WEBVTT

NOTE Confidence: 0.6984148475

00:00:00.000 --> 00:00:02.382 It's my great pleasure to introduce

NOTE Confidence: 0.6984148475

00:00:02.382 --> 00:00:06.340 Doctor Naresh, Carrie to Yale Yale grants.

NOTE Confidence: 0.6984148475

00:00:06.340 --> 00:00:08.435 Naresh completed his Bachelor of

NOTE Confidence: 0.6984148475

00:00:08.435 --> 00:00:10.530 Medicine and Bachelor of Surgery

NOTE Confidence: 0.6984148475

00:00:10.594 --> 00:00:12.426 at Government Government Medical

NOTE Confidence: 0.6984148475

00:00:12.426 --> 00:00:14.716 College where he also received.

NOTE Confidence: 0.6984148475

00:00:14.720 --> 00:00:17.210 Also received my in clinical pathology

NOTE Confidence: 0.6984148475

00:00:17.210 --> 00:00:20.562 he he then did his training in pathology

NOTE Confidence: 0.6984148475

00:00:20.562 --> 00:00:24.137 theology at the prestigious Jipmer Institute.

NOTE Confidence: 0.6984148475

00:00:24.140 --> 00:00:26.877 Nourish began his his anger at Tata

NOTE Confidence: 0.6984148475

00:00:26.877 --> 00:00:28.817 Memorial Hospital where he quickly

NOTE Confidence: 0.6984148475

00:00:28.817 --> 00:00:30.567 rose and banged to become.

NOTE Confidence: 0.6984148475

00:00:30.570 --> 00:00:33.100 Full professor in in pathology,

NOTE Confidence: 0.6984148475

00:00:33.100 --> 00:00:35.410 he moved in 2004 to London,

NOTE Confidence: 0.6984148475

00:00:35.410 --> 00:00:37.181 where he was a professor and a

NOTE Confidence: 0.6984148475

00:00:37.181 --> 00:00:38.858 professor in the cellular and

NOTE Confidence: 0.6984148475

00:00:38.858 --> 00:00:42.540 molecular pathology Imperial Condon.

NOTE Confidence: 0.6984148475

00:00:42.540 --> 00:00:46.818 In 2020 actually move the middle

NOTE Confidence: 0.6984148475

00:00:46.818 --> 00:00:47.949 to pandemic pandemic.

NOTE Confidence: 0.6984148475

00:00:47.950 --> 00:00:50.020 He professor and section head of

NOTE Confidence: 0.6984148475

00:00:50.020 --> 00:00:51.897 pathology in the Clinical Research

NOTE Confidence: 0.6984148475

00:00:51.897 --> 00:00:54.067 Division Vision Hutchinson Cancer Center

NOTE Confidence: 0.6984148475

00:00:54.067 --> 00:00:56.316 with appointment at the University

NOTE Confidence: 0.6984148475

00:00:56.316 --> 00:00:58.546 of Washington Department of Labor.

NOTE Confidence: 0.668894304

00:01:00.590 --> 00:01:02.782 Now Russia has authored over 250

NOTE Confidence: 0.668894304

00:01:02.782 --> 00:01:04.692 original manuscripts and use scripts

NOTE Confidence: 0.668894304

00:01:04.692 --> 00:01:07.050 with on the biology of lymphoma.

NOTE Confidence: 0.668894304

00:01:07.050 --> 00:01:09.246 Developing new items to improve lymphoma,

NOTE Confidence: 0.668894304

00:01:09.250 --> 00:01:12.208 lymphoma and the study of the

NOTE Confidence: 0.668894304

00:01:12.208 --> 00:01:13.687 lymphoma lymphoma microenvironment.

NOTE Confidence: 0.668894304

00:01:13.690 --> 00:01:15.205 His other research in research

NOTE Confidence: 0.668894304

00:01:15.205 --> 00:01:17.120 interest in a focus in lymphoma

NOTE Confidence: 0.668894304

00:01:17.120 --> 00:01:18.835 causing infectious agents which is

NOTE Confidence: 0.668894304

00:01:18.835 --> 00:01:21.348 the topic of his talk to talk today.

NOTE Confidence: 0.668894304

00:01:21.350 --> 00:01:23.588 In addition to his extensive scholarship,

NOTE Confidence: 0.668894304

00:01:23.590 --> 00:01:25.396 nourish has taken on leadership roles

NOTE Confidence: 0.668894304

00:01:25.396 --> 00:01:27.382 in several roles in several large

NOTE Confidence: 0.668894304

00:01:27.382 --> 00:01:29.202 internationals including our next edition

NOTE Confidence: 0.668894304

00:01:29.202 --> 00:01:32.026 of The Who in Hematopathology mythology.

NOTE Confidence: 0.668894304

00:01:32.026 --> 00:01:34.122 Atlas of Blood Cancer

NOTE Confidence: 0.668894304

00:01:34.122 --> 00:01:36.148 Genomics which has met him.

NOTE Confidence: 0.668894304

00:01:36.150 --> 00:01:38.380 Please join please join me in a rush to yell.

NOTE Confidence: 0.668894304

00:01:38.380 --> 00:01:38.970 Thank you,

NOTE Confidence: 0.856045399166667

00:01:39.940 --> 00:01:40.933 thank you Mina.

NOTE Confidence: 0.856045399166667

00:01:40.933 --> 00:01:43.250 It's been a pleasure and thanks for

00:01:43.324 --> 00:01:45.690 inviting me and it gives me great

00:01:45.690 --> 00:01:47.340 pleasure to give this presentation.

00:01:47.340 --> 00:01:49.596 Obviously I would have loved to

00:01:49.596 --> 00:01:52.254 be there in person but under the

00:01:52.254 --> 00:01:53.942 current prevailing circumstances I

00:01:53.942 --> 00:01:56.727 think this is the best we can do.

00:01:56.730 --> 00:02:00.872 And I chose this topic of lymphoid

00:02:00.872 --> 00:02:03.456 proliferations in infectious agents.

00:02:03.460 --> 00:02:05.056 Because over a period of time though,

00:02:05.060 --> 00:02:07.628 my lymphoma research across many different

00:02:07.628 --> 00:02:10.140 types of lymphomas has gone ahead.

00:02:10.140 --> 00:02:11.736 This is something which I started with.

00:02:11.740 --> 00:02:14.188 My research started with a particular

00:02:14.188 --> 00:02:16.747 aspect of Epstein Barr virus in

00:02:16.747 --> 00:02:19.032 Hodgkin lymphoma and later on I've

00:02:19.032 --> 00:02:21.180 had opportunity to work on post

00:02:21.263 --> 00:02:23.934 transplant lymphoproliferative and

00:02:23.934 --> 00:02:26.304 then the HIV associated lymphomas

00:02:26.304 --> 00:02:28.790 and my interest in infectious agents

00:02:28.790 --> 00:02:31.451 and informers has been kept alive

00:02:31.451 --> 00:02:33.759 through these research opportunities.

00:02:33.760 --> 00:02:34.410 So.

00:02:41.080 --> 00:02:43.840 So this was the first work of mine,

00:02:43.840 --> 00:02:45.964 which really caught a lot of

00:02:45.964 --> 00:02:48.130 attention but also gave me a

00:02:48.130 --> 00:02:50.170 very good platform to continue my

00:02:50.170 --> 00:02:52.487 research in the field of lymphomas.

00:02:52.490 --> 00:02:55.802 And this was when we were looking

00:02:55.802 --> 00:02:57.412 at Hodgkin lymphoma and that was

00:02:57.412 --> 00:02:59.274 the early time when Eber in situ

00:02:59.274 --> 00:03:00.778 hybridization had come into place and

NOTE Confidence: 0.8584335075

00:03:00.778 --> 00:03:02.326 then we were looking at proliferation.

NOTE Confidence: 0.8584335075

00:03:02.330 --> 00:03:04.146 At that time we didn't use Key 67,

NOTE Confidence: 0.8584335075

00:03:04.150 --> 00:03:06.465 we were using something called

NOTE Confidence: 0.8584335075

00:03:06.465 --> 00:03:08.317 proliferation cell nuclear antigen

NOTE Confidence: 0.8584335075

00:03:08.320 --> 00:03:10.300 and thing that struck me was.

NOTE Confidence: 0.8584335075

00:03:10.300 --> 00:03:14.100 That Hodgkin's which worry baby

NOTE Confidence: 0.8584335075

00:03:14.100 --> 00:03:16.880 positive those had a higher P CNA

NOTE Confidence: 0.8584335075

00:03:16.880 --> 00:03:19.779 expression in the Reed Sternberg cells.

NOTE Confidence: 0.8584335075

00:03:19.780 --> 00:03:22.556 And if you can see that those cases

NOTE Confidence: 0.8584335075

00:03:22.556 --> 00:03:25.004 those which were PC and a low had

NOTE Confidence: 0.8584335075

00:03:25.004 --> 00:03:27.548 nearly 50% cases for EBV negative

NOTE Confidence: 0.8584335075

00:03:27.548 --> 00:03:30.500 but those which were PC and a high

NOTE Confidence: 0.8584335075

00:03:30.500 --> 00:03:32.900 most of them worry be positive.

NOTE Confidence: 0.8584335075

00:03:32.900 --> 00:03:35.908 So then we let on to the hypothesis

NOTE Confidence: 0.8584335075

00:03:35.908 --> 00:03:38.556 thinking that expression of PC keeps

NOTE Confidence: 0.8584335075

00:03:38.556 --> 00:03:40.926 maintains the Reed Sternberg cells.

NOTE Confidence: 0.8584335075

00:03:40.930 --> 00:03:41.932 In cell cycle,

NOTE Confidence: 0.8584335075

00:03:41.932 --> 00:03:44.270 although it goes through a cell cycle

NOTE Confidence: 0.8584335075

00:03:44.341 --> 00:03:46.976 called endocytosis or endo reduplication,

NOTE Confidence: 0.8584335075

00:03:46.980 --> 00:03:49.536 but that makes the cells more

NOTE Confidence: 0.8584335075

00:03:49.536 --> 00:03:50.814 susceptible to chemotherapy.

NOTE Confidence: 0.8584335075

00:03:50.820 --> 00:03:53.186 And then we looked at the outcomes

NOTE Confidence: 0.8584335075

00:03:53.186 --> 00:03:55.109 in these patients and patients.

NOTE Confidence: 0.8584335075

00:03:55.110 --> 00:03:56.142 With EBV,

NOTE Confidence: 0.8584335075

00:03:56.142 --> 00:03:58.206 positive Hodgkin lymphoma did

NOTE Confidence: 0.8584335075

00:03:58.206 --> 00:04:00.826 exclude mean much better than

NOTE Confidence: 0.8584335075

00:04:00.826 --> 00:04:03.176 those which worry be negative.

NOTE Confidence: 0.8584335075

00:04:03.180 --> 00:04:03.582 Again.

NOTE Confidence: 0.8584335075

00:04:03.582 --> 00:04:06.798 If you look at subsequent to our publication,

NOTE Confidence: 0.8584335075

00:04:06.800 --> 00:04:08.600 there have been many other studies

NOTE Confidence: 0.8584335075

00:04:08.600 --> 00:04:10.145 which have come from different

NOTE Confidence: 0.8584335075

00:04:10.145 --> 00:04:11.993 parts of the world and different

NOTE Confidence: 0.8584335075

00:04:11.993 --> 00:04:13.958 people have had different reasons.

NOTE Confidence: 0.8584335075

00:04:13.960 --> 00:04:16.616 Some people have in many parts the Western.

NOTE Confidence: 0.8584335075

00:04:16.620 --> 00:04:18.804 You know Western Europe and in the US

NOTE Confidence: 0.8584335075

00:04:18.804 --> 00:04:21.198 people have shown that EBV positive disease.

NOTE Confidence: 0.8584335075

00:04:21.200 --> 00:04:22.236 How about Porter survival?

NOTE Confidence: 0.8584335075

00:04:22.236 --> 00:04:24.161 But in the setting of the developing

NOTE Confidence: 0.8584335075

00:04:24.161 --> 00:04:26.057 country with these patients are all

NOTE Confidence: 0.8584335075

00:04:26.057 --> 00:04:28.178 from India eBay be positive disease

NOTE Confidence: 0.8584335075

00:04:28.178 --> 00:04:30.410 had a superior survival to EBV,

NOTE Confidence: 0.8584335075

00:04:30.410 --> 00:04:32.174 negative disease and also.

NOTE Confidence: 0.8584335075

00:04:32.174 --> 00:04:34.820 And this was independent of patients

NOTE Confidence: 0.8584335075

00:04:34.890 --> 00:04:38.150 age and stage of Hodgkin lymphoma.

NOTE Confidence: 0.8584335075

00:04:38.150 --> 00:04:40.299 We also showed at the same time

NOTE Confidence: 0.8584335075

00:04:40.299 --> 00:04:43.860 that almost 98% I think only there

NOTE Confidence: 0.8584335075

00:04:43.860 --> 00:04:46.150 was only one case out of the 50

NOTE Confidence: 0.8584335075

00:04:46.150 --> 00:04:47.740 cases of pediatric Hodgkin lymphoma

NOTE Confidence: 0.8584335075

00:04:47.740 --> 00:04:49.436 which was even with negative the

NOTE Confidence: 0.8584335075

00:04:49.436 --> 00:04:51.350 rest of the 49 or 50 cases.

NOTE Confidence: 0.8584335075

00:04:51.350 --> 00:04:53.030 Bloody may be positive,

NOTE Confidence: 0.8584335075

00:04:53.030 --> 00:04:55.174 so you may be positive ITI was is

NOTE Confidence: 0.8584335075

00:04:55.174 --> 00:04:57.338 very high in the pediatric setting,

NOTE Confidence: 0.8584335075

00:04:57.340 --> 00:05:00.084 especially in a developing

NOTE Confidence: 0.8584335075

00:05:00.084 --> 00:05:01.460 country like India.

NOTE Confidence: 0.8584335075

00:05:01.460 --> 00:05:04.220 So this was the first one which really

NOTE Confidence: 0.8584335075

00:05:04.295 --> 00:05:06.957 led on to this part of my research and

NOTE Confidence: 0.8584335075

00:05:06.957 --> 00:05:10.166 then I will take you through other areas,

NOTE Confidence: 0.8584335075

00:05:10.170 --> 00:05:12.726 partly from translational research and and

NOTE Confidence: 0.8584335075

00:05:12.726 --> 00:05:16.238 most and quite a lot of clinical aspects.

NOTE Confidence: 0.8584335075

00:05:16.240 --> 00:05:18.208 So if you look at infectious

NOTE Confidence: 0.8584335075

00:05:18.208 --> 00:05:19.520 agents in lymphoid proliferations,

NOTE Confidence: 0.8584335075

00:05:19.520 --> 00:05:21.278 we have a list of viruses.

NOTE Confidence: 0.8584335075

00:05:21.280 --> 00:05:23.240 EBV was the first to be recognized then.

NOTE Confidence: 0.8584335075

00:05:23.240 --> 00:05:25.536 Of course we have the Kaposi sarcoma virus,

NOTE Confidence: 0.8584335075

00:05:25.540 --> 00:05:27.796 or the human herpes type age.

NOTE Confidence: 0.8584335075

00:05:27.800 --> 00:05:29.945 Then hepatitis C and hepatitis

NOTE Confidence: 0.8584335075

00:05:29.945 --> 00:05:32.940 B virus human T cell leukemia.

NOTE Confidence: 0.8584335075

00:05:32.940 --> 00:05:35.664 Wireless one HTLV one and human

NOTE Confidence: 0.8584335075

00:05:35.664 --> 00:05:37.480 immunodeficiency virus or HIV,

NOTE Confidence: 0.8584335075

00:05:37.480 --> 00:05:39.526 but we can't forget the bacteria

NOTE Confidence: 0.8584335075

00:05:39.526 --> 00:05:41.923 which can associated with them for

NOTE Confidence: 0.8584335075

00:05:41.923 --> 00:05:43.855 proliferations like the Helicobacter

NOTE Confidence: 0.8584335075

00:05:43.855 --> 00:05:45.787 campylobacter gorilla and chlamydia.

NOTE Confidence: 0.8584335075

00:05:45.790 --> 00:05:47.750 I'm not going to be discussing these.

NOTE Confidence: 0.604118497777778

00:05:47.750 --> 00:05:49.694 I'll primarily restrict my

NOTE Confidence: 0.604118497777778

00:05:49.694 --> 00:05:52.124 discussion to ebb and HP,

NOTE Confidence: 0.604118497777778

00:05:52.130 --> 00:05:53.740 and partly I will touch on STL.

NOTE Confidence: 0.857521963

00:05:55.870 --> 00:05:57.490 So if you look at infectious

NOTE Confidence: 0.857521963

00:05:57.490 --> 00:05:58.570 agents in these disorders,

NOTE Confidence: 0.857521963

00:05:58.570 --> 00:06:01.162 we have a set of diseases where

NOTE Confidence: 0.857521963

00:06:01.162 --> 00:06:03.292 the infectious agent is present

NOTE Confidence: 0.857521963

00:06:03.292 --> 00:06:05.010 within the neoplastic cells.

NOTE Confidence: 0.857521963

00:06:05.010 --> 00:06:07.250 Classic examples that are EBV

NOTE Confidence: 0.857521963

00:06:07.250 --> 00:06:10.783 HHV 8 and HTLV one and there are

NOTE Confidence: 0.857521963

00:06:10.783 --> 00:06:12.938 others where infectious agents are

NOTE Confidence: 0.857521963

00:06:12.938 --> 00:06:14.942 present outside of the neoplastic

NOTE Confidence: 0.857521963

00:06:14.942 --> 00:06:16.846 cells like HIV like Helicobacter

NOTE Confidence: 0.857521963

00:06:16.846 --> 00:06:20.178 hepatitis virus C so on and so

NOTE Confidence: 0.857521963

00:06:20.178 --> 00:06:22.878 forth where the the tumor cell

NOTE Confidence: 0.857521963

00:06:22.878 --> 00:06:25.980 itself is not infected by the virus.

NOTE Confidence: 0.857521963

00:06:25.980 --> 00:06:27.707 And if you look at again,

NOTE Confidence: 0.857521963

00:06:27.707 --> 00:06:29.996 this is a mix of different types

NOTE Confidence: 0.857521963

00:06:29.996 --> 00:06:31.680 of lymphoid proliferations.

NOTE Confidence: 0.857521963

00:06:31.680 --> 00:06:33.255 You have some acute and

NOTE Confidence: 0.857521963

00:06:33.255 --> 00:06:34.200 non malignant conditions,

NOTE Confidence: 0.857521963

00:06:34.200 --> 00:06:35.564 like the infectious mononucleosis

NOTE Confidence: 0.857521963

00:06:35.564 --> 00:06:37.610 we have heard about this and

NOTE Confidence: 0.857521963

00:06:37.668 --> 00:06:39.540 learned about this for many years.

NOTE Confidence: 0.857521963

00:06:39.540 --> 00:06:41.620 I'm not going to develop much time on

NOTE Confidence: 0.857521963

00:06:41.620 --> 00:06:43.838 this and then we have other chronic

NOTE Confidence: 0.857521963

00:06:43.838 --> 00:06:45.478 and non malignant or polyclonal

NOTE Confidence: 0.857521963

00:06:45.534 --> 00:06:47.739 diseases like chronic active infection,

NOTE Confidence: 0.857521963

00:06:47.740 --> 00:06:49.870 multicentric Castleman disease in the

NOTE Confidence: 0.857521963

00:06:49.870 --> 00:06:53.900 HIV studying and with HV-8 HTLV 1 carriers,

NOTE Confidence: 0.857521963

00:06:53.900 --> 00:06:56.220 States and associated gastritis.

NOTE Confidence: 0.857521963

00:06:56.220 --> 00:06:58.268 These are all polyclonal,

NOTE Confidence: 0.857521963

00:06:58.268 --> 00:06:59.804 non malignant proliferations.

NOTE Confidence: 0.857521963

00:06:59.810 --> 00:07:00.366 Again,

NOTE Confidence: 0.857521963

00:07:00.366 --> 00:07:03.589 the question about malignancy and being

NOTE Confidence: 0.857521963

00:07:03.589 --> 00:07:07.101 non malignant it it gets into a grey

NOTE Confidence: 0.857521963

00:07:07.101 --> 00:07:09.618 area with with chronic active infection.

NOTE Confidence: 0.857521963

00:07:09.618 --> 00:07:12.335 We will discuss that and then we

NOTE Confidence: 0.857521963

00:07:12.335 --> 00:07:15.220 have what we currently call as

NOTE Confidence: 0.857521963

00:07:15.220 --> 00:07:16.280 polymorphic lymphoproliferative

NOTE Confidence: 0.857521963

00:07:16.280 --> 00:07:18.887 disorders and these these came to

NOTE Confidence: 0.857521963

00:07:18.887 --> 00:07:21.260 light and was best exemplified in the

NOTE Confidence: 0.857521963

00:07:21.333 --> 00:07:23.649 post transplant setting but now more

NOTE Confidence: 0.857521963

00:07:23.649 --> 00:07:26.458 and more we recognize this across other.

NOTE Confidence: 0.857521963

00:07:26.460 --> 00:07:27.984 Immune deficiency areas.

NOTE Confidence: 0.857521963

00:07:27.984 --> 00:07:32.036 Then we also have lymphomas allow quite a

NOTE Confidence: 0.857521963

00:07:32.036 --> 00:07:34.813 few are full blown lymphomas which many

NOTE Confidence: 0.857521963

00:07:34.813 --> 00:07:37.074 of these lymphomas look like what one

NOTE Confidence: 0.857521963

00:07:37.074 --> 00:07:39.709 would see in an immune competent setting.

NOTE Confidence: 0.857521963

00:07:39.710 --> 00:07:42.813 So if you put them as those

NOTE Confidence: 0.857521963

00:07:42.813 --> 00:07:46.928 where the informatics agent is.

NOTE Confidence: 0.857521963

00:07:46.930 --> 00:07:49.085 Is always associated with the

NOTE Confidence: 0.857521963

00:07:49.085 --> 00:07:51.240 disease is likely be positive.

NOTE Confidence: 0.857521963

00:07:51.240 --> 00:07:53.890 Diffuse large B cell lymphoma

NOTE Confidence: 0.857521963

00:07:53.890 --> 00:07:55.492 lymphomatoid granulomatosis fibron

NOTE Confidence: 0.857521963

00:07:55.492 --> 00:07:57.660 associated DLBCL primary effusion.

NOTE Confidence: 0.857521963

00:07:57.660 --> 00:07:59.838 Lymphoma so on and so forth.

NOTE Confidence: 0.857521963

00:07:59.840 --> 00:08:03.025 All these diseases are always

NOTE Confidence: 0.857521963

00:08:03.025 --> 00:08:06.210 associated with the infectious agent.

NOTE Confidence: 0.857521963

00:08:06.210 --> 00:08:09.306 Then we have a set of diseases where.

NOTE Confidence: 0.857521963

00:08:09.310 --> 00:08:11.207 Some of them are proportion of them

NOTE Confidence: 0.857521963

00:08:11.207 --> 00:08:12.910 are associated with infectious agent,

NOTE Confidence: 0.857521963

00:08:12.910 --> 00:08:14.250 and the rest are not,

NOTE Confidence: 0.857521963

00:08:14.250 --> 00:08:16.020 and you have the marginal zone

NOTE Confidence: 0.857521963

00:08:16.020 --> 00:08:18.010 lymphoma diffuse large B cell lymphoma,

NOTE Confidence: 0.857521963

00:08:18.010 --> 00:08:20.090 plasmablastic lymphoma, Burkitt lymphoma,

NOTE Confidence: 0.857521963

00:08:20.090 --> 00:08:21.650 plastic Hodgkin lymphoma,

NOTE Confidence: 0.857521963

00:08:21.650 --> 00:08:22.710 so on and so forth.

NOTE Confidence: 0.857521963

00:08:22.710 --> 00:08:25.027 There only a proportion of cases are

NOTE Confidence: 0.857521963

00:08:25.027 --> 00:08:27.160 in positive for the infectious agent

NOTE Confidence: 0.857521963

00:08:27.160 --> 00:08:29.659 then you have some cases where very

NOTE Confidence: 0.857521963

00:08:29.723 --> 00:08:31.631 rarely an association has been found

NOTE Confidence: 0.857521963

00:08:31.631 --> 00:08:33.920 like you as a follicular lymphoma.

NOTE Confidence: 0.857521963

00:08:33.920 --> 00:08:35.940 Rare follicular lymphoma sorry

NOTE Confidence: 0.857521963

00:08:35.940 --> 00:08:38.478 be associated in SL where you

NOTE Confidence: 0.857521963

00:08:38.478 --> 00:08:40.770 can have a hot skin like.

NOTE Confidence: 0.857521963

00:08:40.770 --> 00:08:41.604 Richter transformation,

NOTE Confidence: 0.857521963

00:08:41.604 --> 00:08:43.689 which can be be positive.

NOTE Confidence: 0.857521963

00:08:43.690 --> 00:08:45.190 Then you also have very rarely.

NOTE Confidence: 0.857521963

00:08:45.190 --> 00:08:48.064 You can have another dominant optical

NOTE Confidence: 0.857521963

00:08:48.064 --> 00:08:50.960 lymphoma which is EBV associated.

NOTE Confidence: 0.857521963

00:08:50.960 --> 00:08:53.308 So I'm going to discuss these

NOTE Confidence: 0.857521963

00:08:53.308 --> 00:08:55.660 entities and these situations

NOTE Confidence: 0.857521963

00:08:55.660 --> 00:08:57.354 from different perspectives,

NOTE Confidence: 0.857521963

00:08:57.354 --> 00:09:00.114 partly and videology and pathogenesis.

NOTE Confidence: 0.857521963

00:09:00.120 --> 00:09:02.066 Then a few of the aspects of

NOTE Confidence: 0.857521963

00:09:02.066 --> 00:09:03.900 genomics and and immune aspects.

NOTE Confidence: 0.857521963

00:09:03.900 --> 00:09:06.220 Then we will spend a bit of time

NOTE Confidence: 0.857521963

00:09:06.220 --> 00:09:07.731 about apology and immunophenotype

NOTE Confidence: 0.857521963

00:09:07.731 --> 00:09:09.901 diagnosis or the criteria for

NOTE Confidence: 0.857521963

00:09:09.901 --> 00:09:12.043 diagnosis how these impact on

NOTE Confidence: 0.857521963

00:09:12.043 --> 00:09:13.963 classification and how these impact

NOTE Confidence: 0.857521963

00:09:13.963 --> 00:09:16.930 on outcomes and follow up.

NOTE Confidence: 0.857521963

00:09:16.930 --> 00:09:17.742 So first,

NOTE Confidence: 0.857521963

00:09:17.742 --> 00:09:20.990 if we take Epstein Barr virus and Burkitt

NOTE Confidence: 0.687214403636364

00:09:21.073 --> 00:09:23.950 lymphoma. This was Burkitt when he,

NOTE Confidence: 0.687214403636364

00:09:23.950 --> 00:09:26.020 in his initial descriptions and subsequent

NOTE Confidence: 0.687214403636364

00:09:26.020 --> 00:09:28.568 to that we appreciated the Burkitt lymphoma,

NOTE Confidence: 0.687214403636364

00:09:28.570 --> 00:09:31.192 the endemic form of Burkitt lymphoma

NOTE Confidence: 0.687214403636364

00:09:31.192 --> 00:09:35.191 is seen in a specific Equatorial band

NOTE Confidence: 0.687214403636364

00:09:35.191 --> 00:09:38.418 across the world which includes parts of

NOTE Confidence: 0.687214403636364

00:09:38.418 --> 00:09:41.047 South America and parts of Equatorial

NOTE Confidence: 0.687214403636364

00:09:41.047 --> 00:09:44.350 Africa and most of these are difficult.

NOTE Confidence: 0.687214403636364

00:09:44.350 --> 00:09:46.849 Look at the incidents even within Africa.

NOTE Confidence: 0.687214403636364

00:09:46.850 --> 00:09:49.671 You will see like places like Nigeria

NOTE Confidence: 0.687214403636364

00:09:49.671 --> 00:09:52.460 and Uganda which are within the band.

NOTE Confidence: 0.687214403636364

00:09:52.460 --> 00:09:55.508 Just be across the equator between the Tropic

NOTE Confidence: 0.687214403636364

00:09:55.508 --> 00:09:58.280 of Cancer and the Tropic of Capricorn.

NOTE Confidence: 0.687214403636364

00:09:58.280 --> 00:10:00.158 Those have a very high incidence,

NOTE Confidence: 0.687214403636364

00:10:00.160 --> 00:10:02.290 whereas outside of those areas,

NOTE Confidence: 0.687214403636364

00:10:02.290 --> 00:10:04.000 like if you look at Namibia,

NOTE Confidence: 0.687214403636364

00:10:04.000 --> 00:10:07.258 if you look at Zimbabwe you have a lower

NOTE Confidence: 0.687214403636364

00:10:07.258 --> 00:10:10.067 incidence and again this is data from 1988.

NOTE Confidence: 0.687214403636364

00:10:10.067 --> 00:10:13.746 If you look at the current data it is

NOTE Confidence: 0.687214403636364

00:10:13.746 --> 00:10:15.811 slightly diluted and partly diluted

NOTE Confidence: 0.687214403636364

00:10:15.811 --> 00:10:18.429 and partly changed because of the HIV.

NOTE Confidence: 0.687214403636364

00:10:18.430 --> 00:10:20.789 Epidemic now in South Africa and Bob

NOTE Confidence: 0.687214403636364

00:10:20.789 --> 00:10:22.962 with the incidence might have gone

NOTE Confidence: 0.687214403636364

00:10:22.962 --> 00:10:25.164 higher because of the HIV association,

NOTE Confidence: 0.687214403636364

00:10:25.170 --> 00:10:29.020 but before the HIV epidemic one could

NOTE Confidence: 0.687214403636364

00:10:29.020 --> 00:10:32.574 see that Uganda and Nigeria had a much

NOTE Confidence: 0.687214403636364

00:10:32.574 --> 00:10:34.800 higher incidence compared to the rest

NOTE Confidence: 0.687214403636364

00:10:34.800 --> 00:10:36.920 of African countries and rest of the

NOTE Confidence: 0.687214403636364

00:10:36.920 --> 00:10:40.940 world and in endemic Burkitt lymphoma.

NOTE Confidence: 0.687214403636364

00:10:40.940 --> 00:10:42.878 Almost all cases are EBV positive,

NOTE Confidence: 0.687214403636364

00:10:42.880 --> 00:10:45.065 whereas outside the endemic areas

NOTE Confidence: 0.687214403636364

00:10:45.065 --> 00:10:47.924 only about 25 to 30% REB positive.

NOTE Confidence: 0.687214403636364

00:10:47.924 --> 00:10:50.500 So if you look at it association

NOTE Confidence: 0.687214403636364

00:10:50.574 --> 00:10:52.119 within Berkman Firma,

NOTE Confidence: 0.687214403636364

00:10:52.120 --> 00:10:54.690 it's gotta a differential geographic

NOTE Confidence: 0.687214403636364

00:10:54.690 --> 00:10:56.746 distribution like an African,

NOTE Confidence: 0.687214403636364

00:10:56.750 --> 00:10:57.352 nearly hundred.

NOTE Confidence: 0.687214403636364

00:10:57.352 --> 00:10:59.760 When I say Africa here in Equatorial Africa,

NOTE Confidence: 0.687214403636364

00:10:59.760 --> 00:11:02.140 nearly 100% of them are EBV positive,

NOTE Confidence: 0.687214403636364

00:11:02.140 --> 00:11:04.316 but as when you come outside of Africa,

NOTE Confidence: 0.687214403636364

00:11:04.320 --> 00:11:06.819 it varies from 25% to some areas,

NOTE Confidence: 0.687214403636364

00:11:06.820 --> 00:11:08.164 like in South America,

NOTE Confidence: 0.687214403636364

00:11:08.164 --> 00:11:10.794 where it can be nearly 50% in like

NOTE Confidence: 0.687214403636364

00:11:10.794 --> 00:11:12.329 in Mexico is around 50%,

NOTE Confidence: 0.687214403636364

00:11:12.330 --> 00:11:14.274 but in the he could in the belt

NOTE Confidence: 0.687214403636364

00:11:14.274 --> 00:11:16.559 that I showed you it can be higher

NOTE Confidence: 0.687214403636364

00:11:16.559 --> 00:11:18.340 than 50% and the same thing is true

NOTE Confidence: 0.687214403636364

00:11:18.340 --> 00:11:20.029 if you look at Hodgkin lymphoma.

NOTE Confidence: 0.687214403636364

00:11:20.030 --> 00:11:22.472 And not all Hodgkin's are associated

NOTE Confidence: 0.687214403636364

00:11:22.472 --> 00:11:24.302 with EBV, and if in Africa,

NOTE Confidence: 0.687214403636364

00:11:24.302 --> 00:11:25.567 again in the same regions,

NOTE Confidence: 0.687214403636364

00:11:25.570 --> 00:11:27.082 you will see most of them on

NOTE Confidence: 0.687214403636364

00:11:27.082 --> 00:11:27.730 eBay be positive,

NOTE Confidence: 0.687214403636364

00:11:27.730 --> 00:11:30.796 but outside of Africa and some parts

NOTE Confidence: 0.687214403636364

00:11:30.796 --> 00:11:33.704 of South America you have variable

NOTE Confidence: 0.687214403636364

00:11:33.704 --> 00:11:36.728 incidence of EB within the Hodgkin

NOTE Confidence: 0.687214403636364

00:11:36.728 --> 00:11:39.956 lymphoma in the classic Hodgkin lymphoma.

NOTE Confidence: 0.687214403636364

00:11:39.960 --> 00:11:43.240 So what all these things do tell us is easy.

NOTE Confidence: 0.687214403636364

00:11:43.240 --> 00:11:46.460 Be really relevant for neoplastic,

NOTE Confidence: 0.687214403636364

00:11:46.460 --> 00:11:47.564 for lymphoma Genesis.

NOTE Confidence: 0.687214403636364

00:11:47.564 --> 00:11:49.772 In any of these slim firms,

NOTE Confidence: 0.687214403636364

00:11:49.780 --> 00:11:51.436 so that has always been questioned,

00:11:51.440 --> 00:11:54.356 because not every single case of

00:11:54.356 --> 00:11:56.922 an EBV associated lymphoma is

00:11:56.922 --> 00:11:58.527 associated with Debbie.

00:11:58.530 --> 00:12:00.896 And again this has got an impact

00:12:00.896 --> 00:12:02.804 on the distribution of patients.

00:12:02.804 --> 00:12:06.064 Like if you look at EBV positive diseases

00:12:06.064 --> 00:12:09.424 from from England and here you can see.

00:12:09.430 --> 00:12:10.930 But even the positive disease,

00:12:10.930 --> 00:12:14.446 you get a very early peak in the in the very

00:12:14.446 --> 00:12:16.900 early on in the in the 1st and 2nd decades.

00:12:16.900 --> 00:12:18.598 You can have EBV positive disease.

00:12:18.600 --> 00:12:21.152 Then you have a a second peak around

00:12:21.152 --> 00:12:23.744 40 or 50 years and then a third

00:12:23.744 --> 00:12:26.208 peak in the 6th and 7th decade.

00:12:26.210 --> 00:12:28.082 Whereas when you look at EB

00:12:28.082 --> 00:12:28.706 negative diseases,

NOTE Confidence: 0.687214403636364

00:12:28.710 --> 00:12:31.242 you have a single pick somewhere

NOTE Confidence: 0.687214403636364

00:12:31.242 --> 00:12:32.930 in the early adulthood

NOTE Confidence: 0.738222117333333

00:12:33.013 --> 00:12:36.235 between the 20s and 30s and then the

NOTE Confidence: 0.738222117333333

00:12:36.235 --> 00:12:39.630 incidence decreases and if you put them.

NOTE Confidence: 0.738222117333333

00:12:39.630 --> 00:12:41.670 Across the world, if you see you have

NOTE Confidence: 0.738222117333333

00:12:41.670 --> 00:12:43.926 so you got even the positive disease

NOTE Confidence: 0.738222117333333

00:12:43.926 --> 00:12:46.062 comes with three peaks and even with

NOTE Confidence: 0.738222117333333

00:12:46.062 --> 00:12:47.646 negative disease is a single peak.

NOTE Confidence: 0.738222117333333

00:12:47.650 --> 00:12:49.606 So many people have actually questioned.

NOTE Confidence: 0.738222117333333

00:12:49.610 --> 00:12:51.734 Purely based on epidemiology.

NOTE Confidence: 0.738222117333333

00:12:51.734 --> 00:12:54.389 Whether you have EBV positive,

NOTE Confidence: 0.738222117333333

00:12:54.390 --> 00:12:56.181 Hodgkin lymphoma ribbon,

NOTE Confidence: 0.738222117333333

00:12:56.181 --> 00:12:58.569 negative Hodgkin lymphoma similarly

NOTE Confidence: 0.738222117333333

00:12:58.570 --> 00:12:59.998 positive Burkitt lymphoma,

NOTE Confidence: 0.738222117333333

00:12:59.998 --> 00:13:02.854 EBV negative Burkitt lymphoma would be

NOTE Confidence: 0.738222117333333

00:13:02.854 --> 00:13:05.955 the right way to classify these diseases.

NOTE Confidence: 0.738222117333333

00:13:05.960 --> 00:13:08.438 And again, now this kind of

NOTE Confidence: 0.738222117333333

00:13:08.438 --> 00:13:10.090 classification is getting some

NOTE Confidence: 0.738222117333333

00:13:10.166 --> 00:13:12.586 more traction because of genomics.

NOTE Confidence: 0.738222117333333

00:13:12.590 --> 00:13:14.942 And the same thing is true if you

NOTE Confidence: 0.738222117333333

00:13:14.942 --> 00:13:17.534 look at the HTLV 1 HTLV 1 positive

NOTE Confidence: 0.738222117333333

00:13:17.534 --> 00:13:19.736 aitl is again seen in specific

NOTE Confidence: 0.738222117333333

00:13:19.736 --> 00:13:21.408 areas across the world,

NOTE Confidence: 0.738222117333333

00:13:21.410 --> 00:13:24.672 but in today's migration and and with

NOTE Confidence: 0.738222117333333

00:13:24.672 --> 00:13:27.364 the immigration that happens one should

NOTE Confidence: 0.738222117333333

00:13:27.364 --> 00:13:30.728 not be surprised if one sees an HTLV

NOTE Confidence: 0.738222117333333

00:13:30.728 --> 00:13:33.058 positive ATL outside these endemic

NOTE Confidence: 0.738222117333333

00:13:33.058 --> 00:13:36.670 areas like where I used to work in the UK.

NOTE Confidence: 0.738222117333333

00:13:36.670 --> 00:13:38.365 It was we used to

NOTE Confidence: 0.738222117333333

00:13:38.365 --> 00:13:40.060 frequently see cases of ATL.

NOTE Confidence: 0.738222117333333

23

00:13:40.060 --> 00:13:41.935 Most of the patients were

NOTE Confidence: 0.738222117333333

00:13:41.935 --> 00:13:43.060 of Caribbean origin.

NOTE Confidence: 0.738222117333333

00:13:43.060 --> 00:13:45.256 And somewhere off of African origin,

NOTE Confidence: 0.738222117333333

00:13:45.260 --> 00:13:47.438 but most were of Caribbean knowledge.

NOTE Confidence: 0.738222117333333

00:13:47.440 --> 00:13:51.227 So similarly in the US there is.

NOTE Confidence: 0.738222117333333

00:13:51.230 --> 00:13:53.750 There are many cases of ATL

NOTE Confidence: 0.738222117333333

00:13:53.750 --> 00:13:55.646 which go underdiagnosed because

NOTE Confidence: 0.738222117333333

00:13:55.646 --> 00:13:59.342 it shall be one is not tested.

NOTE Confidence: 0.738222117333333

00:13:59.350 --> 00:14:01.843 If you look at when we come to pathogenesis

NOTE Confidence: 0.738222117333333

00:14:01.843 --> 00:14:04.290 of how does EBV contribute to the

NOTE Confidence: 0.738222117333333

00:14:04.290 --> 00:14:06.990 classic example is Burkitt lymphoma.

NOTE Confidence: 0.738222117333333

00:14:06.990 --> 00:14:08.670 Often we think that EBV doesn't

NOTE Confidence: 0.738222117333333

00:14:08.670 --> 00:14:10.984 act on its own, along with EBV.

NOTE Confidence: 0.738222117333333

00:14:10.984 --> 00:14:13.372 You have cofactors like malaria and

NOTE Confidence: 0.738222117333333

00:14:13.372 --> 00:14:16.333 HIV which results in enhanced B

NOTE Confidence: 0.738222117333333

00:14:16.333 --> 00:14:18.325 cell activation and proliferation,

NOTE Confidence: 0.738222117333333

00:14:18.330 --> 00:14:19.870 and when these activities going

NOTE Confidence: 0.738222117333333

00:14:19.870 --> 00:14:21.410 on in the general center,

NOTE Confidence: 0.738222117333333

00:14:21.410 --> 00:14:23.845 you have these translate translocation

NOTE Confidence: 0.738222117333333

00:14:23.845 --> 00:14:26.181 of immuno globulin and C.

NOTE Confidence: 0.738222117333333

00:14:26.181 --> 00:14:26.943 MYC occurs.

NOTE Confidence: 0.738222117333333

00:14:26.943 --> 00:14:29.610 Usually most of these cells are expected.

NOTE Confidence: 0.738222117333333

00:14:29.610 --> 00:14:30.486 Don't die,

NOTE Confidence: 0.738222117333333

00:14:30.486 --> 00:14:33.552 but some of these cells because of

NOTE Confidence: 0.738222117333333

00:14:33.552 --> 00:14:36.318 Debbie Gene products can can survive

NOTE Confidence: 0.738222117333333

00:14:36.318 --> 00:14:38.742 and these gene products will suppress

NOTE Confidence: 0.738222117333333

00:14:38.742 --> 00:14:41.000 the appetite ossis program and these

NOTE Confidence: 0.738222117333333

00:14:41.000 --> 00:14:43.730 cells go on to become Burkitt lymphoma.

NOTE Confidence: 0.738222117333333

00:14:43.730 --> 00:14:44.374 Of course,

NOTE Confidence: 0.738222117333333

00:14:44.374 --> 00:14:46.306 this is a very simplistic view,

NOTE Confidence: 0.738222117333333

00:14:46.310 --> 00:14:49.030 but if you again look at the within,

NOTE Confidence: 0.738222117333333

00:14:49.030 --> 00:14:51.206 if you look at the the breakpoints in

NOTE Confidence: 0.738222117333333

00:14:51.206 --> 00:14:53.561 the C MYC and in the immuno global

NOTE Confidence: 0.738222117333333

00:14:53.561 --> 00:14:55.714 engine you do see differences between

NOTE Confidence: 0.738222117333333

00:14:55.714 --> 00:14:58.486 African Burkitt lymphoma and the non

NOTE Confidence: 0.738222117333333

00:14:58.486 --> 00:15:00.354 endemic sporadic Burkitt lymphoma.

NOTE Confidence: 0.738222117333333

00:15:00.354 --> 00:15:02.714 In the African Burkitt lymphoma,

NOTE Confidence: 0.738222117333333

00:15:02.720 --> 00:15:04.852 the endemic Burkitt lymphoma

NOTE Confidence: 0.738222117333333

00:15:04.852 --> 00:15:07.517 within the immunoglobulin gene the

NOTE Confidence: 0.738222117333333

00:15:07.517 --> 00:15:10.117 the break is in the J region,

NOTE Confidence: 0.738222117333333

00:15:10.120 --> 00:15:11.692 whereas in the non endemic Burkitt

NOTE Confidence: 0.738222117333333

00:15:11.692 --> 00:15:13.400 lymphoma most of them have a break.

NOTE Confidence: 0.738222117333333

00:15:13.400 --> 00:15:14.528 In this which region.

NOTE Confidence: 0.738222117333333

00:15:14.528 --> 00:15:16.604 So when you put this on to

NOTE Confidence: 0.738222117333333

00:15:16.604 --> 00:15:17.860 the what could happen,

NOTE Confidence: 0.738222117333333

00:15:17.860 --> 00:15:20.870 where does the J region more

NOTE Confidence: 0.738222117333333

00:15:20.870 --> 00:15:22.310 susceptible for a translocation

NOTE Confidence: 0.738222117333333

00:15:22.310 --> 00:15:24.518 it would appear that most of

NOTE Confidence: 0.738222117333333

00:15:24.518 --> 00:15:25.934 the African Burkitt lymphoma,

NOTE Confidence: 0.738222117333333

00:15:25.940 --> 00:15:27.625 the translocation is likely to

NOTE Confidence: 0.738222117333333

00:15:27.625 --> 00:15:29.310 happen in the bone marrow,

NOTE Confidence: 0.738222117333333

00:15:29.310 --> 00:15:31.470 whereas in most of the non endemic Burkitt.

NOTE Confidence: 0.738222117333333

00:15:31.470 --> 00:15:31.779 Comma,

NOTE Confidence: 0.738222117333333

00:15:31.779 --> 00:15:33.633 it should be happening in the

NOTE Confidence: 0.738222117333333

00:15:33.633 --> 00:15:35.450 germinal center when the class

NOTE Confidence: 0.738222117333333

00:15:35.450 --> 00:15:36.689 switch recombination occurs.

NOTE Confidence: 0.738222117333333

00:15:36.690 --> 00:15:39.126 So there are these kind of differences

NOTE Confidence: 0.738222117333333

00:15:39.126 --> 00:15:41.630 even at A at a genetic level.

NOTE Confidence: 0.738222117333333

00:15:41.630 --> 00:15:44.409 This was a recognized way back in

NOTE Confidence: 0.738222117333333

00:15:44.409 --> 00:15:48.550 the early late 90s and early 2000s.

NOTE Confidence: 0.907924388571429

00:15:48.550 --> 00:15:50.174 So with all these things in mind,

NOTE Confidence: 0.907924388571429

00:15:50.180 --> 00:15:53.029 so does how does EBV really contribute

NOTE Confidence: 0.907924388571429

00:15:53.029 --> 00:15:55.240 to the pathogenesis of lymphomas?

NOTE Confidence: 0.907924388571429

00:15:55.240 --> 00:15:57.354 So I'm going to present to you

NOTE Confidence: 0.907924388571429

00:15:57.354 --> 00:15:59.254 three pieces of information of

NOTE Confidence: 0.907924388571429

00:15:59.254 --> 00:16:01.554 evidence which would support that.

NOTE Confidence: 0.907924388571429

00:16:01.560 --> 00:16:05.640 EB is crucial for lymphoma Genesis.

NOTE Confidence: 0.907924388571429

00:16:05.640 --> 00:16:07.752 We and others have shown that

NOTE Confidence: 0.907924388571429

00:16:07.752 --> 00:16:09.600 the association reduces the need

NOTE Confidence: 0.907924388571429

00:16:09.600 --> 00:16:11.084 for additional somatic mutations

NOTE Confidence: 0.907924388571429

00:16:11.084 --> 00:16:13.560 in the host genome for lymphoma,

NOTE Confidence: 0.907924388571429

00:16:13.560 --> 00:16:14.652 GENESIS 2 AKA,

NOTE Confidence: 0.907924388571429

00:16:14.652 --> 00:16:17.200 and we have also shown that that

NOTE Confidence: 0.907924388571429

00:16:17.277 --> 00:16:20.217 altered the genome is far more potent,

NOTE Confidence: 0.907924388571429

00:16:20.220 --> 00:16:23.584 and Informa Genesis than EB0

NOTE Confidence: 0.907924388571429

00:16:23.584 --> 00:16:25.360 which is not altered.

NOTE Confidence: 0.907924388571429

00:16:25.360 --> 00:16:27.971 Then we have also shown that type

NOTE Confidence: 0.907924388571429

00:16:27.971 --> 00:16:30.738 EB is far more oncogenic than

28

NOTE Confidence: 0.907924388571429

00:16:30.738 --> 00:16:32.616 type BEPB and I will take you

NOTE Confidence: 0.907924388571429

00:16:32.616 --> 00:16:34.000 through these pieces of evidence.

NOTE Confidence: 0.907924388571429

00:16:34.000 --> 00:16:35.352 So currently what we?

NOTE Confidence: 0.907924388571429

00:16:35.352 --> 00:16:37.380 I believe is that when EBV

NOTE Confidence: 0.907924388571429

00:16:37.454 --> 00:16:39.710 infection occurs on a beat cell,

NOTE Confidence: 0.907924388571429

00:16:39.710 --> 00:16:42.062 most of these cells are under the

NOTE Confidence: 0.907924388571429

00:16:42.062 --> 00:16:43.965 control of teasel both CD four

NOTE Confidence: 0.907924388571429

00:16:43.965 --> 00:16:46.260 and CD 8 positive T cells and it

NOTE Confidence: 0.907924388571429

00:16:46.260 --> 00:16:48.000 goes into a steady state where

NOTE Confidence: 0.907924388571429

00:16:48.000 --> 00:16:49.722 you have a latent infection,

NOTE Confidence: 0.907924388571429

00:16:49.722 --> 00:16:52.278 very low level infection of memory

NOTE Confidence: 0.907924388571429

00:16:52.280 --> 00:16:54.570 B cells are persistent infection,

NOTE Confidence: 0.907924388571429

00:16:54.570 --> 00:16:56.946 but some change within the IBD

NOTE Confidence: 0.907924388571429

00:16:56.950 --> 00:16:58.534 is likely to happen,

NOTE Confidence: 0.907924388571429

00:16:58.534 --> 00:17:02.132 and this is important for making the cell

NOTE Confidence: 0.907924388571429

00:17:02.132 --> 00:17:05.369 not susceptible to the T cell control.

NOTE Confidence: 0.907924388571429

00:17:05.370 --> 00:17:11.730 And giving rise to EBV positive lymphoma.

NOTE Confidence: 0.907924388571429

00:17:11.730 --> 00:17:12.678 So this is 1.

NOTE Confidence: 0.907924388571429

00:17:12.678 --> 00:17:15.506 This is a work which we did on

NOTE Confidence: 0.907924388571429

00:17:15.506 --> 00:17:17.510 posttransplant lymphoproliferative disorders,

NOTE Confidence: 0.907924388571429

00:17:17.510 --> 00:17:17.917 primarily.

NOTE Confidence: 0.907924388571429

00:17:17.917 --> 00:17:21.173 Here you can see these are EBP negative.

NOTE Confidence: 0.907924388571429

00:17:21.180 --> 00:17:22.830 This is a mutational landscape

NOTE Confidence: 0.907924388571429

00:17:22.830 --> 00:17:24.126 of EBV negative, diffuse,

NOTE Confidence: 0.907924388571429

00:17:24.126 --> 00:17:26.268 large B cell lymphoma and here is

NOTE Confidence: 0.907924388571429

00:17:26.268 --> 00:17:27.849 the mutational landscape of EBV.

NOTE Confidence: 0.907924388571429

00:17:27.850 --> 00:17:28.634 Positive, diffuse,

NOTE Confidence: 0.907924388571429

00:17:28.634 --> 00:17:31.378 large B cell lymphoma and you can

NOTE Confidence: 0.907924388571429

00:17:31.378 --> 00:17:33.406 easily recognize that the number

NOTE Confidence: 0.907924388571429

00:17:33.406 --> 00:17:35.758 of mutations seen in EBV positive

NOTE Confidence: 0.907924388571429

00:17:35.827 --> 00:17:38.214 DLBCL is far fewer than EB negative.

NOTE Confidence: 0.907924388571429

00:17:38.220 --> 00:17:39.918 If you flash piece or lymphoma,

NOTE Confidence: 0.907924388571429

00:17:39.920 --> 00:17:42.548 thereby suggesting that if we can.

NOTE Confidence: 0.907924388571429

00:17:42.550 --> 00:17:46.246 Substitute the role of many driver gene

NOTE Confidence: 0.907924388571429

00:17:46.246 --> 00:17:50.188 mutations in the development of lymphoma.

NOTE Confidence: 0.907924388571429

00:17:50.190 --> 00:17:52.694 The same thing is true what we see

NOTE Confidence: 0.907924388571429

00:17:52.694 --> 00:17:54.396 what we saw in post transplant

NOTE Confidence: 0.907924388571429

00:17:54.396 --> 00:17:55.761 studying is also true outside

NOTE Confidence: 0.907924388571429

00:17:55.761 --> 00:17:57.450 of the post transplant study.

NOTE Confidence: 0.907924388571429

00:17:57.450 --> 00:17:58.788 When you look at me positive,

NOTE Confidence: 0.907924388571429

00:17:58.790 --> 00:18:00.310 diffuse large B cell lymphoma,

NOTE Confidence: 0.907924388571429

00:18:00.310 --> 00:18:01.402 there's a lower mutational

NOTE Confidence: 0.907924388571429

00:18:01.402 --> 00:18:02.767 burden as compared to EBV.

NOTE Confidence: 0.907924388571429

00:18:02.770 --> 00:18:03.542 Negative issues,

NOTE Confidence: 0.907924388571429

00:18:03.542 --> 00:18:06.425 large piece of lymphoma and again EBV.

NOTE Confidence: 0.907924388571429

00:18:06.425 --> 00:18:08.650 Positivity is almost mutually exclusive

NOTE Confidence: 0.907924388571429

00:18:08.650 --> 00:18:11.490 with mediate mutations or CD 79 eight

NOTE Confidence: 0.907924388571429

00:18:11.490 --> 00:18:13.930 mutations and often it involves the

NOTE Confidence: 0.907924388571429

00:18:13.930 --> 00:18:16.370 alterations in Africa be wind and

NOTE Confidence: 0.907924388571429

00:18:16.370 --> 00:18:18.989 L6 taxed at both way and there are

NOTE Confidence: 0.907924388571429

00:18:18.989 --> 00:18:20.854 some specific mutations that occur.

NOTE Confidence: 0.907924388571429

00:18:20.860 --> 00:18:23.305 Positive ITI fueled large pizza

NOTE Confidence: 0.907924388571429

00:18:23.305 --> 00:18:26.400 lymphoma which makes it quite unique.

NOTE Confidence: 0.907924388571429

00:18:26.400 --> 00:18:29.808 When you look at EBV positive

NOTE Confidence: 0.907924388571429

00:18:29.808 --> 00:18:31.512 Burkitt lymphoma similar.

NOTE Confidence: 0.907924388571429

00:18:31.520 --> 00:18:32.864 A similar trend occurs.

NOTE Confidence: 0.907924388571429

00:18:32.864 --> 00:18:34.208 The driver gene mutations

NOTE Confidence: 0.907924388571429

00:18:34.208 --> 00:18:35.899 may be positive bucketing for

NOTE Confidence: 0.907924388571429

00:18:35.899 --> 00:18:38.125 mice far fewer than he may be.

NOTE Confidence: 0.907924388571429

00:18:38.130 --> 00:18:39.570 Negative Burkitt lymphoma.

NOTE Confidence: 0.907924388571429

00:18:39.570 --> 00:18:40.530 Of course,

NOTE Confidence: 0.907924388571429

00:18:40.530 --> 00:18:42.870 other mutations within the which

NOTE Confidence: 0.907924388571429

00:18:42.870 --> 00:18:45.210 are non driver mutations occurring

NOTE Confidence: 0.907924388571429

00:18:45.284 --> 00:18:47.486 as a result of activation induced

NOTE Confidence: 0.907924388571429

00:18:47.486 --> 00:18:50.200 cited in that is far more frequent

NOTE Confidence: 0.907924388571429

00:18:50.200 --> 00:18:51.784 in positive Burkitt lymphoma,

NOTE Confidence: 0.907924388571429

00:18:51.790 --> 00:18:53.445 again bringing to question that

NOTE Confidence: 0.907924388571429

00:18:53.445 --> 00:18:55.959 this may be because EBV gives a

NOTE Confidence: 0.907924388571429

00:18:55.959 --> 00:18:57.150 proliferative advantage within

NOTE Confidence: 0.907924388571429

00:18:57.150 --> 00:18:59.550 the germinal center and are those

NOTE Confidence: 0.907924388571429

00:18:59.550 --> 00:19:00.588 cells to survive,

NOTE Confidence: 0.907924388571429

00:19:00.590 --> 00:19:03.254 but the driver gene mutations are far fewer.

NOTE Confidence: 0.907924388571429

00:19:03.260 --> 00:19:06.340 Any positive bucket info?

NOTE Confidence: 0.799687382222222

00:19:06.340 --> 00:19:08.937 Another piece of evidence which we looked

NOTE Confidence: 0.799687382222222

00:19:08.937 --> 00:19:12.468 at was to look at the EBD subtypes in

NOTE Confidence: 0.799687382222222

00:19:12.468 --> 00:19:15.202 post transplant EBV positive PTLD Sandy.

NOTE Confidence: 0.799687382222222

00:19:15.202 --> 00:19:17.154 Be positive HIV influence

NOTE Confidence: 0.799687382222222

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00:19:17.160 --> 00:19:19.844 within the PTLD setting.

NOTE Confidence: 0.799687382222222

00:19:19.844 --> 00:19:23.956 Most of the positive Pete Liz harbored

NOTE Confidence: 0.799687382222222

00:19:23.956 --> 00:19:29.210 Taipei EBV virus whereas in HIV, HIV.

NOTE Confidence: 0.799687382222222

00:19:29.210 --> 00:19:30.324 Already infamous,

NOTE Confidence: 0.799687382222222

00:19:30.324 --> 00:19:33.109 there was an even distribution

NOTE Confidence: 0.799687382222222

00:19:33.109 --> 00:19:34.795 between Taipei and Taipei,

NOTE Confidence: 0.799687382222222

00:19:34.795 --> 00:19:37.420 but more importantly what we saw was

NOTE Confidence: 0.799687382222222

00:19:37.492 --> 00:19:39.538 those cases which are associated with

NOTE Confidence: 0.799687382222222

00:19:39.538 --> 00:19:42.947 type B had a very long period of HIV

NOTE Confidence: 0.799687382222222

00:19:42.947 --> 00:19:45.375 positive ITI before they developed lymphoma,

NOTE Confidence: 0.799687382222222

00:19:45.375 --> 00:19:48.935 so we tend to we from this we

NOTE Confidence: 0.799687382222222

00:19:48.935 --> 00:19:51.076 hypothesize that Taipei is far

NOTE Confidence: 0.799687382222222

00:19:51.076 --> 00:19:53.482 more on Pjanic than type P.

NOTE Confidence: 0.799687382222222

00:19:53.490 --> 00:19:56.618 Then we let down to look at mutations

NOTE Confidence: 0.799687382222222

00:19:56.618 --> 00:19:59.786 within the IBD and we identified.

NOTE Confidence: 0.799687382222222

00:19:59.790 --> 00:20:02.289 And we showed that in a in

NOTE Confidence: 0.799687382222222

00:20:02.289 --> 00:20:06.440 a mouse model having EBV.

NOTE Confidence: 0.799687382222222

00:20:06.440 --> 00:20:09.880 3B Knockout would make the

NOTE Confidence: 0.799687382222222

00:20:09.880 --> 00:20:12.632 mouse susceptible for lymphoma.

NOTE Confidence: 0.799687382222222

00:20:12.640 --> 00:20:14.260 For the development of a lymphoma,

NOTE Confidence: 0.799687382222222

00:20:14.260 --> 00:20:15.175 here are mice.

NOTE Confidence: 0.799687382222222

00:20:15.175 --> 00:20:17.310 The three types of my swan which

NOTE Confidence: 0.799687382222222

00:20:17.377 --> 00:20:19.603 are infected with the wild type web

NOTE Confidence: 0.799687382222222

00:20:19.603 --> 00:20:22.107 and then when it was infected with

NOTE Confidence: 0.799687382222222

00:20:22.107 --> 00:20:24.507 Aetna Trib Knockout virus and then

NOTE Confidence: 0.799687382222222

00:20:24.507 --> 00:20:27.081 in another step we reintroduced Abner

NOTE Confidence: 0.799687382222222

00:20:27.081 --> 00:20:29.993 3B from into the stock out and you

NOTE Confidence: 0.799687382222222

00:20:29.993 --> 00:20:33.260 can see that 50% of the mice were

NOTE Confidence: 0.799687382222222

00:20:33.260 --> 00:20:35.180 infected with ethnicity knockout

NOTE Confidence: 0.799687382222222

00:20:35.180 --> 00:20:37.947 developed lymphomas whereas those which were.

NOTE Confidence: 0.799687382222222

00:20:37.950 --> 00:20:40.323 Infected with the wild type virus or

NOTE Confidence: 0.799687382222222

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00:20:40.323 --> 00:20:42.334 the revertant virus did not develop

NOTE Confidence: 0.799687382222222

00:20:42.334 --> 00:20:44.188 any lymphomas in spleen and then

NOTE Confidence: 0.799687382222222

00:20:44.188 --> 00:20:46.555 we also went on to look at human

NOTE Confidence: 0.799687382222222

00:20:46.555 --> 00:20:48.583 lymphomas to look at Abernathy B

NOTE Confidence: 0.799687382222222

00:20:48.583 --> 00:20:50.929 mutations and a large variety of

NOTE Confidence: 0.799687382222222

00:20:50.929 --> 00:20:53.459 AB positive human infamous showed

NOTE Confidence: 0.799687382222222

00:20:53.459 --> 00:20:56.024 mutations in their blood 3B.

NOTE Confidence: 0.799687382222222

00:20:56.030 --> 00:20:57.530 And here are the.

NOTE Confidence: 0.799687382222222

00:20:57.530 --> 00:20:59.405 Photomicrographs that we saw in

NOTE Confidence: 0.799687382222222

00:20:59.405 --> 00:21:01.797 in this in the spleens of these

NOTE Confidence: 0.799687382222222

00:21:01.797 --> 00:21:04.178 mice and here is the the white,

NOTE Confidence: 0.799687382222222

00:21:04.180 --> 00:21:06.050 those which are infected wild

NOTE Confidence: 0.799687382222222

00:21:06.050 --> 00:21:08.440 type virus and those which are

NOTE Confidence: 0.799687382222222

00:21:08.440 --> 00:21:10.670 infected with the revertant viruses.

NOTE Confidence: 0.799687382222222

00:21:10.670 --> 00:21:12.670 And here is the one with the knockout

NOTE Confidence: 0.799687382222222

00:21:12.670 --> 00:21:14.828 in the knockout mouse we found that

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NOTE Confidence: 0.799687382222222

00:21:14.828 --> 00:21:17.118 there is a proliferation of what would

NOTE Confidence: 0.799687382222222

00:21:17.118 --> 00:21:19.351 be very similar to an EB positive

NOTE Confidence: 0.799687382222222

00:21:19.351 --> 00:21:21.800 monomorphic diffuse large B cell lymphoma.

NOTE Confidence: 0.799687382222222

00:21:21.800 --> 00:21:24.176 And which were richly be positive,

NOTE Confidence: 0.799687382222222

00:21:24.180 --> 00:21:27.753 large B cells and very low in T cells.

NOTE Confidence: 0.799687382222222

00:21:27.760 --> 00:21:30.273 Then we did some experiments to see

NOTE Confidence: 0.799687382222222

00:21:30.273 --> 00:21:33.310 why are they so few T cells in the

NOTE Confidence: 0.799687382222222

00:21:33.310 --> 00:21:35.766 knockout mice and we could show that

NOTE Confidence: 0.799687382222222

00:21:35.766 --> 00:21:37.780 they they had very little chemokine.

NOTE Confidence: 0.799687382222222

00:21:37.780 --> 00:21:41.130 CXCL 10 and CXCL 10, which was

NOTE Confidence: 0.799687382222222

00:21:41.130 --> 00:21:43.620 required for attracting the T cells,

NOTE Confidence: 0.799687382222222

00:21:43.620 --> 00:21:45.996 was absent in the knockout mice.

NOTE Confidence: 0.799687382222222

00:21:46.000 --> 00:21:48.690 And if we supplemented with

NOTE Confidence: 0.799687382222222

00:21:48.690 --> 00:21:51.780 lten this could be reverted so.

NOTE Confidence: 0.799687382222222

00:21:51.780 --> 00:21:53.930 Not only was EBV responsible,

NOTE Confidence: 0.799687382222222

00:21:53.930 --> 00:21:55.490 but the microenvironment which it

NOTE Confidence: 0.799687382222222

00:21:55.490 --> 00:21:57.832 induced or which we which it suppressed

NOTE Confidence: 0.799687382222222

00:21:57.832 --> 00:21:59.632 while responsible for the development

NOTE Confidence: 0.799687382222222

00:21:59.632 --> 00:22:02.430 of diffuse large B cell lymphoma's.

NOTE Confidence: 0.799687382222222

00:22:02.430 --> 00:22:06.417 Then we went on to look at differences in

NOTE Confidence: 0.799687382222222

00:22:06.417 --> 00:22:08.769 microenvironment in HIV positive classic.

NOTE Confidence: 0.799687382222222

00:22:08.770 --> 00:22:11.236 Of course here it is difficult

NOTE Confidence: 0.799687382222222

00:22:11.236 --> 00:22:13.432 because almost all HIV positive,

NOTE Confidence: 0.799687382222222

00:22:13.432 --> 00:22:16.318 classic Hodgkin lymphoma or EBV positive,

NOTE Confidence: 0.799687382222222

00:22:16.320 --> 00:22:19.245 so we had a set of HIV positive EBV

NOTE Confidence: 0.799687382222222

00:22:19.245 --> 00:22:21.429 positive classic article Informa.

NOTE Confidence: 0.799687382222222

00:22:21.430 --> 00:22:22.680 We tried to compare that.

NOTE Confidence: 0.799687382222222

00:22:22.680 --> 00:22:25.355 With HIV negative EBV negative

NOTE Confidence: 0.799687382222222

00:22:25.355 --> 00:22:26.960 classic Hodgkin lymphoma,

NOTE Confidence: 0.799687382222222

00:22:26.960 --> 00:22:30.136 not only did we find differences in the

NOTE Confidence: 0.799687382222222

00:22:30.140 --> 00:22:32.620 numbers of the microenvironment cells,

NOTE Confidence: 0.9141250075

00:22:32.620 --> 00:22:33.805 but there was a difference

NOTE Confidence: 0.9141250075

00:22:33.805 --> 00:22:35.519 in the in the type of cells.

NOTE Confidence: 0.9141250075

00:22:35.520 --> 00:22:37.620 We found a unique population of CD

NOTE Confidence: 0.9141250075

00:22:37.620 --> 00:22:40.517 8 foxp 3 positive cells in the HIV

NOTE Confidence: 0.9141250075

00:22:40.517 --> 00:22:43.130 positive setting which we did not see

NOTE Confidence: 0.9141250075

00:22:43.130 --> 00:22:45.450 in the HIV negative set and similarly

NOTE Confidence: 0.9141250075

00:22:45.450 --> 00:22:48.506 we found that there were more CD 57.

NOTE Confidence: 0.9141250075

00:22:48.506 --> 00:22:51.117 There were fewer CD 57 positive cells.

NOTE Confidence: 0.9141250075

00:22:51.120 --> 00:22:53.910 There was fewer plasmacytoid dendritic cells.

NOTE Confidence: 0.9141250075

00:22:53.910 --> 00:22:55.818 Facility 123 positive cells

NOTE Confidence: 0.9141250075

00:22:55.818 --> 00:22:58.203 in the HIV positive setting,

NOTE Confidence: 0.9141250075

00:22:58.210 --> 00:23:01.140 so the microenvironment of EBV

NOTE Confidence: 0.9141250075

00:23:01.140 --> 00:23:03.484 positive disease is different.

NOTE Confidence: 0.9141250075

00:23:03.490 --> 00:23:05.380 We also then went on to look in the

NOTE Confidence: 0.9141250075

00:23:05.380 --> 00:23:06.817 post transplant setting comparing

NOTE Confidence: 0.9141250075

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00:23:06.817 --> 00:23:08.762 post transplant diffuse large B

NOTE Confidence: 0.9141250075

00:23:08.762 --> 00:23:10.532 cell lymphoma with the immune

NOTE Confidence: 0.9141250075

00:23:10.532 --> 00:23:12.082 competent diffuse large B cell

NOTE Confidence: 0.9141250075

00:23:12.082 --> 00:23:14.560 lymphoma and there were more T cells,

NOTE Confidence: 0.9141250075

00:23:14.560 --> 00:23:16.708 particularly CD 8 positive T cells

NOTE Confidence: 0.9141250075

00:23:16.708 --> 00:23:18.949 in the post transplant EBV positive

NOTE Confidence: 0.9141250075

00:23:18.949 --> 00:23:20.794 diffuse large B cell lymphoma

NOTE Confidence: 0.9141250075

00:23:20.794 --> 00:23:22.948 this and if you look at these we

NOTE Confidence: 0.9141250075

00:23:22.948 --> 00:23:24.955 wanted to make sure that these were

NOTE Confidence: 0.9141250075

00:23:24.955 --> 00:23:27.097 not easy be infected T cells and

NOTE Confidence: 0.9141250075

00:23:27.097 --> 00:23:28.607 these T cells look larger.

NOTE Confidence: 0.9141250075

00:23:28.610 --> 00:23:30.094 They look more stimulated

NOTE Confidence: 0.9141250075

00:23:30.094 --> 00:23:32.320 but and they are clearly EBV

NOTE Confidence: 0.9141250075

00:23:32.390 --> 00:23:34.800 negative and when we looked at.

NOTE Confidence: 0.9141250075

00:23:34.800 --> 00:23:36.620 Whether there was clonal expansion

NOTE Confidence: 0.9141250075

00:23:36.620 --> 00:23:39.250 of these reactive T cell populations,

00:23:39.250 --> 00:23:41.116 we could demonstrate that in a

00:23:41.116 --> 00:23:43.015 good proportion of post transplant

00:23:43.015 --> 00:23:44.788 liver proliferative disorders,

00:23:44.790 --> 00:23:48.126 there was a monoclonal expansion of T cells,

00:23:48.130 --> 00:23:50.360 which possibly those which were

00:23:50.360 --> 00:23:53.425 reactive to the to the EBV present

00:23:53.425 --> 00:23:57.378 in the monoclonal B cell population.

00:23:57.380 --> 00:24:00.105 Similar stories are similar kind

00:24:00.105 --> 00:24:03.346 of of pathogenic involvement of

00:24:03.346 --> 00:24:06.716 hedge viatour or Kaposi sarcoma

00:24:06.716 --> 00:24:09.449 herpesvirus also been identified.

00:24:09.450 --> 00:24:12.570 Much of this work has come from other

00:24:12.570 --> 00:24:14.649 investigators for the major investigator

00:24:14.649 --> 00:24:17.103 in this area is Ethel Merman.

00:24:17.110 --> 00:24:17.740 Tough.

00:24:17.740 --> 00:24:20.260 Along with Amy Chapman,

NOTE Confidence: 0.9141250075

00:24:20.260 --> 00:24:22.514 who have shown that the key uncle

NOTE Confidence: 0.9141250075

00:24:22.514 --> 00:24:25.044 proteins of the HP 8 drives the

NOTE Confidence: 0.9141250075

00:24:25.044 --> 00:24:26.909 lymphoma Genesis which includes the

NOTE Confidence: 0.9141250075

00:24:26.910 --> 00:24:29.532 Lana Lana protein than the recycling

NOTE Confidence: 0.9141250075

00:24:29.532 --> 00:24:32.791 and we flip and various other key

NOTE Confidence: 0.9141250075

00:24:32.791 --> 00:24:34.115 uncle proteins are responsible

NOTE Confidence: 0.9141250075

00:24:34.115 --> 00:24:36.270 for this kind of lymphoma genesis,

NOTE Confidence: 0.9141250075

00:24:36.270 --> 00:24:39.620 which happens in the study.

NOTE Confidence: 0.9141250075

00:24:39.620 --> 00:24:41.692 But when we look at the lymphoid

NOTE Confidence: 0.9141250075

00:24:41.692 --> 00:24:43.495 lesions within the which are

NOTE Confidence: 0.9141250075

00:24:43.495 --> 00:24:45.199 associated with infectious agents,

NOTE Confidence: 0.9141250075

00:24:45.200 --> 00:24:48.128 we see a variety and and a whole

NOTE Confidence: 0.9141250075

00:24:48.128 --> 00:24:51.359 range of aggressiveness and disease.

NOTE Confidence: 0.9141250075

00:24:51.360 --> 00:24:51.722 Biology.

NOTE Confidence: 0.9141250075

00:24:51.722 --> 00:24:54.256 At one end of the spectrum you

NOTE Confidence: 0.9141250075

00:24:54.256 --> 00:24:56.780 have self limiting diseases like

NOTE Confidence: 0.9141250075

00:24:56.780 --> 00:24:59.480 infectious mono nucleosis are very

NOTE Confidence: 0.9141250075

00:24:59.480 --> 00:25:02.014 benign conditions like the EBV

NOTE Confidence: 0.9141250075

00:25:02.014 --> 00:25:04.404 positive cutaneous ulcer of the

NOTE Confidence: 0.9141250075

00:25:04.410 --> 00:25:07.380 positive German or Tropic LPD.

NOTE Confidence: 0.9141250075

00:25:07.380 --> 00:25:08.895 Then you have something which

NOTE Confidence: 0.9141250075

00:25:08.895 --> 00:25:10.410 falls in the Gray zone.

NOTE Confidence: 0.9141250075

00:25:10.410 --> 00:25:12.965 Like the immediate positive polymorphous

NOTE Confidence: 0.9141250075

00:25:12.965 --> 00:25:13.987 lymphoproliferative disorder,

NOTE Confidence: 0.9141250075

00:25:13.990 --> 00:25:16.122 the Castleman disease inflammatory

NOTE Confidence: 0.9141250075

00:25:16.122 --> 00:25:17.721 granulomatosis fibron associated

NOTE Confidence: 0.9141250075

00:25:17.721 --> 00:25:20.290 diffuse large B cell lymphoma,

NOTE Confidence: 0.9141250075

00:25:20.290 --> 00:25:21.794 chronic active EBV infection.

NOTE Confidence: 0.9141250075

00:25:21.794 --> 00:25:24.050 Then you have the classic lymphomas

NOTE Confidence: 0.9141250075

00:25:24.116 --> 00:25:26.546 without associated with infectious agents,

NOTE Confidence: 0.9141250075

00:25:26.550 --> 00:25:28.139 and then you have some very aggressive

NOTE Confidence: 0.9141250075

00:25:28.139 --> 00:25:29.569 disease like the Burkitt lymphoma,

NOTE Confidence: 0.9141250075

00:25:29.570 --> 00:25:30.406 plasmablastic lymphoma,

NOTE Confidence: 0.9141250075

00:25:30.406 --> 00:25:32.496 so on and so forth.

NOTE Confidence: 0.9141250075

00:25:32.500 --> 00:25:34.716 I also what is important with these diseases.

NOTE Confidence: 0.9141250075

00:25:34.720 --> 00:25:36.688 There is a risk of overdiagnosis,

NOTE Confidence: 0.9141250075

00:25:36.690 --> 00:25:38.839 we know for a long time that

NOTE Confidence: 0.9141250075

00:25:38.839 --> 00:25:39.760 infectious mononucleosis can

NOTE Confidence: 0.9141250075

00:25:39.814 --> 00:25:41.429 be misdiagnosed as a lymphoma.

NOTE Confidence: 0.9141250075

00:25:41.430 --> 00:25:43.656 And so also is true about the

NOTE Confidence: 0.9141250075

00:25:43.660 --> 00:25:46.790 positive cricket aneus ulcer or

NOTE Confidence: 0.9141250075

00:25:46.790 --> 00:25:48.882 associate Germany Tropic disease.

NOTE Confidence: 0.9141250075

00:25:48.882 --> 00:25:51.497 So understanding these diseases is

NOTE Confidence: 0.9141250075

00:25:51.497 --> 00:25:53.936 important from the point of view

NOTE Confidence: 0.9141250075

00:25:53.936 --> 00:25:55.781 of recognizing them properly and

NOTE Confidence: 0.790849840923077

00:25:55.849 --> 00:25:58.129 not overdosing them as them first.

NOTE Confidence: 0.790849840923077

00:25:58.130 --> 00:26:00.658 I, I think most of you know very

NOTE Confidence: 0.790849840923077

00:26:00.658 --> 00:26:03.209 well about infectious mononucleosis,

NOTE Confidence: 0.790849840923077

00:26:03.210 --> 00:26:06.858 and I will skip this slide.

NOTE Confidence: 0.790849840923077

00:26:06.860 --> 00:26:08.883 Even the positive continuous also is is

NOTE Confidence: 0.790849840923077

00:26:08.883 --> 00:26:11.658 a is an important entity to recognize,

NOTE Confidence: 0.790849840923077

00:26:11.660 --> 00:26:14.460 because this have a very indolent behavior.

NOTE Confidence: 0.790849840923077

00:26:14.460 --> 00:26:15.810 These are circumscribed,

NOTE Confidence: 0.790849840923077

00:26:15.810 --> 00:26:17.160 painful but shadow.

NOTE Confidence: 0.790849840923077

00:26:17.160 --> 00:26:19.165 Shallow ulcer ative lesions which

NOTE Confidence: 0.790849840923077

00:26:19.165 --> 00:26:21.707 frequently occur in the orphan genetic

NOTE Confidence: 0.790849840923077

00:26:21.707 --> 00:26:24.360 causes skin or gastrointestinal tract most.

NOTE Confidence: 0.790849840923077

00:26:24.360 --> 00:26:26.460 It's not only mean it can be

NOTE Confidence: 0.790849840923077

00:26:26.460 --> 00:26:28.944 associated with the variety of immune

NOTE Confidence: 0.790849840923077

00:26:28.944 --> 00:26:30.768 suppressive conditions like medication

NOTE Confidence: 0.790849840923077

00:26:30.768 --> 00:26:32.820 associated like with methotrexate.

NOTE Confidence: 0.790849840923077

00:26:32.820 --> 00:26:34.654 Sometimes it can be just age related,

NOTE Confidence: 0.790849840923077

00:26:34.660 --> 00:26:35.196 immune senescence.

NOTE Confidence: 0.790849840923077

00:26:35.196 --> 00:26:37.072 It can occur in the background of.

NOTE Confidence: 0.790849840923077

00:26:37.080 --> 00:26:38.466 Community post transplantation.

NOTE Confidence: 0.790849840923077

00:26:38.466 --> 00:26:41.700 Also, it can occur with various malignancies.

NOTE Confidence: 0.790849840923077

00:26:41.700 --> 00:26:43.569 You can see a patient with lymphoma

NOTE Confidence: 0.790849840923077

00:26:43.569 --> 00:26:44.840 developing, ambiguities also,

NOTE Confidence: 0.790849840923077

00:26:44.840 --> 00:26:47.840 and many of these regress spontaneously,

NOTE Confidence: 0.790849840923077

00:26:47.840 --> 00:26:51.504 and some of them respond to withdrawal of

NOTE Confidence: 0.790849840923077

00:26:51.504 --> 00:26:54.408 immune suppression or immune reconstitution.

NOTE Confidence: 0.790849840923077

00:26:54.410 --> 00:26:55.352 And classically,

NOTE Confidence: 0.790849840923077

00:26:55.352 --> 00:26:57.707 this has a polymorphous infiltrate,

NOTE Confidence: 0.790849840923077

00:26:57.710 --> 00:27:00.230 and it got a typical large B cells,

NOTE Confidence: 0.790849840923077

00:27:00.230 --> 00:27:02.306 and some of them can resemble

NOTE Confidence: 0.790849840923077

00:27:02.306 --> 00:27:03.690 Hodgkin Reed Sternberg cells.

NOTE Confidence: 0.790849840923077

00:27:03.690 --> 00:27:06.650 It shows strong CD 30 Andy Barr expression.

NOTE Confidence: 0.790849840923077

00:27:06.650 --> 00:27:08.225 Many of the things in the past

NOTE Confidence: 0.790849840923077

00:27:08.225 --> 00:27:09.838 which might have been called as

NOTE Confidence: 0.790849840923077

00:27:09.838 --> 00:27:11.308 extranodal are because of *******.

NOTE Confidence: 0.790849840923077

00:27:11.310 --> 00:27:13.300 Informa need to be revisited

NOTE Confidence: 0.790849840923077

00:27:13.300 --> 00:27:15.729 whether there's many of them could

NOTE Confidence: 0.790849840923077

00:27:15.729 --> 00:27:17.898 be EBV positive Catania's ulcers.

NOTE Confidence: 0.790849840923077

00:27:17.898 --> 00:27:20.568 They can also explicitly 15,

NOTE Confidence: 0.790849840923077

00:27:20.570 --> 00:27:22.870 and they often express opto,

NOTE Confidence: 0.790849840923077

00:27:22.870 --> 00:27:24.436 but most of them lack Bob.

NOTE Confidence: 0.790849840923077

00:27:24.440 --> 00:27:26.220 One city Trinity expression

NOTE Confidence: 0.790849840923077

00:27:26.220 --> 00:27:27.555 is usually reduced,

NOTE Confidence: 0.790849840923077

00:27:27.560 --> 00:27:29.624 and typically there's a band of CD 3

NOTE Confidence: 0.790849840923077

00:27:29.624 --> 00:27:31.520 positive T cells and the periphery,

NOTE Confidence: 0.790849840923077

00:27:31.520 --> 00:27:33.440 and if one does clonality,

NOTE Confidence: 0.790849840923077

00:27:33.440 --> 00:27:36.075 there can be plotted both

NOTE Confidence: 0.790849840923077

00:27:36.075 --> 00:27:38.087 immunoglobulin or diesel gene

NOTE Confidence: 0.790849840923077

00:27:38.087 --> 00:27:40.222 rearrangements and nearly one half

NOTE Confidence: 0.790849840923077

00:27:40.222 --> 00:27:41.930 of them progress spontaneously.

NOTE Confidence: 0.790849840923077

00:27:41.930 --> 00:27:44.373 These are some of the pictures from

NOTE Confidence: 0.790849840923077

00:27:44.373 --> 00:27:46.098 the publication by Stephen Dodge

NOTE Confidence: 0.790849840923077

00:27:46.098 --> 00:27:48.530 Channel and you can see here is a

NOTE Confidence: 0.790849840923077

00:27:48.597 --> 00:27:50.537 shallow ulcer and the periphery

NOTE Confidence: 0.790849840923077

00:27:50.537 --> 00:27:52.840 you have a diesel infiltrate but

NOTE Confidence: 0.790849840923077

00:27:52.840 --> 00:27:55.000 towards the ulcer you see large.

NOTE Confidence: 0.790849840923077

00:27:55.000 --> 00:27:56.464 EBV positive B cells,

NOTE Confidence: 0.790849840923077

00:27:56.464 --> 00:27:58.660 which can show an article clone,

NOTE Confidence: 0.790849840923077

00:27:58.660 --> 00:28:02.290 another monoclonal expansion of TRB cells.

NOTE Confidence: 0.790849840923077

00:28:02.290 --> 00:28:04.162 And here's another case which shows

NOTE Confidence: 0.790849840923077

00:28:04.162 --> 00:28:06.335 not only CD 30 positivity but

NOTE Confidence: 0.790849840923077

00:28:06.335 --> 00:28:08.475 also profound city 15 expression.

NOTE Confidence: 0.899476258333333

00:28:11.990 --> 00:28:14.650 This is an entity which we for a

NOTE Confidence: 0.899476258333333

00:28:14.650 --> 00:28:16.700 long time we appreciated polymorphic

NOTE Confidence: 0.899476258333333

00:28:16.700 --> 00:28:18.712 type of post, transplant liver,

NOTE Confidence: 0.899476258333333

00:28:18.712 --> 00:28:19.494 proliferative disorders,

NOTE Confidence: 0.899476258333333

00:28:19.494 --> 00:28:21.449 but now more and more.

NOTE Confidence: 0.899476258333333

00:28:21.450 --> 00:28:23.964 We are seeing this in outside

NOTE Confidence: 0.899476258333333

00:28:23.964 --> 00:28:26.370 of the post transplant setting.

NOTE Confidence: 0.899476258333333

00:28:26.370 --> 00:28:28.930 We can see that in in the setting

NOTE Confidence: 0.899476258333333

00:28:28.930 --> 00:28:31.209 of autoimmune diseases or therapy

NOTE Confidence: 0.899476258333333

00:28:31.209 --> 00:28:32.775 related immune deficiency,

NOTE Confidence: 0.899476258333333

00:28:32.780 --> 00:28:34.418 but rarely we can also see it

NOTE Confidence: 0.899476258333333

00:28:34.418 --> 00:28:36.091 in the setting of a child here

NOTE Confidence: 0.899476258333333

00:28:36.091 --> 00:28:38.377 architecture of the node of the

NOTE Confidence: 0.899476258333333

00:28:38.377 --> 00:28:40.947 extra node log lesion is a faced.

NOTE Confidence: 0.899476258333333

00:28:40.950 --> 00:28:42.860 There's a heterogeneous of polymorphous.

NOTE Confidence: 0.899476258333333

00:28:42.860 --> 00:28:45.040 Infiltrate of immune cells,

NOTE Confidence: 0.899476258333333

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00:28:45.040 --> 00:28:47.642 which includes B cells which has got a

NOTE Confidence: 0.899476258333333

00:28:47.642 --> 00:28:49.979 full spectrum of B cell differentiation.

NOTE Confidence: 0.899476258333333

00:28:49.980 --> 00:28:51.996 You will see large immuno blasts.

NOTE Confidence: 0.899476258333333

00:28:52.000 --> 00:28:54.888 You will see plasma cells so the whole

NOTE Confidence: 0.899476258333333

00:28:54.888 --> 00:28:56.784 range of visual differentiation is seen

NOTE Confidence: 0.899476258333333

00:28:56.784 --> 00:28:58.719 within this polymorphous infiltrate.

NOTE Confidence: 0.899476258333333

00:28:58.720 --> 00:29:00.952 And many of these large beetles can have

NOTE Confidence: 0.899476258333333

00:29:00.952 --> 00:29:03.120 features of Hodgkin Reed Sternberg cells.

NOTE Confidence: 0.899476258333333

00:29:03.120 --> 00:29:04.630 And these are EBV positive.

NOTE Confidence: 0.899476258333333

00:29:04.630 --> 00:29:07.955 Most often some people debate whether there

NOTE Confidence: 0.899476258333333

00:29:07.955 --> 00:29:10.420 could be any be negative polymorphous LPD,

NOTE Confidence: 0.899476258333333

00:29:10.420 --> 00:29:13.030 but defining that can be difficult.

NOTE Confidence: 0.899476258333333

00:29:13.030 --> 00:29:16.690 And distinguishing them from other

NOTE Confidence: 0.899476258333333

00:29:16.690 --> 00:29:18.675 reactive conditions can be difficult

NOTE Confidence: 0.899476258333333

00:29:18.675 --> 00:29:20.660 even with positive disease is

NOTE Confidence: 0.899476258333333

00:29:20.727 --> 00:29:21.902 more easily identified,

NOTE Confidence: 0.899476258333333

00:29:21.902 --> 00:29:23.438 and they can.

NOTE Confidence: 0.899476258333333

00:29:23.438 --> 00:29:25.870 Also, it can have monoclonal article,

NOTE Confidence: 0.899476258333333

00:29:25.870 --> 00:29:29.022 clonal proliferation of B cells and

NOTE Confidence: 0.899476258333333

00:29:29.022 --> 00:29:31.582 both nodal and external deliberations

NOTE Confidence: 0.899476258333333

00:29:31.582 --> 00:29:34.066 are presentations are known and

NOTE Confidence: 0.899476258333333

00:29:34.066 --> 00:29:36.593 some of them may also present with.

NOTE Confidence: 0.899476258333333

00:29:36.600 --> 00:29:39.279 For history cytosis.

NOTE Confidence: 0.899476258333333

00:29:39.280 --> 00:29:42.453 I'll take you through a few examples and

NOTE Confidence: 0.899476258333333

00:29:42.453 --> 00:29:44.957 I think it brings out the issues well.

NOTE Confidence: 0.899476258333333

00:29:44.960 --> 00:29:47.921 Here is a woman in 60s who had been

NOTE Confidence: 0.899476258333333

00:29:47.921 --> 00:29:50.423 treated with pancreatic cancer two

NOTE Confidence: 0.899476258333333

00:29:50.423 --> 00:29:52.438 years prior to this presentation

NOTE Confidence: 0.899476258333333

00:29:52.440 --> 00:29:54.480 and patient presented with fever and

NOTE Confidence: 0.899476258333333

00:29:54.480 --> 00:29:56.860 weight loss of three months duration,

NOTE Confidence: 0.899476258333333

00:29:56.860 --> 00:29:59.182 and there was a large periodic

NOTE Confidence: 0.899476258333333

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00:29:59.182 --> 00:30:01.670 mass sub in centimeter dimension

NOTE Confidence: 0.899476258333333

00:30:01.670 --> 00:30:04.820 and patient also had right axilla

NOTE Confidence: 0.899476258333333

00:30:04.908 --> 00:30:07.208 re lymph adenopathy and needle

NOTE Confidence: 0.899476258333333

00:30:07.208 --> 00:30:09.336 core biopsy was undertake.

NOTE Confidence: 0.899476258333333

00:30:09.340 --> 00:30:11.563 And here you can see on on the left

NOTE Confidence: 0.899476258333333

00:30:11.563 --> 00:30:12.946 you can see predominantly small

NOTE Confidence: 0.899476258333333

00:30:12.946 --> 00:30:15.137 to medium sized cells and on the

NOTE Confidence: 0.899476258333333

00:30:15.137 --> 00:30:16.915 right you see amidst these small

NOTE Confidence: 0.899476258333333

00:30:16.915 --> 00:30:19.039 to medium sized cells you see some

NOTE Confidence: 0.899476258333333

00:30:19.039 --> 00:30:20.699 cells which look like mononuclear.

NOTE Confidence: 0.899476258333333

00:30:20.700 --> 00:30:23.150 Hodgkin cells are lacunar cells.

NOTE Confidence: 0.899476258333333

00:30:23.150 --> 00:30:25.556 You also know fields were completely

NOTE Confidence: 0.899476258333333

00:30:25.556 --> 00:30:27.542 lacking in this infiltrate and

NOTE Confidence: 0.899476258333333

00:30:27.542 --> 00:30:29.768 plasma cells were also not too many.

NOTE Confidence: 0.899476258333333

00:30:29.770 --> 00:30:31.905 And you can see these cells are

NOTE Confidence: 0.899476258333333

00:30:31.905 --> 00:30:33.350 rich in T cells.

NOTE Confidence: 0.899476258333333

00:30:33.350 --> 00:30:35.435 And they are predominantly city

NOTE Confidence: 0.899476258333333

00:30:35.435 --> 00:30:38.310 8 positive T cells and there were

NOTE Confidence: 0.899476258333333

00:30:38.310 --> 00:30:39.910 many evil positive cells.

NOTE Confidence: 0.899476258333333

00:30:39.910 --> 00:30:42.528 You have some larger Lieber positive cells.

NOTE Confidence: 0.899476258333333

00:30:42.530 --> 00:30:45.446 And many smaller evil positive cells.

NOTE Confidence: 0.899476258333333

00:30:45.450 --> 00:30:47.722 And then we did further and you also

NOTE Confidence: 0.899476258333333

00:30:47.722 --> 00:30:50.072 had large CD 20 positive cells which

NOTE Confidence: 0.899476258333333

00:30:50.072 --> 00:30:52.218 were also both positive and these

NOTE Confidence: 0.899476258333333

00:30:52.218 --> 00:30:55.290 cells for CD30 and CD15 and Oct 2000.

NOTE Confidence: 0.899476258333333

00:30:55.290 --> 00:30:56.890 So there were some areas,

NOTE Confidence: 0.899476258333333

00:30:56.890 --> 00:30:58.450 those things which looked like

NOTE Confidence: 0.899476258333333

00:30:58.450 --> 00:31:00.502 Hodgkin's cells had a phenotype not

NOTE Confidence: 0.899476258333333

00:31:00.502 --> 00:31:02.962 too different from Hodgkin apart

NOTE Confidence: 0.899476258333333

00:31:02.962 --> 00:31:05.489 from strong expression of CD 20.

NOTE Confidence: 0.899476258333333

00:31:05.490 --> 00:31:07.250 Oneba as you see here,

NOTE Confidence: 0.899476258333333

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00:31:07.250 --> 00:31:09.644 many cells are even positive and this

NOTE Confidence: 0.899476258333333

00:31:09.644 --> 00:31:11.870 includes both large cells like Hodgkin.

NOTE Confidence: 0.899476258333333

00:31:11.870 --> 00:31:13.952 Look like large cells and many

NOTE Confidence: 0.899476258333333

00:31:13.952 --> 00:31:16.159 smaller cells and medium sized cells.

NOTE Confidence: 0.899476258333333

00:31:16.160 --> 00:31:19.037 And when we did double state you

NOTE Confidence: 0.899476258333333

00:31:19.037 --> 00:31:20.270 can see that.

NOTE Confidence: 0.899476258333333

00:31:20.270 --> 00:31:22.406 These large cells libre positive CD,

NOTE Confidence: 0.899476258333333

00:31:22.410 --> 00:31:24.534 three negative but many of the

NOTE Confidence: 0.899476258333333

00:31:24.534 --> 00:31:25.950 small and medium sized

NOTE Confidence: 0.793170691666667

00:31:26.021 --> 00:31:28.829 cells were CD three and Eva dual positive.

NOTE Confidence: 0.793170691666667

00:31:28.830 --> 00:31:31.294 And here you can see that many of

NOTE Confidence: 0.793170691666667

00:31:31.294 --> 00:31:33.486 the smaller and medium sized Eber

NOTE Confidence: 0.793170691666667

00:31:33.486 --> 00:31:35.742 positive cells are CD 8 positive.

NOTE Confidence: 0.793170691666667

00:31:35.750 --> 00:31:37.772 So here's a situation where you

NOTE Confidence: 0.793170691666667

00:31:37.772 --> 00:31:40.184 have both CD 8 positive either

NOTE Confidence: 0.793170691666667

00:31:40.184 --> 00:31:42.644 positive cells and other facts.

NOTE Confidence: 0.793170691666667

00:31:42.650 --> 00:31:45.092 Fire CD 20 positive either positive

NOTE Confidence: 0.793170691666667

00:31:45.092 --> 00:31:47.720 cells and this is a classic exam

NOTE Confidence: 0.793170691666667

00:31:47.720 --> 00:31:50.204 and we try to we also undertook.

NOTE Confidence: 0.793170691666667

00:31:50.204 --> 00:31:52.294 Immunoglobulin T cell receptor gene

NOTE Confidence: 0.793170691666667

00:31:52.294 --> 00:31:54.160 rearrangement studies and we could

NOTE Confidence: 0.793170691666667

00:31:54.160 --> 00:31:55.775 not identify any particular clone,

NOTE Confidence: 0.793170691666667

00:31:55.780 --> 00:31:58.756 and the patients EBV levels waxed and vein.

NOTE Confidence: 0.793170691666667

00:31:58.760 --> 00:32:00.118 Then it fell off on its own,

NOTE Confidence: 0.793170691666667

00:32:00.120 --> 00:32:02.312 so this is a classic case of a

NOTE Confidence: 0.793170691666667

00:32:02.312 --> 00:32:03.800 polymorphism for polar disorder,

NOTE Confidence: 0.793170691666667

00:32:03.800 --> 00:32:06.230 with some features overlapping with a

NOTE Confidence: 0.793170691666667

00:32:06.230 --> 00:32:08.959 chronic EBV infection of the T cell type.

NOTE Confidence: 0.793170691666667

00:32:08.960 --> 00:32:11.096 And then there are some features

NOTE Confidence: 0.793170691666667

00:32:11.096 --> 00:32:12.935 which raises the possibility of

NOTE Confidence: 0.793170691666667

00:32:12.935 --> 00:32:14.685 an evolving fortune like process.

NOTE Confidence: 0.793170691666667

00:32:14.690 --> 00:32:15.109 However,

NOTE Confidence: 0.793170691666667

00:32:15.109 --> 00:32:17.204 this patient was not treated

NOTE Confidence: 0.793170691666667

00:32:17.204 --> 00:32:18.880 for any Hodgkin lymphoma,

NOTE Confidence: 0.793170691666667

00:32:18.880 --> 00:32:20.956 but eventually within two months time

NOTE Confidence: 0.793170691666667

00:32:20.956 --> 00:32:22.810 patient developed a treatment related.

NOTE Confidence: 0.793170691666667

00:32:22.810 --> 00:32:24.970 I could buy leukemia,

NOTE Confidence: 0.793170691666667

00:32:24.970 --> 00:32:27.737 but so this gives you an impression in a

NOTE Confidence: 0.793170691666667

00:32:27.737 --> 00:32:29.956 patient with a post Trump a patient who

NOTE Confidence: 0.793170691666667

00:32:29.956 --> 00:32:31.828 had been treated for pancreatic cancer,

NOTE Confidence: 0.793170691666667

00:32:31.830 --> 00:32:36.238 had a reduced immune.

NOTE Confidence: 0.793170691666667

00:32:36.240 --> 00:32:40.608 Capacity and then develop an EBV positive

NOTE Confidence: 0.793170691666667

00:32:40.608 --> 00:32:42.480 polymorphous lymphoproliferative disorder.

NOTE Confidence: 0.793170691666667

00:32:42.480 --> 00:32:43.624 In contrast to that,

NOTE Confidence: 0.793170691666667

00:32:43.624 --> 00:32:45.340 here is another case where the

NOTE Confidence: 0.793170691666667

00:32:45.400 --> 00:32:47.371 fact is a is a man in 60s who

NOTE Confidence: 0.793170691666667

00:32:47.371 --> 00:32:48.754 presented with pancytopenia with

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NOTE Confidence: 0.793170691666667

00:32:48.754 --> 00:32:50.571 a clinical diagnosis of HLH.

NOTE Confidence: 0.793170691666667

00:32:50.571 --> 00:32:53.299 I had lower hemoglobin at a low white

NOTE Confidence: 0.793170691666667

00:32:53.299 --> 00:32:56.376 cell count and a low platelets and

NOTE Confidence: 0.793170691666667

00:32:56.376 --> 00:32:58.788 bone marrow investigations were done

NOTE Confidence: 0.793170691666667

00:32:58.788 --> 00:33:01.613 which showed a hypercellular marrow

NOTE Confidence: 0.793170691666667

00:33:01.613 --> 00:33:03.898 with trilineage hematopoiesis flow on.

NOTE Confidence: 0.793170691666667

00:33:03.898 --> 00:33:05.368 The peripheral blood showed that

NOTE Confidence: 0.793170691666667

00:33:05.368 --> 00:33:07.332 there was an increase in the cur

NOTE Confidence: 0.793170691666667

00:33:07.332 --> 00:33:09.197 gamma delta T cells and the same

NOTE Confidence: 0.793170691666667

00:33:09.197 --> 00:33:11.101 thing was also there in bone marrow

NOTE Confidence: 0.793170691666667

00:33:11.101 --> 00:33:13.010 and these cells were a bit larger.

NOTE Confidence: 0.793170691666667

00:33:13.010 --> 00:33:14.768 Here are the flow plots focus

NOTE Confidence: 0.793170691666667

00:33:14.768 --> 00:33:16.330 on the red cells here.

NOTE Confidence: 0.793170691666667

00:33:16.330 --> 00:33:18.808 These were larger cells with a

NOTE Confidence: 0.793170691666667

00:33:18.808 --> 00:33:20.880 slightly higher side scatter and

NOTE Confidence: 0.793170691666667

00:33:20.880 --> 00:33:22.980 these were gamma delta T cells.

NOTE Confidence: 0.793170691666667

00:33:22.980 --> 00:33:24.273 Which were CD,

NOTE Confidence: 0.793170691666667

00:33:24.273 --> 00:33:26.859 four negative and CD eight was

NOTE Confidence: 0.793170691666667

00:33:26.859 --> 00:33:29.467 mostly negative of weak CD 8 and

NOTE Confidence: 0.793170691666667

00:33:29.467 --> 00:33:32.534 these were CD 56 positive cells and

NOTE Confidence: 0.793170691666667

00:33:32.534 --> 00:33:35.179 CD five was completely negative.

NOTE Confidence: 0.793170691666667

00:33:35.180 --> 00:33:37.091 And here's the border from the patient

NOTE Confidence: 0.793170691666667

00:33:37.091 --> 00:33:39.440 and you can see there were an atypical,

NOTE Confidence: 0.793170691666667

00:33:39.440 --> 00:33:41.328 slightly larger lymphoid infiltrate

NOTE Confidence: 0.793170691666667

00:33:41.328 --> 00:33:44.540 which you can see here with CD3.

NOTE Confidence: 0.793170691666667

00:33:44.540 --> 00:33:46.574 These are the lymphoid cells and

NOTE Confidence: 0.793170691666667

00:33:46.574 --> 00:33:48.951 then this was CD 3 positive and

NOTE Confidence: 0.793170691666667

00:33:48.951 --> 00:33:51.111 this here is evil and here you

NOTE Confidence: 0.793170691666667

00:33:51.111 --> 00:33:52.893 can see with a double strain.

NOTE Confidence: 0.793170691666667

00:33:52.900 --> 00:33:54.226 These were not only CD 8.

NOTE Confidence: 0.793170691666667

00:33:54.230 --> 00:33:54.584 Positive,

NOTE Confidence: 0.793170691666667

00:33:54.584 --> 00:33:57.062 but these were also CD 56 positive

NOTE Confidence: 0.793170691666667

00:33:57.062 --> 00:34:00.061 CD 3 positive and CD 56 positive

NOTE Confidence: 0.793170691666667

00:34:00.061 --> 00:34:03.138 either positive cells and this is a

NOTE Confidence: 0.793170691666667

00:34:03.138 --> 00:34:05.754 classic example of a chronic active

NOTE Confidence: 0.793170691666667

00:34:05.754 --> 00:34:08.658 EBV infection of CD8 Gamma Delta type

NOTE Confidence: 0.793170691666667

00:34:08.658 --> 00:34:11.834 and we can see the viral levels of

NOTE Confidence: 0.793170691666667

00:34:11.834 --> 00:34:14.550 waxed and waned in this patient and

NOTE Confidence: 0.793170691666667

00:34:14.636 --> 00:34:17.606 patient did with conservative measures.

NOTE Confidence: 0.793170691666667

00:34:17.610 --> 00:34:18.650 Patient did quite well.

NOTE Confidence: 0.9657866

00:34:20.940 --> 00:34:24.340 So. We move on to a few other

NOTE Confidence: 0.9657866

00:34:24.340 --> 00:34:25.367 TB positive lymphomas, like.

NOTE Confidence: 0.9657866

00:34:25.367 --> 00:34:27.343 Here is I want to discuss about it.

NOTE Confidence: 0.9657866

00:34:27.350 --> 00:34:31.060 Be positive diffuse large B cell lymphoma.

NOTE Confidence: 0.9657866

00:34:31.060 --> 00:34:32.653 For the definition of EBV, positive,

NOTE Confidence: 0.9657866

00:34:32.653 --> 00:34:34.318 diffuse, large B cell lymphoma,

NOTE Confidence: 0.9657866

00:34:34.320 --> 00:34:36.931 there should be no history of a

NOTE Confidence: 0.9657866

00:34:36.931 --> 00:34:39.369 previous and informal or of any

NOTE Confidence: 0.9657866

00:34:39.369 --> 00:34:41.439 inborn or acquired immune deficiency.

NOTE Confidence: 0.9657866

00:34:41.440 --> 00:34:43.918 But age is not a criteria.

NOTE Confidence: 0.9657866

00:34:43.920 --> 00:34:46.685 And the the disease should not fulfill

NOTE Confidence: 0.9657866

00:34:46.685 --> 00:34:49.838 any criteria for other EBV positive news

NOTE Confidence: 0.9657866

00:34:49.838 --> 00:34:52.208 for proliferative disorders like you

NOTE Confidence: 0.9657866

00:34:52.208 --> 00:34:55.252 can't have limited granulomatosis or it

NOTE Confidence: 0.9657866

00:34:55.252 --> 00:34:57.304 should not be a plasmablastic lymphoma.

NOTE Confidence: 0.9657866

00:34:57.310 --> 00:34:59.585 So when you exclude all those things,

NOTE Confidence: 0.9657866

00:34:59.590 --> 00:35:01.710 what remains would be easy.

NOTE Confidence: 0.9657866

00:35:01.710 --> 00:35:03.887 Be positive. That would be be positive,

NOTE Confidence: 0.9657866

00:35:03.890 --> 00:35:05.570 diffuse large B cell lymphoma.

NOTE Confidence: 0.9657866

00:35:05.570 --> 00:35:07.370 Most of these patients are over the age

NOTE Confidence: 0.9657866

00:35:07.370 --> 00:35:09.526 of 50 years, but age is not a criterion.

NOTE Confidence: 0.9657866

00:35:09.530 --> 00:35:11.350 It can happen even in patients less

NOTE Confidence: 0.9657866

00:35:11.350 --> 00:35:13.147 than 50 years of age and a peak.

NOTE Confidence: 0.9657866

00:35:13.150 --> 00:35:14.686 Incidences in the 7th and the.

NOTE Confidence: 0.9657866

00:35:14.690 --> 00:35:17.370 8 decades.

NOTE Confidence: 0.9657866

00:35:17.370 --> 00:35:19.743 More than 50% of the patients present

NOTE Confidence: 0.9657866

00:35:19.743 --> 00:35:22.700 with a high IPI and a High E Cox scope,

NOTE Confidence: 0.9657866

00:35:22.700 --> 00:35:24.210 and as I said earlier,

NOTE Confidence: 0.9657866

00:35:24.210 --> 00:35:25.974 they show a lower mutational burden

NOTE Confidence: 0.9657866

00:35:25.974 --> 00:35:28.086 as compared to maybe negative diffuse

NOTE Confidence: 0.9657866

00:35:28.086 --> 00:35:30.868 large B cell lymphoma's and frequently

NOTE Confidence: 0.9657866

00:35:30.868 --> 00:35:34.221 show over expression of PD L1 and

NOTE Confidence: 0.9657866

00:35:34.221 --> 00:35:36.571 they may also harbor structural

NOTE Confidence: 0.9657866

00:35:36.571 --> 00:35:39.518 variations in PDL one and PDL 2

NOTE Confidence: 0.9657866

00:35:39.520 --> 00:35:42.622 Chainz 2 subsets are identified,

NOTE Confidence: 0.9657866

00:35:42.622 --> 00:35:44.620 one is a polymorphous variant and

NOTE Confidence: 0.9657866

00:35:44.682 --> 00:35:46.656 other one is a monomorphic variant.

NOTE Confidence: 0.9657866

00:35:46.660 --> 00:35:48.450 The polymorphic variant is important

00:35:48.450 --> 00:35:50.640 to recognize because this can be

00:35:50.640 --> 00:35:52.355 misdiagnosed as a Hodgkin lymphoma.

00:35:52.360 --> 00:35:53.880 Other type of lymphomas.

00:35:53.880 --> 00:35:56.160 Here you have large transform cells,

00:35:56.160 --> 00:35:59.580 immuno blast including cells resembling Reed,

00:35:59.580 --> 00:36:01.470 Sternberg cells all inside predominant

00:36:01.470 --> 00:36:04.608 cells and these are seen in a very

00:36:04.608 --> 00:36:06.810 polymorphous background of small lymphocytes,

00:36:06.810 --> 00:36:08.220 plasma cells histiocytes.

00:36:08.220 --> 00:36:10.252 So you can see that there is an

00:36:10.252 --> 00:36:12.747 overlapping in overlap in the differential

00:36:12.747 --> 00:36:14.671 diagnosis with a polymorphous

00:36:14.671 --> 00:36:15.633 lymphoproliferative disorder.

00:36:15.640 --> 00:36:16.678 And other lymphomas.

00:36:16.678 --> 00:36:19.462 It can be also be mistaken for a

NOTE Confidence: 0.9657866

00:36:19.462 --> 00:36:21.506 T cell rich piece of lymphoma if

NOTE Confidence: 0.9657866

00:36:21.506 --> 00:36:23.386 the baby is not tested often,

NOTE Confidence: 0.9657866

00:36:23.386 --> 00:36:25.808 you see I'm just centric and the

NOTE Confidence: 0.9657866

00:36:25.808 --> 00:36:27.999 destructive areas and you have extensive

NOTE Confidence: 0.9657866

00:36:27.999 --> 00:36:30.579 coagulative necrosis and they can be CD 30.

NOTE Confidence: 0.9657866

00:36:30.580 --> 00:36:32.995 Positive City 15 can also be positive.

NOTE Confidence: 0.9657866

00:36:33.000 --> 00:36:35.292 Often you have a latency of

NOTE Confidence: 0.9657866

00:36:35.292 --> 00:36:37.759 type 2 and rarely of type 3.

NOTE Confidence: 0.9657866

00:36:37.760 --> 00:36:40.200 By type two I would mean that they

NOTE Confidence: 0.9657866

00:36:40.200 --> 00:36:42.431 should also be expressing LMP one and

NOTE Confidence: 0.9657866

00:36:42.431 --> 00:36:44.919 Type 3 in addition to Eber and LMP.

NOTE Confidence: 0.9657866

00:36:44.920 --> 00:36:47.400 One they would express.

NOTE Confidence: 0.9657866

00:36:47.400 --> 00:36:48.020 Who?

NOTE Confidence: 0.9657866

00:36:48.020 --> 00:36:50.024 Again, the impact on outcomes is

NOTE Confidence: 0.9657866

00:36:50.024 --> 00:36:52.638 not very clear in the Asian setting,

NOTE Confidence: 0.9657866

00:36:52.640 --> 00:36:53.292 EBV positive,

NOTE Confidence: 0.9657866

00:36:53.292 --> 00:36:54.922 diffuse large B cell lymphoma

NOTE Confidence: 0.9657866

00:36:54.922 --> 00:36:55.900 as adverse prognosis.

NOTE Confidence: 0.9657866

00:36:55.900 --> 00:36:58.160 The Neb negative diffuse large

NOTE Confidence: 0.9657866

00:36:58.160 --> 00:36:59.516 B cell lymphoma.

NOTE Confidence: 0.9657866

00:36:59.520 --> 00:37:00.604 Here is an example.

NOTE Confidence: 0.9657866

00:37:00.604 --> 00:37:03.122 He can see there are areas of neck

NOTE Confidence: 0.9657866

00:37:03.122 --> 00:37:03.948 regulative necrosis.

NOTE Confidence: 0.9657866

00:37:03.950 --> 00:37:06.050 Then here's the viability areas,

NOTE Confidence: 0.9657866

00:37:06.050 --> 00:37:08.330 and these cells can be

NOTE Confidence: 0.9657866

00:37:08.330 --> 00:37:09.696 quite polymorphic in nature.

NOTE Confidence: 0.9657866

00:37:09.696 --> 00:37:11.206 There are many other cells,

NOTE Confidence: 0.9657866

00:37:11.210 --> 00:37:12.626 including granulocytes,

NOTE Confidence: 0.9657866

00:37:12.626 --> 00:37:14.042 plasma cells,

NOTE Confidence: 0.9657866

00:37:14.042 --> 00:37:18.290 lymphocytes along with large atypical cells.

NOTE Confidence: 0.9657866

00:37:18.290 --> 00:37:21.146 Sorry and these are CD 20 positive,

NOTE Confidence: 0.9657866

00:37:21.150 --> 00:37:23.886 either positive and there are many

NOTE Confidence: 0.9657866

00:37:23.886 --> 00:37:26.062 histiocytes which are brought out

NOTE Confidence: 0.9657866

00:37:26.062 --> 00:37:28.734 by City 68 are here and then if you

NOTE Confidence: 0.9657866

00:37:28.734 --> 00:37:30.364 look light chain restriction study,

NOTE Confidence: 0.767819538956522

00:37:30.370 --> 00:37:32.526 there's a lot of background but these

NOTE Confidence: 0.767819538956522

00:37:32.526 --> 00:37:34.139 cells clearly show capital light

NOTE Confidence: 0.767819538956522

00:37:34.139 --> 00:37:36.023 chain restriction and they often have

NOTE Confidence: 0.767819538956522

00:37:36.023 --> 00:37:38.138 a non germinal center phenotype.

NOTE Confidence: 0.767819538956522

00:37:38.140 --> 00:37:40.730 Mum 1 positive there were negative for

NOTE Confidence: 0.767819538956522

00:37:40.730 --> 00:37:43.511 city 10 and possibly for BCL 6 and

NOTE Confidence: 0.767819538956522

00:37:43.511 --> 00:37:46.220 they have a high key 67 expression.

NOTE Confidence: 0.767819538956522

00:37:46.220 --> 00:37:47.616 In contrast to this,

NOTE Confidence: 0.767819538956522

00:37:47.616 --> 00:37:49.710 this is another EBV positive lymphoma,

NOTE Confidence: 0.767819538956522

00:37:49.710 --> 00:37:51.535 but in a completely different

NOTE Confidence: 0.767819538956522

00:37:51.535 --> 00:37:52.265 clinical context.

NOTE Confidence: 0.767819538956522

00:37:52.270 --> 00:37:55.700 This is a patient at 7070 year old lady

NOTE Confidence: 0.767819538956522

00:37:55.700 --> 00:37:57.800 who presented with an adrenal mass

NOTE Confidence: 0.767819538956522

00:37:57.870 --> 00:37:59.808 so that hemorrhagic mass and there

NOTE Confidence: 0.767819538956522

00:37:59.808 --> 00:38:02.628 was a a pseudo cyst with brown fluid,

NOTE Confidence: 0.767819538956522

00:38:02.630 --> 00:38:05.584 and when we accept when we examine

NOTE Confidence: 0.767819538956522

00:38:05.584 --> 00:38:07.690 multiple blocks from the pseudo cyst,

NOTE Confidence: 0.767819538956522

00:38:07.690 --> 00:38:09.734 there were some areas where we see

NOTE Confidence: 0.767819538956522

00:38:09.734 --> 00:38:11.859 these kind of large atypical cells

NOTE Confidence: 0.767819538956522

00:38:11.859 --> 00:38:13.834 and these large atypical cells.

NOTE Confidence: 0.767819538956522

00:38:13.840 --> 00:38:16.145 As you can see here, these were all.

NOTE Confidence: 0.767819538956522

00:38:16.145 --> 00:38:18.472 Keep a positive and they are they

NOTE Confidence: 0.767819538956522

00:38:18.472 --> 00:38:20.500 had a non germinal center phenotype.

NOTE Confidence: 0.767819538956522

00:38:20.500 --> 00:38:22.508 They were seen in 20 probably Mum 1

NOTE Confidence: 0.767819538956522

00:38:22.508 --> 00:38:24.217 positive but negative for CD 10 and

NOTE Confidence: 0.767819538956522

00:38:24.220 --> 00:38:27.270 six and a very high K 67 expression.

NOTE Confidence: 0.767819538956522

00:38:27.270 --> 00:38:29.580 It's important not to call these AB

NOTE Confidence: 0.767819538956522

00:38:29.644 --> 00:38:32.116 positive diffuse large B cell lymphoma.

NOTE Confidence: 0.767819538956522

00:38:32.120 --> 00:38:35.704 This is a fibron associated EBV positive

NOTE Confidence: 0.767819538956522

00:38:35.704 --> 00:38:38.518 large B cell lymphoma that these have

NOTE Confidence: 0.767819538956522

00:38:38.518 --> 00:38:41.466 a very different disease cause most

NOTE Confidence: 0.767819538956522

00:38:41.466 --> 00:38:44.238 of these don't require any chemotherapy.

NOTE Confidence: 0.767819538956522

00:38:44.240 --> 00:38:47.480 They do exceedingly well.

NOTE Confidence: 0.767819538956522

00:38:47.480 --> 00:38:49.465 Rarely be negative cases have

NOTE Confidence: 0.767819538956522

00:38:49.465 --> 00:38:51.053 also been described here.

NOTE Confidence: 0.767819538956522

00:38:51.060 --> 00:38:53.625 These two muscles are sit

NOTE Confidence: 0.767819538956522

00:38:53.625 --> 00:38:56.190 within the mesh of fibrin.

NOTE Confidence: 0.767819538956522

00:38:56.190 --> 00:38:58.926 And you can also get these in in

NOTE Confidence: 0.767819538956522

00:38:58.926 --> 00:39:01.438 catheters and whenever you have a

NOTE Confidence: 0.767819538956522

00:39:01.438 --> 00:39:03.536 thrombus within within that thrombus,

NOTE Confidence: 0.767819538956522

00:39:03.536 --> 00:39:06.650 we can get these EBV positive large B cells.

NOTE Confidence: 0.767819538956522

00:39:06.650 --> 00:39:10.026 So it occurs in specific clinical context and

NOTE Confidence: 0.767819538956522

00:39:10.026 --> 00:39:13.828 one has to be careful not to over diagnosis.

NOTE Confidence: 0.767819538956522

00:39:13.830 --> 00:39:15.706 Inflammation is very little as you can,

NOTE Confidence: 0.767819538956522

00:39:15.710 --> 00:39:18.370 as you saw in this particular case

NOTE Confidence: 0.767819538956522

00:39:18.370 --> 00:39:20.342 they have immuno plastic features

NOTE Confidence: 0.767819538956522

00:39:20.342 --> 00:39:23.170 and they have a non GC phenotype.

NOTE Confidence: 0.767819538956522

00:39:23.170 --> 00:39:26.026 The CD ten negative mum 1 positive

NOTE Confidence: 0.767819538956522

00:39:26.030 --> 00:39:28.228 six can be positive in some cases.

NOTE Confidence: 0.767819538956522

00:39:28.230 --> 00:39:31.275 And they can rarely express City 138,

NOTE Confidence: 0.767819538956522

00:39:31.275 --> 00:39:34.250 and they have a very favorable outcome.

NOTE Confidence: 0.767819538956522

00:39:34.250 --> 00:39:36.180 And accession alone is sufficient

NOTE Confidence: 0.767819538956522

00:39:36.180 --> 00:39:38.110 in most of these cases.

NOTE Confidence: 0.767819538956522

00:39:38.110 --> 00:39:39.590 In contrast to this season,

NOTE Confidence: 0.767819538956522

00:39:39.590 --> 00:39:41.415 here is a very aggressive

NOTE Confidence: 0.767819538956522

00:39:41.415 --> 00:39:42.510 EBV positive lymphoma.

NOTE Confidence: 0.767819538956522

00:39:42.510 --> 00:39:43.542 The Plasmablastic lymphoma,

NOTE Confidence: 0.767819538956522

00:39:43.542 --> 00:39:45.950 which is got diffused in a plastic

NOTE Confidence: 0.767819538956522

00:39:46.010 --> 00:39:48.110 which shows diffused in a plastic

NOTE Confidence: 0.767819538956522

00:39:48.110 --> 00:39:49.510 proliferation of tumor cells,

NOTE Confidence: 0.767819538956522

00:39:49.510 --> 00:39:51.520 which I've got plasmacytic features,

NOTE Confidence: 0.767819538956522

00:39:51.520 --> 00:39:53.355 typically occurs in an extranodal

NOTE Confidence: 0.767819538956522

00:39:53.355 --> 00:39:55.608 setting occurring in the oral cavity

NOTE Confidence: 0.767819538956522

00:39:55.608 --> 00:39:57.367 and other mucosal sites rarely

NOTE Confidence: 0.767819538956522

00:39:57.367 --> 00:39:59.866 can also occur in in lymph nodes,

NOTE Confidence: 0.767819538956522

00:39:59.870 --> 00:40:02.798 it classically occurs.

NOTE Confidence: 0.767819538956522

00:40:02.800 --> 00:40:04.215 It typically occurs in the

NOTE Confidence: 0.767819538956522

00:40:04.215 --> 00:40:05.064 HIV positive patient,

NOTE Confidence: 0.767819538956522

00:40:05.070 --> 00:40:08.166 but can also occur outside the HIV study.

NOTE Confidence: 0.767819538956522

00:40:08.170 --> 00:40:10.005 And can also occur in

NOTE Confidence: 0.767819538956522

00:40:10.005 --> 00:40:11.106 post transplant patients.

NOTE Confidence: 0.767819538956522

00:40:11.110 --> 00:40:14.470 It can also occur in in elderly people.

NOTE Confidence: 0.767819538956522

00:40:14.470 --> 00:40:17.627 Some may occur as a transformational event.

NOTE Confidence: 0.767819538956522

00:40:17.630 --> 00:40:19.832 In a previous case of follicular

NOTE Confidence: 0.767819538956522

00:40:19.832 --> 00:40:22.131 lymphoma or CLL and rarely following

NOTE Confidence: 0.767819538956522

00:40:22.131 --> 00:40:24.770 CD 19 CAR T cell therapy again.

NOTE Confidence: 0.767819538956522

00:40:24.770 --> 00:40:27.345 Patients present with advanced stage

NOTE Confidence: 0.767819538956522

00:40:27.345 --> 00:40:30.340 with advanced with a high IPI.

NOTE Confidence: 0.767819538956522

00:40:30.340 --> 00:40:32.590 Nearly 60% of Kesari be associated

NOTE Confidence: 0.767819538956522

00:40:32.590 --> 00:40:34.977 and those which are EBR associate

NOTE Confidence: 0.767819538956522

00:40:34.977 --> 00:40:37.022 typically have latency type one

NOTE Confidence: 0.767819538956522

00:40:37.022 --> 00:40:39.985 or type 280% of the cases of

NOTE Confidence: 0.767819538956522

00:40:39.985 --> 00:40:42.130 associated case or HIV positive.

NOTE Confidence: 0.767819538956522

00:40:42.130 --> 00:40:44.566 And rarely we can get in

NOTE Confidence: 0.767819538956522

00:40:44.566 --> 00:40:45.784 between negative cases.

NOTE Confidence: 0.549947888

00:40:45.790 --> 00:40:47.510 You running HIV studying rarely.

NOTE Confidence: 0.549947888

00:40:47.510 --> 00:40:49.492 It can be even be negative and

NOTE Confidence: 0.549947888

00:40:49.492 --> 00:40:51.202 milk translocation is present in

NOTE Confidence: 0.549947888

00:40:51.202 --> 00:40:53.330 nearly 80% of these patients.

NOTE Confidence: 0.549947888

00:40:53.330 --> 00:40:55.250 In of these cases,

NOTE Confidence: 0.549947888

00:40:55.250 --> 00:40:57.460 they typically suppress the Bissell

NOTE Confidence: 0.549947888

00:40:57.460 --> 00:40:59.228 program that negative facility,

NOTE Confidence: 0.549947888

00:40:59.230 --> 00:41:01.614 20 packs file and city 45 and they

NOTE Confidence: 0.549947888

00:41:01.614 --> 00:41:03.570 expressed a plasma cell program.

NOTE Confidence: 0.549947888

00:41:03.570 --> 00:41:06.520 The positive facility 138 city

NOTE Confidence: 0.549947888

00:41:06.520 --> 00:41:09.966 38 blimp one mom one XBP one

NOTE Confidence: 0.549947888

00:41:09.970 --> 00:41:11.480 and they express light chains.

NOTE Confidence: 0.549947888

00:41:11.480 --> 00:41:13.104 They express imina globulin.

NOTE Confidence: 0.549947888

00:41:13.104 --> 00:41:15.540 They you can demonstrate your globulin.

NOTE Confidence: 0.549947888

00:41:15.540 --> 00:41:18.860 Restriction like chain restriction and

NOTE Confidence: 0.549947888

00:41:18.860 --> 00:41:21.149 they can rarely also express CD 56,

NOTE Confidence: 0.549947888

00:41:21.150 --> 00:41:23.518 so often one would think the CD 56

NOTE Confidence: 0.549947888

00:41:23.518 --> 00:41:25.943 expression would be a good way to

NOTE Confidence: 0.549947888

00:41:25.943 --> 00:41:27.713 distinguish this from plasmablastic myeloma,

NOTE Confidence: 0.549947888

00:41:27.720 --> 00:41:30.078 but they can rarely be positive,

NOTE Confidence: 0.549947888

00:41:30.080 --> 00:41:32.341 or city 56 cyclin D1 expression would

NOTE Confidence: 0.549947888

00:41:32.341 --> 00:41:34.568 be negative in these cases and that

NOTE Confidence: 0.549947888

00:41:34.568 --> 00:41:36.920 could be a useful marker if present.

NOTE Confidence: 0.549947888

00:41:36.920 --> 00:41:39.422 They are more indicative of a

NOTE Confidence: 0.549947888

00:41:39.422 --> 00:41:41.385 plasmablastic myeloma mic is often

NOTE Confidence: 0.549947888

00:41:41.385 --> 00:41:43.260 positive because these carry MC

NOTE Confidence: 0.549947888

00:41:43.260 --> 00:41:45.630 transportation. PDL one is often positive.

NOTE Confidence: 0.549947888

00:41:45.630 --> 00:41:48.678 They show loss of MHC Class 2 expression

NOTE Confidence: 0.549947888

00:41:48.678 --> 00:41:52.426 and K 67 expression is usually very high.

NOTE Confidence: 0.549947888

00:41:52.430 --> 00:41:54.572 This is a classic example of

NOTE Confidence: 0.549947888

00:41:54.572 --> 00:41:55.643 Blossom plasmablastic lymphoma.

NOTE Confidence: 0.549947888

00:41:55.650 --> 00:41:58.709 You can see these are blast immuno

NOTE Confidence: 0.549947888

00:41:58.709 --> 00:42:00.578 blaster plasmablasts and these

NOTE Confidence: 0.549947888

00:42:00.578 --> 00:42:03.696 are typically as I said CD 138

NOTE Confidence: 0.549947888

00:42:03.696 --> 00:42:05.634 positive and it can very easily

NOTE Confidence: 0.549947888

00:42:05.634 --> 00:42:07.280 demonstrate like to instructions.

NOTE Confidence: 0.549947888

00:42:07.280 --> 00:42:08.840 Yet scapolite chin restricted.

NOTE Confidence: 0.783067412

00:42:10.940 --> 00:42:13.460 As against the Plasmablastic lymphoma,

NOTE Confidence: 0.783067412

00:42:13.460 --> 00:42:16.596 you have the. Just create associated.

NOTE Confidence: 0.783067412

00:42:16.596 --> 00:42:19.200 Sorry before I go into situate associated

NOTE Confidence: 0.783067412

00:42:19.262 --> 00:42:21.522 lymphoma is worthwhile to discuss

NOTE Confidence: 0.783067412

00:42:21.522 --> 00:42:23.330 situate associated Castleman disease.

NOTE Confidence: 0.700351148571429

00:42:26.210 --> 00:42:28.450 This occurs usually in HIV positive patients.

NOTE Confidence: 0.700351148571429

00:42:28.450 --> 00:42:31.110 Nearly 80% of them are HIV positive.

NOTE Confidence: 0.700351148571429

00:42:31.110 --> 00:42:34.176 Rarely it can occur in HIV negative

NOTE Confidence: 0.700351148571429

00:42:34.176 --> 00:42:35.933 setting in in specific areas,

NOTE Confidence: 0.700351148571429

00:42:35.933 --> 00:42:37.970 but most of them are HIV positive.

NOTE Confidence: 0.700351148571429

00:42:37.970 --> 00:42:40.850 Typically these patients are in.

NOTE Confidence: 0.700351148571429

00:42:40.850 --> 00:42:43.250 That early 40s in middle aged

NOTE Confidence: 0.700351148571429

00:42:43.250 --> 00:42:45.658 patients and have relatively low

NOTE Confidence: 0.700351148571429

00:42:45.658 --> 00:42:48.168 or undetectable HIV viral loads.

NOTE Confidence: 0.700351148571429

00:42:48.170 --> 00:42:50.228 So CD 4 counts are reasonably OK.

NOTE Confidence: 0.700351148571429

00:42:50.230 --> 00:42:52.967 These patients milk there's a huge male

NOTE Confidence: 0.700351148571429

00:42:52.967 --> 00:42:54.970 predominance and different morphologies.

NOTE Confidence: 0.700351148571429

00:42:54.970 --> 00:42:56.570 Those of Castleman disease

NOTE Confidence: 0.700351148571429

00:42:56.570 --> 00:42:57.770 of plasmacytic type,

NOTE Confidence: 0.700351148571429

00:42:57.770 --> 00:43:01.074 other mixed mixed pattern and they are

NOTE Confidence: 0.700351148571429

00:43:01.074 --> 00:43:03.623 you classically see plasmablasts which

NOTE Confidence: 0.700351148571429

00:43:03.623 --> 00:43:07.270 are medium to large sized lymphoid cells

NOTE Confidence: 0.700351148571429

00:43:07.270 --> 00:43:09.651 with nuclei and amphiphilic cytoplasm,

NOTE Confidence: 0.700351148571429

00:43:09.651 --> 00:43:11.359 and these cells are.

NOTE Confidence: 0.700351148571429

00:43:11.360 --> 00:43:13.436 Being typically in the mantle zones,

NOTE Confidence: 0.700351148571429

00:43:13.440 --> 00:43:15.048 but rarely they can be seen

NOTE Confidence: 0.700351148571429

00:43:15.048 --> 00:43:16.120 in into follicular interest.

NOTE Confidence: 0.700351148571429

00:43:16.120 --> 00:43:18.328 They can be intrafollicular,

NOTE Confidence: 0.700351148571429

00:43:18.328 --> 00:43:20.300 perifollicular, and these lymph nodes.

NOTE Confidence: 0.700351148571429

00:43:20.300 --> 00:43:22.075 One it's important to recognize

NOTE Confidence: 0.700351148571429

00:43:22.075 --> 00:43:23.960 that many of these lymph nodes

NOTE Confidence: 0.700351148571429

00:43:23.960 --> 00:43:25.980 can have foci of Kaposi sarcoma.

NOTE Confidence: 0.700351148571429

00:43:25.980 --> 00:43:29.502 When these patients are treated with anti CD,

NOTE Confidence: 0.700351148571429

00:43:29.502 --> 00:43:32.344 20 Kaposi sarcoma tends to explode so

NOTE Confidence: 0.700351148571429

00:43:32.344 --> 00:43:35.227 it's important to recognize that if

NOTE Confidence: 0.700351148571429

00:43:35.227 --> 00:43:38.340 the patients also have Kaposi sarcoma.

NOTE Confidence: 0.700351148571429

00:43:38.340 --> 00:43:42.020 Alchemize also concomitantly treated.

NOTE Confidence: 0.700351148571429

00:43:42.020 --> 00:43:42.911 This the the,

NOTE Confidence: 0.700351148571429

00:43:42.911 --> 00:43:44.693 the number and the density of

NOTE Confidence: 0.700351148571429

00:43:44.693 --> 00:43:46.659 copper brass can be very variable.

NOTE Confidence: 0.700351148571429

00:43:46.660 --> 00:43:49.549 It can be few or it can form large

NOTE Confidence: 0.700351148571429

00:43:49.549 --> 00:43:51.590 sheets like what people used to

NOTE Confidence: 0.700351148571429

00:43:51.590 --> 00:43:53.450 describe as micro infamous in the

NOTE Confidence: 0.700351148571429

00:43:53.450 --> 00:43:55.176 past and these plasmablasts our

NOTE Confidence: 0.700351148571429

00:43:55.176 --> 00:43:57.300 mum one and blimp and positive.

NOTE Confidence: 0.700351148571429

00:43:57.300 --> 00:43:59.680 But they often are negative for CD,

NOTE Confidence: 0.700351148571429

00:43:59.680 --> 00:44:02.668 20 have very low expression of CD 20 and

NOTE Confidence: 0.700351148571429

00:44:02.668 --> 00:44:05.660 they typically laxity 1:30 at expression.

NOTE Confidence: 0.700351148571429

00:44:05.660 --> 00:44:07.868 The express IG M and they are Lambda

NOTE Confidence: 0.700351148571429

00:44:07.868 --> 00:44:09.732 light chain restricted though there

NOTE Confidence: 0.700351148571429

00:44:09.732 --> 00:44:11.817 are Lambda light chain restricted.

NOTE Confidence: 0.700351148571429

00:44:11.820 --> 00:44:12.788 They are not born.

NOTE Confidence: 0.700351148571429

00:44:12.788 --> 00:44:13.894 Well, there polyclonal,

NOTE Confidence: 0.700351148571429

00:44:13.894 --> 00:44:15.190 so they're monotypic,

NOTE Confidence: 0.700351148571429

00:44:15.190 --> 00:44:17.178 but polyclonal and patients

NOTE Confidence: 0.700351148571429

00:44:17.178 --> 00:44:19.663 usually have a detectable plasma,

NOTE Confidence: 0.700351148571429

00:44:19.670 --> 00:44:21.728 which case which we are judged

NOTE Confidence: 0.700351148571429

00:44:21.728 --> 00:44:23.891 by DNA and that's a useful

NOTE Confidence: 0.700351148571429

00:44:23.891 --> 00:44:25.482 marker outside of the Histology.

NOTE Confidence: 0.700351148571429

00:44:25.482 --> 00:44:27.747 Here is a typical case where you

NOTE Confidence: 0.700351148571429

00:44:27.747 --> 00:44:29.507 can see castlemans like features.

NOTE Confidence: 0.700351148571429

00:44:29.510 --> 00:44:31.615 You got follicles which somewhat

NOTE Confidence: 0.700351148571429

00:44:31.615 --> 00:44:33.795 resemble the they had in vascular

NOTE Confidence: 0.700351148571429

00:44:33.795 --> 00:44:35.199 type of Castleman disease.

NOTE Confidence: 0.700351148571429

00:44:35.200 --> 00:44:37.290 But more importantly you have

NOTE Confidence: 0.700351148571429

00:44:37.290 --> 00:44:38.920 plasma cells in the inter,

NOTE Confidence: 0.700351148571429

00:44:38.920 --> 00:44:40.788 follicular and medullary areas.

NOTE Confidence: 0.700351148571429

00:44:40.788 --> 00:44:42.650 These plasma cells are.

NOTE Confidence: 0.700351148571429

00:44:42.650 --> 00:44:44.030 Are not plasmablasts,

NOTE Confidence: 0.700351148571429

00:44:44.030 --> 00:44:45.870 they're reactive plasma cells,

NOTE Confidence: 0.700351148571429

00:44:45.870 --> 00:44:47.405 which are both Kappa and

NOTE Confidence: 0.700351148571429

00:44:47.405 --> 00:44:48.633 Lambda light chain positive,

NOTE Confidence: 0.700351148571429

00:44:48.640 --> 00:44:50.460 but the typical plasmablasts are

NOTE Confidence: 0.700351148571429

00:44:50.460 --> 00:44:52.680 seen here in the mantle zone.

NOTE Confidence: 0.700351148571429

00:44:52.680 --> 00:44:54.220 As you can see here,

NOTE Confidence: 0.700351148571429

00:44:54.220 --> 00:44:55.620 and these are huge,

NOTE Confidence: 0.700351148571429

00:44:55.620 --> 00:44:58.345 8 positive and CD 21 will highlight

NOTE Confidence: 0.700351148571429

00:44:58.345 --> 00:45:01.400 this FTC meshworks and here with you

NOTE Confidence: 0.700351148571429

00:45:01.400 --> 00:45:03.530 can identify plasmablasts in the mantle

NOTE Confidence: 0.700351148571429

00:45:03.602 --> 00:45:06.042 cell and these are IG M positive and

NOTE Confidence: 0.700351148571429

00:45:06.042 --> 00:45:08.158 their Lambda light chain restricted,

NOTE Confidence: 0.700351148571429

00:45:08.160 --> 00:45:09.860 whereas the plasma cells in

NOTE Confidence: 0.700351148571429

00:45:09.860 --> 00:45:10.880 the interfollicular area.

NOTE Confidence: 0.700351148571429

00:45:10.880 --> 00:45:14.786 Those are normal reactive plasma cells.

NOTE Confidence: 0.700351148571429

00:45:14.790 --> 00:45:17.544 Siri 20 this patients respond extremely

NOTE Confidence: 0.700351148571429

00:45:17.544 --> 00:45:20.530 well for anti CD 20 treatment.

NOTE Confidence: 0.700351148571429

00:45:20.530 --> 00:45:22.501 So one of the questions is always been if

NOTE Confidence: 0.700351148571429

00:45:22.501 --> 00:45:24.346 these plasma Blaster CD twenty negative.

NOTE Confidence: 0.700351148571429

00:45:24.350 --> 00:45:25.254 How do they respond?

NOTE Confidence: 0.700351148571429

00:45:25.254 --> 00:45:27.246 So we went on to do some double

NOTE Confidence: 0.700351148571429

00:45:27.246 --> 00:45:29.262 stains and here you can show that

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NOTE Confidence: 0.700351148571429

00:45:29.262 --> 00:45:31.342 while most of the plasma blasts are

NOTE Confidence: 0.700351148571429

00:45:31.342 --> 00:45:33.342 negative like here is positive plasma

NOTE Confidence: 0.700351148571429

00:45:33.342 --> 00:45:35.868 blast which is negative for CD20.

NOTE Confidence: 0.700351148571429

00:45:35.870 --> 00:45:37.835 A good proportion of them

NOTE Confidence: 0.700351148571429

00:45:37.835 --> 00:45:39.800 show expression of CD 20

NOTE Confidence: 0.804032571111111

00:45:39.879 --> 00:45:42.623 and some of them can be quite weak.

NOTE Confidence: 0.804032571111111

00:45:42.630 --> 00:45:46.094 Then we also went on to look at.

NOTE Confidence: 0.804032571111111

00:45:46.100 --> 00:45:47.408 In these lymph nodes,

NOTE Confidence: 0.804032571111111

00:45:47.408 --> 00:45:49.370 many of these lymph nodes show

NOTE Confidence: 0.804032571111111

00:45:49.433 --> 00:45:51.758 follicular dendritic cell mesh works.

NOTE Confidence: 0.804032571111111

00:45:51.760 --> 00:45:54.372 Here is Brown is in the HV

NOTE Confidence: 0.804032571111111

00:45:54.372 --> 00:45:57.634 Atlanta one and red is CD 20,

NOTE Confidence: 0.804032571111111

00:45:57.640 --> 00:46:00.504 city 21 and you can see many of

NOTE Confidence: 0.804032571111111

00:46:00.504 --> 00:46:02.317 the follicular dendritic cell

NOTE Confidence: 0.804032571111111

00:46:02.317 --> 00:46:05.353 processes also show the Lana protein.

NOTE Confidence: 0.804032571111111

00:46:05.360 --> 00:46:07.628 So obviously the nuclei of these

NOTE Confidence: 0.804032571111111

00:46:07.630 --> 00:46:09.500 are negative for Lana one,

NOTE Confidence: 0.804032571111111

00:46:09.500 --> 00:46:11.230 it's only the cytoplasmic processes

NOTE Confidence: 0.804032571111111

00:46:11.230 --> 00:46:13.760 that are showing Lana one positive ITI.

NOTE Confidence: 0.804032571111111

00:46:13.760 --> 00:46:16.049 So there by suggesting that you have.

NOTE Confidence: 0.804032571111111

00:46:16.050 --> 00:46:18.388 In a subset of metric Castleman disease,

NOTE Confidence: 0.804032571111111

00:46:18.390 --> 00:46:20.230 that is presentation of Lana,

NOTE Confidence: 0.804032571111111

00:46:20.230 --> 00:46:21.510 one on the FTC's.

NOTE Confidence: 0.804032571111111

00:46:21.510 --> 00:46:24.169 So then we went on to look at,

NOTE Confidence: 0.804032571111111

00:46:24.170 --> 00:46:25.427 make some associations.

NOTE Confidence: 0.804032571111111

00:46:25.427 --> 00:46:28.360 We showed that those cases will have

NOTE Confidence: 0.804032571111111

00:46:28.360 --> 00:46:32.107 a lower load of huge positive plasma

NOTE Confidence: 0.804032571111111

00:46:32.107 --> 00:46:35.726 blasts are more likely to have HSV

NOTE Confidence: 0.804032571111111

00:46:35.726 --> 00:46:38.549 positivity in the FDC processes,

NOTE Confidence: 0.804032571111111

00:46:38.550 --> 00:46:40.870 and these cases also had fewer CD 3

NOTE Confidence: 0.804032571111111

00:46:40.870 --> 00:46:43.350 positive T cells within these follicles.

NOTE Confidence: 0.804032571111111

00:46:43.350 --> 00:46:45.570 So there was an inverse correlation

NOTE Confidence: 0.804032571111111

00:46:45.570 --> 00:46:47.050 between the number eventuate.

NOTE Confidence: 0.804032571111111

00:46:47.050 --> 00:46:49.054 All the new cells.

NOTE Confidence: 0.804032571111111

00:46:49.054 --> 00:46:51.838 And presence of antigen on the

NOTE Confidence: 0.804032571111111

00:46:51.838 --> 00:46:53.968 left and this this positively

NOTE Confidence: 0.804032571111111

00:46:53.968 --> 00:46:56.345 correlated with the number of T

NOTE Confidence: 0.804032571111111

00:46:56.345 --> 00:46:58.160 cells within the folly truths.

NOTE Confidence: 0.804032571111111

00:46:58.160 --> 00:46:59.024 As I said,

NOTE Confidence: 0.804032571111111

00:46:59.024 --> 00:47:00.752 there can be microscopic Kaposi sarcoma.

NOTE Confidence: 0.804032571111111

00:47:00.760 --> 00:47:03.064 Here is the lymph node capsule of a

NOTE Confidence: 0.804032571111111

00:47:03.064 --> 00:47:05.402 patient with multicentric Castleman disease

NOTE Confidence: 0.804032571111111

00:47:05.402 --> 00:47:07.666 showing microscopic Kaposi sarcoma.

NOTE Confidence: 0.728047215294118

00:47:10.570 --> 00:47:12.852 A good a good proportion of patients

NOTE Confidence: 0.728047215294118

00:47:12.852 --> 00:47:14.672 of multicentric Castleman disease also

NOTE Confidence: 0.728047215294118

00:47:14.672 --> 00:47:16.627 present with primary effusion lymphoma,

NOTE Confidence: 0.728047215294118

00:47:16.630 --> 00:47:19.450 and typically these are serious effusions,

NOTE Confidence: 0.728047215294118

00:47:19.450 --> 00:47:21.350 but some cases and more,

NOTE Confidence: 0.728047215294118

00:47:21.350 --> 00:47:23.897 and many of them will not have any solid

NOTE Confidence: 0.728047215294118

00:47:23.897 --> 00:47:26.234 tumor analysis but a subset of them

NOTE Confidence: 0.728047215294118

00:47:26.234 --> 00:47:28.282 present with solid tumor masses and

NOTE Confidence: 0.728047215294118

00:47:28.282 --> 00:47:30.578 and these may not have any effusions,

NOTE Confidence: 0.728047215294118

00:47:30.580 --> 00:47:32.428 and these are called extra cavitary,

NOTE Confidence: 0.728047215294118

00:47:32.430 --> 00:47:33.672 primary fusion infamous,

NOTE Confidence: 0.728047215294118

00:47:33.672 --> 00:47:35.742 and these patients usually have

NOTE Confidence: 0.728047215294118

00:47:35.742 --> 00:47:38.308 a low CD 4 count in contrast to

NOTE Confidence: 0.728047215294118

00:47:38.310 --> 00:47:39.603 multicentric Castleman disease.

NOTE Confidence: 0.728047215294118

00:47:39.603 --> 00:47:43.159 And though most of these are seen in HIV,

NOTE Confidence: 0.728047215294118

00:47:43.160 --> 00:47:44.850 positive patients rarely just can

NOTE Confidence: 0.728047215294118

00:47:44.850 --> 00:47:47.059 be seen in other immune suppression

NOTE Confidence: 0.728047215294118

00:47:47.059 --> 00:47:49.765 settings like the post transplant setting

NOTE Confidence: 0.728047215294118

00:47:49.765 --> 00:47:51.780 operations with immune sentences,

00:47:51.780 --> 00:47:54.356 and again typical ages 40 to 50.

00:47:54.360 --> 00:47:56.474 Rarely you can see this outside of

00:47:56.474 --> 00:47:58.673 the HIV setting in the in endemic

00:47:58.673 --> 00:48:00.521 areas like the Sub Saharan Africa

00:48:00.583 --> 00:48:01.669 and Mediterranean,

00:48:01.670 --> 00:48:03.596 and they're accompanied by at the

00:48:03.596 --> 00:48:06.372 same time by Kaposi sarcoma and the

00:48:06.372 --> 00:48:07.797 Multicentric Castleman disease.

00:48:07.800 --> 00:48:09.546 In nearly one half of cases.

00:48:11.650 --> 00:48:14.303 Here the self the important thing about

00:48:14.303 --> 00:48:16.978 this entity is they are dually infected

00:48:16.978 --> 00:48:20.020 both with HHV 8 and Epstein Barr virus,

00:48:20.020 --> 00:48:22.344 but largely the malignant

00:48:22.344 --> 00:48:24.668 process is driven by.

00:48:24.670 --> 00:48:27.532 So by Minister chemistry you can

00:48:27.532 --> 00:48:29.774 demonstrate edges and by in situ

NOTE Confidence: 0.656019058636364

00:48:29.774 --> 00:48:31.379 hybridization you can identify Eva.

NOTE Confidence: 0.656019058636364

00:48:31.380 --> 00:48:34.004 You usually the EBV latency is type one,

NOTE Confidence: 0.656019058636364

00:48:34.010 --> 00:48:35.538 so you'll be LMP.

NOTE Confidence: 0.656019058636364

00:48:35.538 --> 00:48:38.390 One is usually absent in these cells.

NOTE Confidence: 0.656019058636364

00:48:38.390 --> 00:48:40.574 This again a large amount of plastic

NOTE Confidence: 0.656019058636364

00:48:40.574 --> 00:48:42.599 cells are plastic plastic cells and

NOTE Confidence: 0.656019058636364

00:48:42.599 --> 00:48:44.645 they show prominent and aplasia cells

NOTE Confidence: 0.656019058636364

00:48:44.645 --> 00:48:46.788 can resemble Reed Sternberg cells.

NOTE Confidence: 0.656019058636364

00:48:46.790 --> 00:48:47.478 And again,

NOTE Confidence: 0.656019058636364

00:48:47.478 --> 00:48:49.198 like in the plasmablastic lymphoma,

NOTE Confidence: 0.656019058636364

00:48:49.200 --> 00:48:51.156 there is suppression of the bezel

NOTE Confidence: 0.656019058636364

00:48:51.156 --> 00:48:53.435 program and what you see is often

NOTE Confidence: 0.656019058636364

00:48:53.435 --> 00:48:54.945 a plasma cell program with.

NOTE Confidence: 0.656019058636364

00:48:54.950 --> 00:48:57.659 It's only 138 mum one and blimp,

NOTE Confidence: 0.656019058636364

00:48:57.660 --> 00:49:00.480 but unlike the plasmablastic lymphomas,

NOTE Confidence: 0.656019058636364

00:49:00.480 --> 00:49:03.252 these do not express immunoglobulin so

NOTE Confidence: 0.656019058636364

00:49:03.252 --> 00:49:06.289 the immuno globulin negative and some of

NOTE Confidence: 0.656019058636364

00:49:06.289 --> 00:49:08.893 them can express aberrant T cell antigens.

NOTE Confidence: 0.656019058636364

00:49:08.900 --> 00:49:11.098 Nearly a third of them do that.

NOTE Confidence: 0.656019058636364

00:49:11.100 --> 00:49:13.356 And here is a typical case of an

NOTE Confidence: 0.656019058636364

00:49:13.356 --> 00:49:15.000 extra cavitary primary effusion.

NOTE Confidence: 0.656019058636364

00:49:15.000 --> 00:49:16.986 Lymphoma showing on a plastic or

NOTE Confidence: 0.656019058636364

00:49:16.986 --> 00:49:18.985 even a plastic type cells which

NOTE Confidence: 0.656019058636364

00:49:18.985 --> 00:49:21.120 are positive for in this case it

NOTE Confidence: 0.656019058636364

00:49:21.120 --> 00:49:23.211 was CD 45 positive but most often

NOTE Confidence: 0.656019058636364

00:49:23.211 --> 00:49:24.787 city 45 is also negative.

NOTE Confidence: 0.656019058636364

00:49:24.787 --> 00:49:28.490 CD 38 and mum one were positive and you

NOTE Confidence: 0.656019058636364

00:49:28.490 --> 00:49:30.620 can see there is minimal expression

NOTE Confidence: 0.656019058636364

00:49:30.620 --> 00:49:33.297 of 79 and a proportion of cells.

NOTE Confidence: 0.656019058636364

00:49:33.300 --> 00:49:34.992 Express CD 30.

NOTE Confidence: 0.656019058636364

00:49:34.992 --> 00:49:36.120 Most importantly,

NOTE Confidence: 0.656019058636364

00:49:36.120 --> 00:49:38.885 these cells are dually infected with EBV,

NOTE Confidence: 0.656019058636364

00:49:38.890 --> 00:49:40.975 demonstrated by Eva and Batch

NOTE Confidence: 0.656019058636364

00:49:40.975 --> 00:49:42.643 were demonstrated by LENOVA.

NOTE Confidence: 0.690439316666667

00:49:44.920 --> 00:49:47.800 And more, many of them

NOTE Confidence: 0.690439316666667

00:49:47.800 --> 00:49:50.104 also overexpressed PDL 1.

NOTE Confidence: 0.690439316666667

00:49:50.110 --> 00:49:52.936 So we do not know whether all of these

NOTE Confidence: 0.690439316666667

00:49:52.936 --> 00:49:55.886 carry structural abnormalities in PDL one,

NOTE Confidence: 0.690439316666667

00:49:55.890 --> 00:50:00.658 but most of them have overexpression of PDL.

NOTE Confidence: 0.690439316666667

00:50:00.660 --> 00:50:01.820 There is also another entity

NOTE Confidence: 0.690439316666667

00:50:01.820 --> 00:50:02.748 known as the case.

NOTE Confidence: 0.690439316666667

00:50:02.750 --> 00:50:04.310 Such great positive diffuse

NOTE Confidence: 0.690439316666667

00:50:04.310 --> 00:50:05.870 large B cell lymphoma.

NOTE Confidence: 0.690439316666667

00:50:05.870 --> 00:50:07.935 Most of these men can

NOTE Confidence: 0.690439316666667

00:50:07.935 --> 00:50:09.587 develop in patients who.

NOTE Confidence: 0.690439316666667

00:50:09.590 --> 00:50:12.326 Have been of who had medical

NOTE Confidence: 0.690439316666667

00:50:12.326 --> 00:50:13.694 centric Castleman disease.

NOTE Confidence: 0.690439316666667

00:50:13.700 --> 00:50:15.005 These patients are

NOTE Confidence: 0.690439316666667

00:50:15.005 --> 00:50:16.310 profound immune deficiency.

NOTE Confidence: 0.690439316666667

00:50:16.310 --> 00:50:18.466 The most of them are HIV positive.

NOTE Confidence: 0.690439316666667

00:50:18.470 --> 00:50:21.412 Rarely it occurs in other other immune

NOTE Confidence: 0.690439316666667

00:50:21.412 --> 00:50:23.167 compromised settings are very rarely.

NOTE Confidence: 0.690439316666667

00:50:23.170 --> 00:50:24.334 It can occur.

NOTE Confidence: 0.690439316666667

00:50:24.334 --> 00:50:26.208 Non immune compromised setting and

NOTE Confidence: 0.690439316666667

00:50:26.208 --> 00:50:28.116 this is singley infected with HPV.

NOTE Confidence: 0.690439316666667

00:50:28.120 --> 00:50:30.352 There is no infection in these

NOTE Confidence: 0.690439316666667

00:50:30.352 --> 00:50:31.468 patients and characteristically

NOTE Confidence: 0.690439316666667

00:50:31.468 --> 00:50:33.110 involves lymph nodes and spleen.

NOTE Confidence: 0.690439316666667

00:50:33.110 --> 00:50:35.834 Same areas where Multicentric

NOTE Confidence: 0.690439316666667

00:50:35.834 --> 00:50:37.877 Castleman disease presents.

NOTE Confidence: 0.690439316666667

00:50:37.880 --> 00:50:40.704 They are variably positive of 45 and 20.

NOTE Confidence: 0.690439316666667

00:50:40.710 --> 00:50:42.870 Unlike the Multicentric Castleman disease,

NOTE Confidence: 0.690439316666667

00:50:42.870 --> 00:50:45.138 they express AGM and Lambda light chains.

NOTE Confidence: 0.868253375714286

00:50:47.670 --> 00:50:49.987 So this is quite a rare disease.

NOTE Confidence: 0.868253375714286

00:50:49.990 --> 00:50:51.916 You can and look if we

NOTE Confidence: 0.868253375714286

00:50:51.916 --> 00:50:54.330 move on to the next entity,

NOTE Confidence: 0.868253375714286

00:50:54.330 --> 00:50:56.890 which is extremely exceedingly uncommon,

NOTE Confidence: 0.868253375714286

00:50:56.890 --> 00:50:59.235 but it's important to know about this

NOTE Confidence: 0.868253375714286

00:50:59.240 --> 00:51:03.286 because this is a perfectly benign disease.

NOTE Confidence: 0.868253375714286

00:51:03.290 --> 00:51:07.518 Here we got cake and EBV positive.

NOTE Confidence: 0.868253375714286

00:51:07.518 --> 00:51:11.408 This can be again Dooley infected by EBV

NOTE Confidence: 0.868253375714286

00:51:11.408 --> 00:51:14.898 and what's known as the Associated German

NOTE Confidence: 0.868253375714286

00:51:14.898 --> 00:51:17.010 or Tropic lymphoproliferative disorder.

NOTE Confidence: 0.868253375714286

00:51:17.010 --> 00:51:19.446 Most of these patients are HIV negative.

NOTE Confidence: 0.868253375714286

00:51:19.450 --> 00:51:20.746 They present with neck,

NOTE Confidence: 0.868253375714286

00:51:20.746 --> 00:51:22.690 lymph adenopathy and they are asymptomatic.

NOTE Confidence: 0.868253375714286

00:51:22.690 --> 00:51:25.534 Here the germinal centers are partially

NOTE Confidence: 0.868253375714286

00:51:25.534 --> 00:51:28.151 or completely replaced by large blasts

NOTE Confidence: 0.868253375714286

00:51:28.151 --> 00:51:30.828 which are as I said ebb and positive.

NOTE Confidence: 0.868253375714286

00:51:30.828 --> 00:51:32.868 They are mum 1 positive.

NOTE Confidence: 0.868253375714286

00:51:32.870 --> 00:51:34.900 They've got many features which

NOTE Confidence: 0.868253375714286

00:51:34.900 --> 00:51:38.652 could be similar to the similar to

NOTE Confidence: 0.868253375714286

00:51:38.652 --> 00:51:41.483 the primary effusion lymphoma but

NOTE Confidence: 0.868253375714286

00:51:41.483 --> 00:51:44.525 these cells are right within the.

NOTE Confidence: 0.868253375714286

00:51:44.530 --> 00:51:46.567 In the germinal centers and the important

NOTE Confidence: 0.868253375714286

00:51:46.567 --> 00:51:48.309 difference from the primary effusion,

NOTE Confidence: 0.868253375714286

00:51:48.310 --> 00:51:50.560 enforma is that they express

NOTE Confidence: 0.868253375714286

00:51:50.560 --> 00:51:51.910 monotypic immunoglobulin expression

NOTE Confidence: 0.868253375714286

00:51:51.910 --> 00:51:54.478 is seen in nearly 2/3 of cases,

NOTE Confidence: 0.868253375714286

00:51:54.478 --> 00:51:56.554 whereas in primary effusion lymphoma you

NOTE Confidence: 0.868253375714286

00:51:56.554 --> 00:51:58.810 can't demonstrate him in a globe date,

NOTE Confidence: 0.868253375714286

00:51:58.810 --> 00:52:01.770 and if you do PCR study for immuno

NOTE Confidence: 0.868253375714286

00:52:01.770 --> 00:52:03.670 globulin gene rearrangement,

NOTE Confidence: 0.868253375714286

00:52:03.670 --> 00:52:05.378 they're calling clonal and

NOTE Confidence: 0.868253375714286

00:52:05.378 --> 00:52:07.086 expressing itself is sufficient,

NOTE Confidence: 0.868253375714286

00:52:07.090 --> 00:52:11.199 and prognosis is excellent in these patients.

NOTE Confidence: 0.868253375714286

00:52:11.200 --> 00:52:12.240 There's another entity which

NOTE Confidence: 0.868253375714286

00:52:12.240 --> 00:52:13.800 people need to be aware of.

NOTE Confidence: 0.868253375714286

00:52:13.800 --> 00:52:15.876 Many of the patients are nearly

NOTE Confidence: 0.868253375714286

00:52:15.880 --> 00:52:17.788 one in 10 patients of MULTICENTRIC.

NOTE Confidence: 0.868253375714286

00:52:17.790 --> 00:52:20.102 Castleman disease can develop

NOTE Confidence: 0.868253375714286

00:52:20.102 --> 00:52:21.836 hemophagocytic invoice cytosis,

NOTE Confidence: 0.868253375714286

00:52:21.840 --> 00:52:23.196 and if you get a spleen,

NOTE Confidence: 0.868253375714286

00:52:23.200 --> 00:52:25.279 or if you get one metal in these patients,

NOTE Confidence: 0.868253375714286

00:52:25.280 --> 00:52:26.102 you can explain.

NOTE Confidence: 0.868253375714286

00:52:26.102 --> 00:52:28.981 You can see this in the red bulk you

NOTE Confidence: 0.868253375714286

00:52:28.981 --> 00:52:30.769 have active phagocytosis occurring

NOTE Confidence: 0.868253375714286

00:52:30.770 --> 00:52:33.149 and you also see this positive

NOTE Confidence: 0.868253375714286

00:52:33.149 --> 00:52:35.294 plasma blast in the surrounding

NOTE Confidence: 0.868253375714286

00:52:35.294 --> 00:52:37.817 areas and the same thing happens

NOTE Confidence: 0.868253375714286

00:52:37.817 --> 00:52:40.729 also in the bone marrow you can see.

NOTE Confidence: 0.868253375714286

00:52:40.730 --> 00:52:43.220 Active phagocytosis along with presence

NOTE Confidence: 0.868253375714286

00:52:43.220 --> 00:52:45.710 of these kind eventuate positive

NOTE Confidence: 0.868253375714286

00:52:45.780 --> 00:52:48.182 plasmablasts and this these patients

NOTE Confidence: 0.868253375714286

00:52:48.182 --> 00:52:51.689 can have if they are not treated well.

NOTE Confidence: 0.868253375714286

00:52:51.690 --> 00:52:53.760 They can have pork survival.

NOTE Confidence: 0.868253375714286

00:52:53.760 --> 00:52:56.072 I just want to touch for the next

NOTE Confidence: 0.868253375714286

00:52:56.072 --> 00:52:58.240 few couple of minutes on HTLV one,

NOTE Confidence: 0.868253375714286

00:52:58.240 --> 00:53:00.280 which is quite a rare entity,

NOTE Confidence: 0.868253375714286

00:53:00.280 --> 00:53:02.220 but people have to recognize

NOTE Confidence: 0.868253375714286

00:53:02.220 --> 00:53:04.053 that this is underdiagnosed in.

NOTE Confidence: 0.868253375714286

00:53:04.053 --> 00:53:06.237 In 2018 there was a a study came

NOTE Confidence: 0.868253375714286

00:53:06.237 --> 00:53:08.463 out from the National Cancer

NOTE Confidence: 0.868253375714286

91

00:53:08.463 --> 00:53:10.818 Database which showed that mycosis

00:53:10.818 --> 00:53:12.858 fungoides occurring in patients.

00:53:12.860 --> 00:53:13.654 I'm sorry,

00:53:13.654 --> 00:53:15.242 330 positive proteinous infamous

00:53:15.242 --> 00:53:17.200 occurring in African American

00:53:17.200 --> 00:53:19.520 patients have portal survival.

00:53:19.520 --> 00:53:20.484 This could be true,

00:53:20.484 --> 00:53:22.284 but in all none of these patients

00:53:22.284 --> 00:53:24.066 they still be one was tested.

00:53:24.070 --> 00:53:25.570 Around the same time you had,

00:53:25.570 --> 00:53:27.424 there was another study which came

00:53:27.424 --> 00:53:29.795 out from the Miami group which showed

00:53:29.795 --> 00:53:31.575 that ATL is indistinguishable from

00:53:31.575 --> 00:53:33.989 many of the common teasel informers.

00:53:33.990 --> 00:53:36.614 So any T cell lymphoma one has to

00:53:36.614 --> 00:53:39.387 keep in mind that the likelihood of

NOTE Confidence: 0.868253375714286

00:53:39.387 --> 00:53:42.021 HTLV one and exclude the possibility

NOTE Confidence: 0.868253375714286

00:53:42.021 --> 00:53:44.008 of HTLV 1 by serology.

NOTE Confidence: 0.868253375714286

00:53:44.010 --> 00:53:46.570 Otherwise one could easily miss,

NOTE Confidence: 0.868253375714286

00:53:46.570 --> 00:53:49.600 diagnose and aitl as some other

NOTE Confidence: 0.868253375714286

00:53:49.600 --> 00:53:51.115 T cell lymphoma.

NOTE Confidence: 0.868253375714286

00:53:51.120 --> 00:53:53.520 ATL is divided into four groups.

NOTE Confidence: 0.868253375714286

00:53:53.520 --> 00:53:54.816 When he was a cute group

NOTE Confidence: 0.868253375714286

00:53:54.816 --> 00:53:55.680 and their infamous group,

NOTE Confidence: 0.868253375714286

00:53:55.680 --> 00:53:57.552 then you have the chronic group

NOTE Confidence: 0.868253375714286

00:53:57.552 --> 00:53:59.310 and the smoldering type of aitl,

NOTE Confidence: 0.868253375714286

00:53:59.310 --> 00:54:00.246 the genomic.

NOTE Confidence: 0.868253375714286

00:54:00.246 --> 00:54:02.118 They're all genomic differences

NOTE Confidence: 0.868253375714286

00:54:02.118 --> 00:54:03.990 between these four groups

NOTE Confidence: 0.813424632666667

00:54:04.062 --> 00:54:06.630 and the genomic differences also have

NOTE Confidence: 0.813424632666667

00:54:06.630 --> 00:54:09.333 an implication on outcomes like the IRF

NOTE Confidence: 0.813424632666667

00:54:09.333 --> 00:54:11.723 4 mutations has a very patient of ATL,

NOTE Confidence: 0.813424632666667

00:54:11.723 --> 00:54:13.121 which I had a four mutations

NOTE Confidence: 0.813424632666667

00:54:13.121 --> 00:54:14.600 have a very poor survival.

NOTE Confidence: 0.813424632666667

00:54:14.600 --> 00:54:16.880 Those will start 3 mutations are

NOTE Confidence: 0.813424632666667

00:54:16.880 --> 00:54:19.489 typically seen in the indolent type of

NOTE Confidence: 0.813424632666667

00:54:19.489 --> 00:54:22.490 ATL and they have a much better survive.

NOTE Confidence: 0.813424632666667

00:54:22.490 --> 00:54:24.206 So again, now people have come

NOTE Confidence: 0.813424632666667

00:54:24.206 --> 00:54:25.789 up with genomic skills in ATL.

NOTE Confidence: 0.813424632666667

00:54:25.790 --> 00:54:28.645 Much of this work has come from Japan

NOTE Confidence: 0.813424632666667

00:54:28.645 --> 00:54:32.035 and the genomic subsets also correlate

NOTE Confidence: 0.813424632666667

00:54:32.035 --> 00:54:35.870 with the clinical subsets and and and

NOTE Confidence: 0.813424632666667

00:54:35.870 --> 00:54:38.990 there are clear indicators of survival.

NOTE Confidence: 0.813424632666667

00:54:38.990 --> 00:54:40.817 I'll just, I think this is the

NOTE Confidence: 0.813424632666667

00:54:40.817 --> 00:54:42.672 last case I'm going to show and

NOTE Confidence: 0.813424632666667

00:54:42.672 --> 00:54:44.216 I will end with this here.

NOTE Confidence: 0.813424632666667

00:54:44.216 --> 00:54:45.932 The HIV positive patient who was

NOTE Confidence: 0.813424632666667

00:54:45.932 --> 00:54:48.010 referred for an allogeneic transplant.

NOTE Confidence: 0.813424632666667

00:54:48.010 --> 00:54:50.264 This was in London and patient had

NOTE Confidence: 0.813424632666667

00:54:50.264 --> 00:54:52.170 already received two courses of ice,

NOTE Confidence: 0.813424632666667

00:54:52.170 --> 00:54:53.322 and when bullmer investigations

NOTE Confidence: 0.813424632666667

00:54:53.322 --> 00:54:54.186 were being done,

NOTE Confidence: 0.813424632666667

00:54:54.190 --> 00:54:56.829 we saw these kind of abnormal cells

NOTE Confidence: 0.813424632666667

00:54:56.830 --> 00:54:59.168 and these cells were CD 3 positive.

NOTE Confidence: 0.813424632666667

00:54:59.170 --> 00:55:01.144 There were CD 4 positive in 25

NOTE Confidence: 0.813424632666667

00:55:01.144 --> 00:55:02.990 positive and most of them were CD,

NOTE Confidence: 0.813424632666667

00:55:02.990 --> 00:55:05.414 eight negative and on flow you

NOTE Confidence: 0.813424632666667

00:55:05.414 --> 00:55:07.700 can see that these were having

NOTE Confidence: 0.813424632666667

00:55:07.700 --> 00:55:10.080 lower expression of CD3 or CD to.

NOTE Confidence: 0.813424632666667

00:55:10.080 --> 00:55:12.306 Positive and there were no CD 4

NOTE Confidence: 0.813424632666667

00:55:12.306 --> 00:55:14.366 positive but CD eight negative and

NOTE Confidence: 0.813424632666667

00:55:14.366 --> 00:55:17.200 you can see City 25 was positive in

NOTE Confidence: 0.813424632666667

00:55:17.200 --> 00:55:19.629 these cells and CD seven was negative.

NOTE Confidence: 0.813424632666667

00:55:19.630 --> 00:55:21.506 So these for ATL cells and these

NOTE Confidence: 0.813424632666667

00:55:21.506 --> 00:55:23.001 sometimes can be difficult to

NOTE Confidence: 0.813424632666667

00:55:23.001 --> 00:55:24.903 diagnose in peripheral red where you

NOTE Confidence: 0.813424632666667

00:55:24.903 --> 00:55:26.669 have the question of whether it's

NOTE Confidence: 0.813424632666667

00:55:26.669 --> 00:55:28.924 an ATL or a chronic HTLV 1 carrier.

NOTE Confidence: 0.813424632666667

00:55:28.924 --> 00:55:30.534 In contrast to that case,

NOTE Confidence: 0.813424632666667

00:55:30.540 --> 00:55:32.472 here is a peripheral blood from a

NOTE Confidence: 0.813424632666667

00:55:32.472 --> 00:55:34.140 patient with cousin STLV 1 carrier.

NOTE Confidence: 0.813424632666667

00:55:34.140 --> 00:55:36.114 Here are the blue cells you can

NOTE Confidence: 0.813424632666667

00:55:36.114 --> 00:55:37.861 see with lower expression of CD

NOTE Confidence: 0.813424632666667

00:55:37.861 --> 00:55:39.972 three and these for CD 4 positive.

NOTE Confidence: 0.813424632666667

00:55:39.972 --> 00:55:42.564 And you can see reduced expression

NOTE Confidence: 0.813424632666667

00:55:42.564 --> 00:55:45.264 of CD5 and importantly these four

NOTE Confidence: 0.813424632666667

00:55:45.264 --> 00:55:48.344 CD 25 positive and CD 26 negative

NOTE Confidence: 0.813424632666667

00:55:48.427 --> 00:55:50.547 and also CD seven negative.

NOTE Confidence: 0.813424632666667

00:55:50.550 --> 00:55:52.209 So this is for the patient with

NOTE Confidence: 0.813424632666667

00:55:52.209 --> 00:55:54.010 chronic HSV 1 carrier and that

NOTE Confidence: 0.813424632666667

00:55:54.010 --> 00:55:55.725 distinction can be quite difficult.

NOTE Confidence: 0.813424632666667

00:55:55.730 --> 00:55:57.629 One may have to do southern blot for STL.

NOTE Confidence: 0.813424632666667

00:55:57.630 --> 00:56:00.078 We want to show that there is a

NOTE Confidence: 0.813424632666667

00:56:00.078 --> 00:56:02.782 monoclonal HTLV one or they're in the

NOTE Confidence: 0.813424632666667

00:56:02.782 --> 00:56:05.970 process from a chronic infection to ATL,

NOTE Confidence: 0.813424632666667

00:56:05.970 --> 00:56:08.028 that is integration of the virus.

NOTE Confidence: 0.813424632666667

00:56:08.030 --> 00:56:09.368 It can be a single integration,

NOTE Confidence: 0.813424632666667

00:56:09.370 --> 00:56:10.750 sometimes there can be more

NOTE Confidence: 0.813424632666667

00:56:10.750 --> 00:56:11.578 than one integration.

NOTE Confidence: 0.813424632666667

00:56:11.580 --> 00:56:15.101 And that's important to recognize the ATL

NOTE Confidence: 0.813424632666667

00:56:15.101 --> 00:56:19.080 and distinguish that from chronic carrier.

NOTE Confidence: 0.813424632666667

00:56:19.080 --> 00:56:20.872 So in the last couple of minutes I

NOTE Confidence: 0.813424632666667

00:56:20.872 --> 00:56:22.591 just want to give you an update on

NOTE Confidence: 0.813424632666667

00:56:22.591 --> 00:56:24.900 The Who classification of tumors.

NOTE Confidence: 0.813424632666667

00:56:24.900 --> 00:56:27.500 So this is in general about

NOTE Confidence: 0.813424632666667

00:56:27.500 --> 00:56:28.860 the classification of tumor.

NOTE Confidence: 0.813424632666667

00:56:28.860 --> 00:56:31.447 This is managed by the classification

NOTE Confidence: 0.813424632666667

00:56:31.447 --> 00:56:32.161 of tumours,

NOTE Confidence: 0.813424632666667

00:56:32.161 --> 00:56:34.303 editorial board and this has got

NOTE Confidence: 0.813424632666667

00:56:34.303 --> 00:56:36.931 a chair or the head of the WHL

NOTE Confidence: 0.813424632666667

00:56:36.931 --> 00:56:38.245 classification of tumors. Dr.

NOTE Confidence: 0.813424632666667

00:56:38.245 --> 00:56:40.800 Ian Cree, who is a pathologist himself.

NOTE Confidence: 0.813424632666667

00:56:40.800 --> 00:56:42.360 Then it has got.

NOTE Confidence: 0.813424632666667

00:56:42.360 --> 00:56:43.140 Standing members,

NOTE Confidence: 0.813424632666667

00:56:43.140 --> 00:56:45.840 these are standing members are common

NOTE Confidence: 0.813424632666667

00:56:45.840 --> 00:56:48.109 across different globe books and

NOTE Confidence: 0.813424632666667

00:56:48.109 --> 00:56:50.461 these are nominated by major societies

NOTE Confidence: 0.813424632666667

00:56:50.461 --> 00:56:51.874 and involving cancer diagnosis

NOTE Confidence: 0.813424632666667

00:56:51.874 --> 00:56:54.630 and they serve on a 3 year term.

NOTE Confidence: 0.813424632666667

00:56:54.630 --> 00:56:57.066 Then you have the expert editorial

NOTE Confidence: 0.813424632666667

00:56:57.066 --> 00:56:58.690 board members for each

NOTE Confidence: 0.836637875

00:56:58.768 --> 00:57:01.616 of these, each of the blue books and the

NOTE Confidence: 0.836637875

00:57:01.616 --> 00:57:04.052 current guideline for these for being an

NOTE Confidence: 0.836637875

00:57:04.052 --> 00:57:06.292 expert member is that people can't be

NOTE Confidence: 0.836637875

00:57:06.292 --> 00:57:08.837 on this board for more than two books.

NOTE Confidence: 0.836637875

00:57:08.840 --> 00:57:11.180 That's the maximum if you serve on one book,

NOTE Confidence: 0.836637875

00:57:11.180 --> 00:57:14.370 you can. So when a second book, but we can't.

NOTE Confidence: 0.836637875

00:57:14.370 --> 00:57:17.149 So beyond two books and all members

NOTE Confidence: 0.836637875

00:57:17.149 --> 00:57:19.858 have equal status and this is the

NOTE Confidence: 0.836637875

00:57:19.858 --> 00:57:22.150 decisions are made more by consensus.

NOTE Confidence: 0.836637875

00:57:22.150 --> 00:57:24.484 There is it's not,

NOTE Confidence: 0.836637875

00:57:24.484 --> 00:57:26.506 there is no hierarchy within the

NOTE Confidence: 0.836637875

00:57:26.506 --> 00:57:28.216 tutorial board and members are

NOTE Confidence: 0.836637875

00:57:28.216 --> 00:57:30.166 chosen based on their expertise and

NOTE Confidence: 0.836637875

00:57:30.166 --> 00:57:32.149 and also geography if possible.

NOTE Confidence: 0.836637875

00:57:32.150 --> 00:57:33.968 Like there is a positive attempt

NOTE Confidence: 0.836637875

00:57:33.968 --> 00:57:36.487 is made to be inclusive to include

NOTE Confidence: 0.836637875

00:57:36.487 --> 00:57:38.547 people from across the world.

NOTE Confidence: 0.836637875

00:57:38.550 --> 00:57:41.035 And the current WHO classification

NOTE Confidence: 0.836637875

00:57:41.035 --> 00:57:44.297 has 25 expert editors and one of

NOTE Confidence: 0.836637875

00:57:44.297 --> 00:57:46.646 them and has about 380 authors,

NOTE Confidence: 0.836637875

00:57:46.646 --> 00:57:49.544 and these authors include not just

NOTE Confidence: 0.836637875

00:57:49.544 --> 00:57:51.966 hematopathologist, but they have clinicians,

NOTE Confidence: 0.836637875

00:57:51.966 --> 00:57:53.130 hematologists, oncologists.

NOTE Confidence: 0.836637875

00:57:53.130 --> 00:57:55.850 We got, geneticists, epidemiologists.

NOTE Confidence: 0.836637875

00:57:55.850 --> 00:58:00.240 All of them are authors. Most of the major.

NOTE Confidence: 0.836637875

00:58:00.240 --> 00:58:02.880 Major chapters have got.

NOTE Confidence: 0.673802238333333

00:58:05.590 --> 00:58:08.665 Otters are beyond just being

NOTE Confidence: 0.673802238333333

00:58:08.665 --> 00:58:10.680 hematopathologist and across these I mean,

NOTE Confidence: 0.673802238333333

00:58:10.680 --> 00:58:13.948 these 380 authors come from 31 different

NOTE Confidence: 0.673802238333333

00:58:13.948 --> 00:58:16.732 countries, so there's a much wider

NOTE Confidence: 0.673802238333333

00:58:16.732 --> 00:58:18.440 representation of across the world,

NOTE Confidence: 0.673802238333333

00:58:18.440 --> 00:58:20.728 so the the timelines and the way

NOTE Confidence: 0.673802238333333

00:58:20.728 --> 00:58:22.840 we are progressing. This was fast.

NOTE Confidence: 0.673802238333333

00:58:22.840 --> 00:58:24.925 We, you know, the editorial board,

NOTE Confidence: 0.673802238333333

00:58:24.925 --> 00:58:27.055 at least the editorial board members

NOTE Confidence: 0.673802238333333

00:58:27.055 --> 00:58:28.808 were contacted. In February,

NOTE Confidence: 0.673802238333333

00:58:28.808 --> 00:58:32.048 we had a very pre meet in April 2021.

NOTE Confidence: 0.673802238333333

00:58:32.048 --> 00:58:33.504 That was the first time we got

NOTE Confidence: 0.673802238333333

00:58:33.504 --> 00:58:34.870 to know who were the other.

NOTE Confidence: 0.673802238333333

00:58:34.870 --> 00:58:37.714 In total board members and then we had a

NOTE Confidence: 0.673802238333333

00:58:37.714 --> 00:58:40.407 content meeting which happened in November,

NOTE Confidence: 0.673802238333333

00:58:40.410 --> 00:58:42.410 so part of it we could not complete.

NOTE Confidence: 0.673802238333333

00:58:42.410 --> 00:58:44.545 So the T cell lymphomas could not

NOTE Confidence: 0.673802238333333

00:58:44.545 --> 00:58:46.332 be discussed because we had three

NOTE Confidence: 0.673802238333333

101

00:58:46.332 --> 00:58:48.229 full days 12 hour meetings each day

NOTE Confidence: 0.673802238333333

00:58:48.289 --> 00:58:50.369 for three days and we are still left

NOTE Confidence: 0.673802238333333

00:58:50.369 --> 00:58:52.750 with some chapters which were left

NOTE Confidence: 0.673802238333333

00:58:52.750 --> 00:58:55.540 and that's being discussed next week.

NOTE Confidence: 0.673802238333333

00:58:55.540 --> 00:58:58.060 And I mean that was the November

NOTE Confidence: 0.673802238333333

00:58:58.060 --> 00:58:58.794 2224 meeting.

NOTE Confidence: 0.673802238333333

00:58:58.794 --> 00:59:00.996 So we have a third editorial

NOTE Confidence: 0.673802238333333

00:59:00.996 --> 00:59:02.780 meeting in in in January,

NOTE Confidence: 0.673802238333333

00:59:02.780 --> 00:59:05.377 but we are likely to have another

NOTE Confidence: 0.673802238333333

00:59:05.377 --> 00:59:07.572 meeting sometime in in spring and

NOTE Confidence: 0.673802238333333

00:59:07.572 --> 00:59:09.924 we are hoping that the towards the

NOTE Confidence: 0.673802238333333

00:59:09.997 --> 00:59:12.181 end of the of the year we will

NOTE Confidence: 0.673802238333333

00:59:12.181 --> 00:59:14.119 have the publication coming out.

NOTE Confidence: 0.673802238333333

00:59:14.119 --> 00:59:16.897 So possibly by October November we

NOTE Confidence: 0.673802238333333

00:59:16.897 --> 00:59:19.068 should be having the 5th edition

NOTE Confidence: 0.673802238333333

00:59:19.068 --> 00:59:21.730 of The Who classification.

NOTE Confidence: 0.673802238333333

00:59:21.730 --> 00:59:24.922 I'll stop that and I'm happy to

NOTE Confidence: 0.673802238333333

00:59:24.922 --> 00:59:25.834 take questions.

NOTE Confidence: 0.930480176363637

00:59:28.200 --> 00:59:29.502 Sorry, I think I took a little

NOTE Confidence: 0.930480176363637

00:59:29.502 --> 00:59:32.260 longer than I expected. I would thank

NOTE Confidence: 0.769444279

00:59:32.270 --> 00:59:35.056 you. So thank you so much for

NOTE Confidence: 0.769444279

00:59:35.056 --> 00:59:36.890 that overview and really,

NOTE Confidence: 0.769444279

00:59:36.890 --> 00:59:39.080 really fascinating case.

NOTE Confidence: 0.769444279

00:59:39.080 --> 00:59:42.496 Needed cases. Allow all the

NOTE Confidence: 0.769444279

00:59:42.496 --> 00:59:45.756 people currently onto to essence,

NOTE Confidence: 0.769444279

00:59:45.760 --> 00:59:46.686 especially trainees.

NOTE Confidence: 0.769444279

00:59:46.686 --> 00:59:49.132 Please feel free to pop up

NOTE Confidence: 0.769444279

00:59:49.132 --> 00:59:50.316 with question with question.

NOTE Confidence: 0.786050025

00:59:55.670 --> 00:59:58.256 See, there's something on the chat,

NOTE Confidence: 0.786050025

00:59:58.260 --> 00:59:59.600 see if there's any question.

NOTE Confidence: 0.786050025

00:59:59.600 --> 01:00:04.658 Those oh those are CME credits. OK so I have

NOTE Confidence: 0.670838205

01:00:04.690 --> 01:00:07.876 a question why that was a a great talk.

NOTE Confidence: 0.670838205

01:00:07.880 --> 01:00:09.500 I really appreciated that

NOTE Confidence: 0.897798416

01:00:09.510 --> 01:00:11.020 my my question is about

NOTE Confidence: 0.745629577222222

01:00:11.650 --> 01:00:13.650 you know the latency versus

NOTE Confidence: 0.745629577222222

01:00:13.650 --> 01:00:15.250 lytic cycles of EBV,

NOTE Confidence: 0.745629577222222

01:00:15.250 --> 01:00:17.469 and that how that plays into lymphoma,

NOTE Confidence: 0.745629577222222

01:00:17.470 --> 01:00:19.950 Genesis, and I know historically,

NOTE Confidence: 0.745629577222222

01:00:19.950 --> 01:00:22.110 we've always talking about these latency

NOTE Confidence: 0.745629577222222

01:00:22.110 --> 01:00:25.052 programs and eborn Debnath course or latency.

NOTE Confidence: 0.745629577222222

01:00:25.052 --> 01:00:27.000 Genes, but recently there's been a

NOTE Confidence: 0.745629577222222

01:00:27.000 --> 01:00:29.020 lot more suggestion that the lytic

NOTE Confidence: 0.745629577222222

01:00:29.020 --> 01:00:31.192 replication of the virus in the near

NOTE Confidence: 0.745629577222222

01:00:31.192 --> 01:00:34.340 term before you know diagnosis is actually,

NOTE Confidence: 0.745629577222222

01:00:34.340 --> 01:00:37.300 you know, very relevant for

NOTE Confidence: 0.745629577222222

01:00:37.300 --> 01:00:38.361 for lymphoma Genesis.

NOTE Confidence: 0.745629577222222

01:00:38.361 --> 01:00:40.769 So just your thoughts on sort of how

NOTE Confidence: 0.745629577222222

01:00:40.769 --> 01:00:43.436 that sort of might integrate into

NOTE Confidence: 0.745629577222222

01:00:43.436 --> 01:00:45.520 these classifications or pathogenesis.

NOTE Confidence: 0.72471833

01:00:45.980 --> 01:00:48.885 Yeah, good that you asked the question,

NOTE Confidence: 0.72471833

01:00:48.890 --> 01:00:52.378 if you use the one you see proportion

NOTE Confidence: 0.72471833

01:00:52.378 --> 01:00:55.750 of cells which are in the lytic phase.

NOTE Confidence: 0.72471833

01:00:55.750 --> 01:00:58.228 And the question that comes up is.

NOTE Confidence: 0.72471833

01:00:58.230 --> 01:01:00.286 Those cells which are in the lytic phase.

NOTE Confidence: 0.72471833

01:01:00.290 --> 01:01:03.430 Can they infect other cells?

NOTE Confidence: 0.72471833

01:01:03.430 --> 01:01:06.772 And can you have multiple EBV

NOTE Confidence: 0.72471833

01:01:06.772 --> 01:01:09.643 positive lymphoma clones occurring

NOTE Confidence: 0.72471833

01:01:09.643 --> 01:01:12.727 within a particular tumor?

NOTE Confidence: 0.72471833

01:01:12.730 --> 01:01:15.810 In most of the. B cell lymphoma's.

NOTE Confidence: 0.72471833

01:01:15.810 --> 01:01:17.770 At least people have not much work

NOTE Confidence: 0.72471833

01:01:17.826 --> 01:01:19.286 has actually happened, though.

NOTE Confidence: 0.72471833

01:01:19.286 --> 01:01:21.654 People have shown that there is a subset

NOTE Confidence: 0.72471833

01:01:21.654 --> 01:01:24.038 of cells which are in the lytic phase.

NOTE Confidence: 0.72471833

01:01:24.040 --> 01:01:26.556 But how that would impinge on

NOTE Confidence: 0.72471833

01:01:26.556 --> 01:01:28.886 the evolution of the tuba.

NOTE Confidence: 0.72471833

01:01:28.890 --> 01:01:30.829 I think it is far from clear.

NOTE Confidence: 0.846749167857143

01:01:33.970 --> 01:01:35.634 I'm probably the lytic.

NOTE Confidence: 0.846749167857143

01:01:35.634 --> 01:01:37.714 Phase is important also because

NOTE Confidence: 0.846749167857143

01:01:37.714 --> 01:01:40.079 if you follow these patients.

NOTE Confidence: 0.846749167857143

01:01:40.080 --> 01:01:42.782 It is only latent TB you wouldn't

NOTE Confidence: 0.846749167857143

01:01:42.782 --> 01:01:45.531 see arising EBV viral level in the

NOTE Confidence: 0.846749167857143

01:01:45.531 --> 01:01:47.662 serum and the very fact that the

NOTE Confidence: 0.846749167857143

01:01:47.662 --> 01:01:49.584 plasma levels keep increasing and

NOTE Confidence: 0.846749167857143

01:01:49.584 --> 01:01:51.614 correlates with the tumor load.

NOTE Confidence: 0.846749167857143

01:01:51.620 --> 01:01:54.446 It means that there is a subset of cells

NOTE Confidence: 0.846749167857143

01:01:54.446 --> 01:01:57.018 where they are lytic infected exactly.

NOTE Confidence: 0.846749167857143

01:01:57.020 --> 01:01:59.228 Yeah and also the the fascinating

NOTE Confidence: 0.846749167857143

01:01:59.228 --> 01:02:01.174 question also comes up is if

01:02:01.174 --> 01:02:03.092 there was a way to convert the

01:02:03.092 --> 01:02:04.838 latent virus into a lytic virus.

01:02:04.840 --> 01:02:07.171 Can you steal the kill the lymphoma

01:02:07.171 --> 01:02:09.260 cell instead of treating patient with

01:02:09.260 --> 01:02:10.660 all the chemotherapeutic agents?

01:02:10.660 --> 01:02:12.300 If you can just trigger.

01:02:12.300 --> 01:02:14.826 And change the latency into lytic,

01:02:14.830 --> 01:02:16.295 or whether the baby itself

01:02:16.295 --> 01:02:17.760 can kill the tumor cells.

01:02:17.760 --> 01:02:19.335 But that has been just

01:02:19.335 --> 01:02:20.280 a fascinating question,

01:02:20.280 --> 01:02:21.486 but nobody has ever done it.

01:02:24.470 --> 01:02:27.240 Thank you, thank you. I

01:02:27.250 --> 01:02:29.336 have a question. This is Jeff Squire.

01:02:31.250 --> 01:02:33.938 You described the mutations

01:02:33.940 --> 01:02:36.099 in EBV in EBV genome,

NOTE Confidence: 0.717284165428571

01:02:36.340 --> 01:02:40.015 in Burkitt's. And wondering whether there are

NOTE Confidence: 0.7224809144

01:02:40.030 --> 01:02:42.370 mutations? Found another

NOTE Confidence: 0.7224809144

01:02:42.370 --> 01:02:44.820 EBV associated lymphomas

NOTE Confidence: 0.87892495

01:02:45.490 --> 01:02:48.920 and also you described cytokine

NOTE Confidence: 0.87892495

01:02:48.920 --> 01:02:50.412 suppression in Burkitt's,

NOTE Confidence: 0.87892495

01:02:50.412 --> 01:02:52.818 and I wonder how widespread that

NOTE Confidence: 0.960165116666667

01:02:52.830 --> 01:02:56.830 is among other. Yeah, that's us.

NOTE Confidence: 0.960165116666667

01:02:56.830 --> 01:02:59.050 Regarding the Abner 3B mutations,

NOTE Confidence: 0.960165116666667

01:02:59.050 --> 01:03:00.037 which we showed,

NOTE Confidence: 0.960165116666667

01:03:00.037 --> 01:03:02.340 we showed that across not just Burkitt

NOTE Confidence: 0.960165116666667

01:03:02.399 --> 01:03:04.660 lymphoma but also in diffuse large B

NOTE Confidence: 0.960165116666667

01:03:04.660 --> 01:03:07.411 cell lymphoma and in post transplant

NOTE Confidence: 0.960165116666667

01:03:07.411 --> 01:03:09.400 lymphoproliferative disorders so that actors,

NOTE Confidence: 0.960165116666667

01:03:09.400 --> 01:03:11.568 even outside of the bucket, look firmer.

NOTE Confidence: 0.960165116666667

01:03:11.568 --> 01:03:13.488 Whereas this cytokine thing that

NOTE Confidence: 0.960165116666667

01:03:13.488 --> 01:03:16.436 I showed you was purely in in the

NOTE Confidence: 0.960165116666667

01:03:16.436 --> 01:03:19.900 mouse model we have not been able to

NOTE Confidence: 0.960165116666667

01:03:20.010 --> 01:03:23.180 show SL 10 differences in patients.

NOTE Confidence: 0.858680108571429

01:03:27.170 --> 01:03:29.240 OK, so that's a rather dramatic

NOTE Confidence: 0.858680108571429

01:03:29.240 --> 01:03:31.846 finding, so it seems to be a

NOTE Confidence: 0.858680108571429

01:03:31.846 --> 01:03:33.340 consistent mutation and ended

NOTE Confidence: 0.460836098

01:03:35.520 --> 01:03:36.670 3833 B mutations we have.

NOTE Confidence: 0.460836098

01:03:36.670 --> 01:03:38.170 We have been able to show

NOTE Confidence: 0.460836098

01:03:38.170 --> 01:03:39.620 outside of the work as well

NOTE Confidence: 0.708532458571429

01:03:39.690 --> 01:03:41.690 and and how. How prevalent

NOTE Confidence: 0.708532458571429

01:03:41.690 --> 01:03:43.190 is that? Is it a friend?

NOTE Confidence: 0.733068255714286

01:03:43.680 --> 01:03:46.102 Most cases? Yeah, we evaluated in about

NOTE Confidence: 0.733068255714286

01:03:46.102 --> 01:03:48.807 40 cases and if I remember correctly.

NOTE Confidence: 0.733068255714286

01:03:48.810 --> 01:03:51.974 More than half of them had mutations

NOTE Confidence: 0.733068255714286

01:03:51.974 --> 01:03:54.239 and these patients were from.

NOTE Confidence: 0.733068255714286

01:03:54.240 --> 01:03:55.520 All over the world now.

NOTE Confidence: 0.733068255714286

01:03:55.520 --> 01:03:57.968 I mean, we had patients from

NOTE Confidence: 0.733068255714286

01:03:57.968 --> 01:04:00.232 Australia to UK to Africa,

NOTE Confidence: 0.733068255714286

01:04:00.232 --> 01:04:01.621 collected from different

NOTE Confidence: 0.733068255714286

01:04:01.621 --> 01:04:04.172 parts of the world and also.

NOTE Confidence: 0.733068255714286

01:04:04.172 --> 01:04:06.098 One of The thing is important.

NOTE Confidence: 0.733068255714286

01:04:06.100 --> 01:04:09.370 Recently my my friend Lorenzo Lucchini.

NOTE Confidence: 0.733068255714286

01:04:09.370 --> 01:04:11.950 He showed a variety of lymphomas

NOTE Confidence: 0.733068255714286

01:04:11.950 --> 01:04:14.538 where using RNA scope they could

NOTE Confidence: 0.733068255714286

01:04:14.538 --> 01:04:17.268 show remnants of EB virus even even

NOTE Confidence: 0.733068255714286

01:04:17.268 --> 01:04:20.217 in those which were ever negative.

NOTE Confidence: 0.733068255714286

01:04:20.220 --> 01:04:21.875 So there is a possibility

NOTE Confidence: 0.733068255714286

01:04:21.875 --> 01:04:23.199 not only mutations occur,

NOTE Confidence: 0.733068255714286

01:04:23.200 --> 01:04:24.752 but eventually many tumors

NOTE Confidence: 0.733068255714286

01:04:24.752 --> 01:04:26.692 may lose the baby virus.

NOTE Confidence: 0.733068255714286

01:04:26.700 --> 01:04:28.765 So what we currently consider

NOTE Confidence: 0.733068255714286

01:04:28.765 --> 01:04:30.417 as EBV negative disease,

NOTE Confidence: 0.733068255714286

01:04:30.420 --> 01:04:32.572 a subset of them may not be be

NOTE Confidence: 0.733068255714286

01:04:32.572 --> 01:04:36.250 negative when from inception, yes.

NOTE Confidence: 0.733068255714286

01:04:36.250 --> 01:04:37.539 Thank you, thank you.

NOTE Confidence: 0.851152315

01:04:45.740 --> 01:04:48.564 So I think we're over 6 minutes over.

NOTE Confidence: 0.851152315

01:04:48.570 --> 01:04:52.188 I just wanted to thank you so much for

NOTE Confidence: 0.613557415714286

01:04:52.520 --> 01:04:55.208 took a little long I could have.

NOTE Confidence: 0.613557415714286

01:04:55.210 --> 01:04:58.080 Cut down on my great thank you. Thank you

NOTE Confidence: 0.769622185

01:04:58.810 --> 01:04:59.838 to the next meeting.

NOTE Confidence: 0.7166406825

01:05:00.290 --> 01:05:03.410 Thank you, thank you. Thank you very much.

NOTE Confidence: 0.763318403333333

01:05:03.440 --> 01:05:03.998 Thank you, bye.