WEBVTT

00:00:00.000 --> 00:00:02.844 So it's my great pleasure to

00:00:02.844 --> 00:00:05.032 introduce Doctor Khari Richard from

00:00:05.032 --> 00:00:06.966 our Yale pathology grand rounds.

00:00:06.966 --> 00:00:10.134 Dr Reichart study molecular biology at

00:00:10.134 --> 00:00:12.859 Princeton University and Medicine at Tufts,

00:00:12.860 --> 00:00:15.779 where she graduated with a OA distinction.

00:00:15.780 --> 00:00:18.657 She completed her AP and CP Residency,

00:00:18.660 --> 00:00:21.733 and also her Empath Fellowship at UT

00:00:21.733 --> 00:00:24.411 Southwestern and after a surge Path

00:00:24.411 --> 00:00:26.238 fellowship at Stanford University,

00:00:26.240 --> 00:00:28.210 she began as assistant professor

00:00:28.210 --> 00:00:30.740 at the University of New Mexico.

00:00:30.740 --> 00:00:32.996 Where she later served as chief

00:00:32.996 --> 00:00:35.260 of their Heat Path division,

NOTE Confidence: 0.813080833

00:00:35.260 --> 00:00:37.570 Doctor Richard was subsequently recruited

NOTE Confidence: 0.813080833

00:00:37.570 --> 00:00:40.644 to Mayo Clinic in Minnesota in 2011

NOTE Confidence: 0.813080833

00:00:40.644 --> 00:00:42.732 as their director of Flow Cytometry

NOTE Confidence: 0.813080833

00:00:42.732 --> 00:00:45.438 and also as their fellowship director.

NOTE Confidence: 0.813080833

00:00:45.440 --> 00:00:47.708 She became professor of lab medicine

NOTE Confidence: 0.813080833

00:00:47.708 --> 00:00:50.272 and pathology at Mayo in 2018 and

NOTE Confidence: 0.813080833

00:00:50.272 --> 00:00:52.228 is currently serving as their Chair

NOTE Confidence: 0.813080833

00:00:52.228 --> 00:00:53.910 of Education Oversight committee

NOTE Confidence: 0.813080833

00:00:53.910 --> 00:00:56.478 in the Division of Heme Path,

NOTE Confidence: 0.813080833

00:00:56.480 --> 00:00:59.497 which she formed over a decade ago.

NOTE Confidence: 0.813080833

00:00:59.500 --> 00:01:00.286 Doctor reichardt.

NOTE Confidence: 0.813080833

00:01:00.286 --> 00:01:02.644 Research focus is in the clinical,

NOTE Confidence: 0.813080833

00:01:02.650 --> 00:01:03.121 pathologic,

NOTE Confidence: 0.813080833

00:01:03.121 --> 00:01:05.947 and genetic features of myeloid disorders,

NOTE Confidence: 0.813080833

00:01:05.950 --> 00:01:08.040 and in particular in diseases

NOTE Confidence: 0.813080833

00:01:08.040 --> 00:01:10.130 that are associated with eastern

NOTE Confidence: 0.813080833

00:01:10.202 --> 00:01:11.888 affilia and mastocytosis.

NOTE Confidence: 0.813080833

00:01:11.890 --> 00:01:14.130 Her work has not only shed light

NOTE Confidence: 0.813080833

00:01:14.130 --> 00:01:15.885 in the pathophysiology of these

NOTE Confidence: 0.813080833

00:01:15.885 --> 00:01:17.357 difficult to diagnose tumors,

NOTE Confidence: 0.813080833

00:01:17.360 --> 00:01:19.120 but also demonstrated practical

NOTE Confidence: 0.813080833

00:01:19.120 --> 00:01:21.320 ways that pathologists can improve

NOTE Confidence: 0.813080833

00:01:21.320 --> 00:01:23.630 test utilization in their work up.

NOTE Confidence: 0.813080833

00:01:23.630 --> 00:01:25.676 She's authored over 100 book chapters

NOTE Confidence: 0.813080833

00:01:25.676 --> 00:01:28.767 and empath and is also coauthor of our

NOTE Confidence: 0.813080833

00:01:28.767 --> 00:01:30.837 beloved bone marrow pathology textbook.

NOTE Confidence: 0.813080833

00:01:30.840 --> 00:01:33.618 With Kathy Fuccaro and David Cholesky,

NOTE Confidence: 0.813080833

00:01:33.620 --> 00:01:35.028 innumerable trainees and junior

NOTE Confidence: 0.813080833

00:01:35.028 --> 00:01:37.140 faculty now all over the country,

NOTE Confidence: 0.813080833

00:01:37.140 --> 00:01:39.408 some of whom I know have

NOTE Confidence: 0.813080833

00:01:39.408 --> 00:01:40.920 flourished under her mentorship,

NOTE Confidence: 0.813080833

00:01:40.920 --> 00:01:43.460 and so if you have much to learn from her.

NOTE Confidence: 0.813080833

00:01:43.460 --> 00:01:44.812 In that regard, Dr.

NOTE Confidence: 0.813080833

00:01:44.812 --> 00:01:46.502 Walker has been an invited

NOTE Confidence: 0.813080833

00:01:46.502 --> 00:01:48.280 speaker for impactful courses,

NOTE Confidence: 0.813080833

00:01:48.280 --> 00:01:50.390 including those given a national

NOTE Confidence: 0.813080833

00:01:50.390 --> 00:01:53.159 meetings of CAP ASCAP and use CAP.

NOTE Confidence: 0.813080833

00:01:53.160 --> 00:01:55.393 So we are greatly honored by her

NOTE Confidence: 0.813080833

00:01:55.393 --> 00:01:58.277 visit today and for her talk on

NOTE Confidence: 0.813080833

00:01:58.277 --> 00:02:00.137 hypereosinophilia evolving our strategy.

NOTE Confidence: 0.813080833

00:02:00.140 --> 00:02:00.630 Thank you.

NOTE Confidence: 0.951842466

00:02:13.680 --> 00:02:16.710 Can you see my screen?

NOTE Confidence: 0.951842466

00:02:16.710 --> 00:02:18.455 Yes, perfect great.

NOTE Confidence: 0.951842466

00:02:18.455 --> 00:02:21.570 Well thank you so much good afternoon

NOTE Confidence: 0.951842466

00:02:21.570 --> 00:02:24.885 everyone and thank you Doctor Chu for that.

NOTE Confidence: 0.951842466

00:02:24.890 --> 00:02:26.069 Very gracious introduction.

NOTE Confidence: 0.951842466

00:02:26.069 --> 00:02:29.308 It's a great honor for me to receive

NOTE Confidence: 0.951842466

00:02:29.308 --> 00:02:31.792 this invitation from from you and

NOTE Confidence: 0.951842466

00:02:31.792 --> 00:02:33.971 I'm very grateful and pleased

NOTE Confidence: 0.951842466

00:02:33.971 --> 00:02:36.126 to have this opportunity today.

NOTE Confidence: 0.951842466

00:02:36.130 --> 00:02:37.873 I'd also like to thank the faculty

NOTE Confidence: 0.951842466

00:02:37.873 --> 00:02:39.629 and the resident fellow that I was

NOTE Confidence: 0.951842466

00:02:39.629 --> 00:02:41.063 able to chat with this morning.

NOTE Confidence: 0.951842466

00:02:41.070 --> 00:02:43.849 I learned a lot about your institution.

NOTE Confidence: 0.951842466

00:02:43.850 --> 00:02:46.160 It was just an absolute pleasure.

NOTE Confidence: 0.951842466

00:02:46.160 --> 00:02:48.260 And while it's unfortunate that I

NOTE Confidence: 0.951842466

00:02:48.260 --> 00:02:50.360 cannot be there today in person,

NOTE Confidence: 0.951842466

00:02:50.360 --> 00:02:52.700 it's still wonderful for me

NOTE Confidence: 0.951842466

00:02:52.700 --> 00:02:54.572 to be here virtually.

NOTE Confidence: 0.951842466

00:02:54.580 --> 00:02:56.584 As I was thinking about a

NOTE Confidence: 0.951842466

00:02:56.584 --> 00:02:57.920 topic for this presentation,

NOTE Confidence: 0.951842466

00:02:57.920 --> 00:03:00.122 I wanted to select something that

NOTE Confidence: 0.951842466

00:03:00.122 --> 00:03:02.280 was both somewhat broadly appealing,

NOTE Confidence: 0.951842466

00:03:02.280 --> 00:03:05.059 yet you also unique and one in

NOTE Confidence: 0.951842466

00:03:05.059 --> 00:03:07.344 which recent advances are pushing

NOTE Confidence: 0.951842466

00:03:07.344 --> 00:03:09.380 our boundaries of diagnosis.

NOTE Confidence: 0.951842466

00:03:09.380 --> 00:03:11.485 So I decided on hypereosinophilic

NOTE Confidence: 0.951842466

00:03:11.485 --> 00:03:13.590 conditions because our knowledge of

NOTE Confidence: 0.951842466

00:03:13.659 --> 00:03:15.857 these disorders as many of you know,

NOTE Confidence: 0.951842466

00:03:15.860 --> 00:03:18.135 has greatly expanded in literally

NOTE Confidence: 0.951842466

00:03:18.135 --> 00:03:19.955 just the past decade,

NOTE Confidence: 0.951842466

00:03:19.960 --> 00:03:22.480 and many of these advances have been

NOTE Confidence: 0.951842466

00:03:22.480 --> 00:03:25.060 incorporated into our current classification.

NOTE Confidence: 0.951842466

00:03:25.060 --> 00:03:27.304 System much of these advances are

NOTE Confidence: 0.951842466

00:03:27.304 --> 00:03:29.909 due to the molecular genetics space,

NOTE Confidence: 0.951842466

00:03:29.910 --> 00:03:31.670 which we will talk about,

NOTE Confidence: 0.951842466

00:03:31.670 --> 00:03:34.322 and because of these advances we

NOTE Confidence: 0.951842466

00:03:34.322 --> 00:03:36.628 are having to continually revise

NOTE Confidence: 0.951842466

00:03:36.628 --> 00:03:39.903 and evolve our strategy in how our

NOTE Confidence: 0.951842466

00:03:39.903 --> 00:03:42.308 diagnosis occurs in these conditions.

NOTE Confidence: 0.951842466

00:03:42.310 --> 00:03:44.506 I personally find that these disorders

NOTE Confidence: 0.951842466

00:03:44.506 --> 00:03:47.240 can be very tricky to diagnose and

NOTE Confidence: 0.951842466

00:03:47.240 --> 00:03:49.245 they can be somewhat overwhelming,

NOTE Confidence: 0.951842466

00:03:49.250 --> 00:03:52.362 and since one of the ways we learn

NOTE Confidence: 0.951842466

00:03:52.362 --> 00:03:54.511 as pathologists is by showing

NOTE Confidence: 0.951842466

00:03:54.511 --> 00:03:55.795 cases and studying.

NOTE Confidence: 0.951842466

00:03:55.800 --> 00:03:58.523 Cases you will see that I have

NOTE Confidence: 0.951842466

00:03:58.523 --> 00:03:59.690 interspersed case presentations

NOTE Confidence: 0.951842466

00:03:59.759 --> 00:04:01.734 throughout today's talk to illustrate

NOTE Confidence: 0.951842466

00:04:01.734 --> 00:04:04.659 some of the concepts that we will cover.

NOTE Confidence: 0.947473108

00:04:07.270 --> 00:04:08.840 I have nothing to disclose.

NOTE Confidence: 0.88264979625

00:04:11.150 --> 00:04:12.500 So there are three learning

NOTE Confidence: 0.88264979625

7

00:04:12.500 --> 00:04:13.310 objectives for today,

NOTE Confidence: 0.88264979625

00:04:13.310 --> 00:04:15.949 two of which focus on the genetics

NOTE Confidence: 0.88264979625

00:04:15.949 --> 00:04:18.619 of primary clonal ES and affiliate

NOTE Confidence: 0.88264979625

00:04:18.619 --> 00:04:20.262 conditions over the past decade.

NOTE Confidence: 0.88264979625

00:04:20.262 --> 00:04:23.078 As I mentioned, it has become clear

NOTE Confidence: 0.88264979625

00:04:23.078 --> 00:04:25.513 that there are demonstrable recurring

NOTE Confidence: 0.88264979625

00:04:25.513 --> 00:04:28.241 genetic abnormalities that underlie a

NOTE Confidence: 0.88264979625

00:04:28.241 --> 00:04:30.946 distinct subset of these disorders.

NOTE Confidence: 0.88264979625

00:04:30.950 --> 00:04:32.594 And these specific abnormalities,

NOTE Confidence: 0.88264979625

00:04:32.594 --> 00:04:35.534 as I mentioned, are currently housed

NOTE Confidence: 0.88264979625

00:04:35.534 --> 00:04:38.374 in our WHO classification system.

NOTE Confidence: 0.88264979625

00:04:38.380 --> 00:04:41.257 So as we have walked this journey

NOTE Confidence: 0.88264979625

00:04:41.257 --> 00:04:43.104 of discovering recurrent genetic

NOTE Confidence: 0.88264979625

00:04:43.104 --> 00:04:45.260 abnormalities and ESN affilia,

NOTE Confidence: 0.88264979625

00:04:45.260 --> 00:04:47.460 it is now becoming clear that there are

NOTE Confidence: 0.88264979625

00:04:47.460 --> 00:04:49.885 new and additional emerging potential

8

NOTE Confidence: 0.88264979625

00:04:49.885 --> 00:04:51.700 recurring genetic abnormalities.

NOTE Confidence: 0.88264979625

00:04:51.700 --> 00:04:53.518 And I will mention them later

NOTE Confidence: 0.88264979625

00:04:53.518 --> 00:04:55.160 in my talk as well.

NOTE Confidence: 0.88264979625

00:04:55.160 --> 00:04:57.328 Thirdly, even though hypereosinophilic

NOTE Confidence: 0.88264979625

00:04:57.328 --> 00:04:58.954 states are uncommon,

NOTE Confidence: 0.88264979625

00:04:58.960 --> 00:05:00.840 they're very it's very unusual

NOTE Confidence: 0.88264979625

00:05:00.840 --> 00:05:03.419 for them to come across our desk.

NOTE Confidence: 0.88264979625

00:05:03.420 --> 00:05:04.508 As you will see,

NOTE Confidence: 0.88264979625

00:05:04.508 --> 00:05:06.574 there is a vast array of ancillary

NOTE Confidence: 0.88264979625

00:05:06.574 --> 00:05:09.470 testing that can be done in such cases,

NOTE Confidence: 0.88264979625

00:05:09.470 --> 00:05:12.522 and because that can become quite costly

NOTE Confidence: 0.88264979625

00:05:12.522 --> 00:05:16.347 and in that cost can incur quite quickly,

NOTE Confidence: 0.88264979625

00:05:16.350 --> 00:05:19.080 I'm going to introduce a judicious

NOTE Confidence: 0.88264979625

00:05:19.080 --> 00:05:20.900 yet comprehensive algorithmic approach

NOTE Confidence: 0.88264979625

00:05:20.962 --> 00:05:22.770 to ESPN affiliate conditions.

NOTE Confidence: 0.735796022

00:05:24.850 --> 00:05:26.970 So what are hypereosinophilic conditions?

NOTE Confidence: 0.735796022

00:05:26.970 --> 00:05:29.945 These are disorders that are defined as

NOTE Confidence: 0.735796022

00:05:29.950 --> 00:05:32.617 disorders of diverse ideology and they can

NOTE Confidence: 0.735796022

00:05:32.617 --> 00:05:35.635 be clonal or non clonal and essentially

NOTE Confidence: 0.735796022

00:05:35.635 --> 00:05:38.335 there is a sustained overproduction of

NOTE Confidence: 0.735796022

00:05:38.413 --> 00:05:40.908 the acidophiles in these conditions.

NOTE Confidence: 0.735796022

00:05:40.910 --> 00:05:42.968 Why is it important to recognize?

NOTE Confidence: 0.735796022

00:05:42.970 --> 00:05:46.281 Because one of the most dire consequences

NOTE Confidence: 0.735796022

00:05:46.281 --> 00:05:48.268 of hypereosinophilic states is

NOTE Confidence: 0.735796022

00:05:48.268 --> 00:05:50.244 what is called Hypereosinophilic

NOTE Confidence: 0.735796022

00:05:50.244 --> 00:05:52.714 syndrome that results in significant

NOTE Confidence: 0.735796022

00:05:52.784 --> 00:05:54.980 patient morbidity and mortality.

NOTE Confidence: 0.735796022

00:05:54.980 --> 00:05:58.039 Due to the end organ damage that's

NOTE Confidence: 0.735796022

00:05:58.039 --> 00:06:01.538 caused by the ESMA Philic infiltrate.

NOTE Confidence: 0.735796022

00:06:01.540 --> 00:06:04.300 The concept of Hypereosinophilic syndrome,

NOTE Confidence: 0.735796022

00:06:04.300 --> 00:06:07.989 abbreviated HES and in fact the term

NOTE Confidence: 0.735796022

00:06:07.989 --> 00:06:11.741 itself HES has its origin in this 1968

NOTE Confidence: 0.735796022

00:06:11.741 --> 00:06:15.047 publication by doctors Hardy and Anderson.

NOTE Confidence: 0.735796022

00:06:15.050 --> 00:06:16.367 In this paper,

NOTE Confidence: 0.735796022

00:06:16.367 --> 00:06:19.780 they report three patients that had H ES,

NOTE Confidence: 0.735796022

00:06:19.780 --> 00:06:22.215 all of whom had extensive

NOTE Confidence: 0.735796022

00:06:22.215 --> 00:06:23.189 systemic involvement,

NOTE Confidence: 0.735796022

00:06:23.190 --> 00:06:25.400 two of whom even died.

NOTE Confidence: 0.735796022

00:06:25.400 --> 00:06:27.216 Based on their findings,

NOTE Confidence: 0.735796022

00:06:27.216 --> 00:06:29.940 these authors propose the term that

NOTE Confidence: 0.735796022

00:06:30.016 --> 00:06:32.551 we still use today Hypereosinophilic

NOTE Confidence: 0.735796022

00:06:32.551 --> 00:06:35.599 syndrome to emphasize that HHS is

NOTE Confidence: 0.735796022

00:06:35.599 --> 00:06:38.227 actually a continuum of disease that

NOTE Confidence: 0.735796022

00:06:38.227 --> 00:06:40.774 can range anywhere from an asymptomatic

NOTE Confidence: 0.735796022

00:06:40.774 --> 00:06:44.110 type of form to a rapidly fatal form.

NOTE Confidence: 0.846271117777778

00:06:46.300 --> 00:06:48.192 Seven years after doctors,

NOTE Confidence: 0.846271117777778

00:06:48.192 --> 00:06:50.557 Harding Anderson published their paper.

NOTE Confidence: 0.846271117777778

00:06:50.560 --> 00:06:53.080 She used it. It all published a much larger

NOTE Confidence: 0.846271117777778

00:06:53.080 --> 00:06:55.139 study of Hypereosinophilic syndrome.

NOTE Confidence: 0.846271117777778

00:06:55.140 --> 00:06:57.954 They reported on the clinical pathologic

NOTE Confidence: 0.846271117777778

00:06:57.954 --> 00:07:01.583 features of 14 patients with HS and they

NOTE Confidence: 0.846271117777778

00:07:01.583 --> 00:07:04.091 showed that the disease presentation was

NOTE Confidence: 0.846271117777778

00:07:04.169 --> 00:07:06.574 heterogeneous and quite variable with

NOTE Confidence: 0.846271117777778

00:07:06.574 --> 00:07:10.028 respect to the number and the type of

NOTE Confidence: 0.846271117777778

00:07:10.028 --> 00:07:12.320 organ systems that could be involved.

NOTE Confidence: 0.846271117777778

00:07:12.320 --> 00:07:15.416 They also reported that individuals that

NOTE Confidence: 0.846271117777778

00:07:15.416 --> 00:07:18.944 have cardiac or central nervous system

NOTE Confidence: 0.846271117777778

00:07:18.944 --> 00:07:22.399 involvement had particularly dismal outcomes,

NOTE Confidence: 0.846271117777778

00:07:22.400 --> 00:07:25.215 and they documented finally that

NOTE Confidence: 0.846271117777778

00:07:25.215 --> 00:07:27.467 most treatments are ineffective.

NOTE Confidence: 0.846271117777778

00:07:27.470 --> 00:07:30.142 Remarkably, their findings that

NOTE Confidence: 0.846271117777778

00:07:30.142 --> 00:07:33.542 they reported in 1975 capture much

NOTE Confidence: 0.846271117777778

00:07:33.542 --> 00:07:36.790 of what we still know today about

NOTE Confidence: 0.846271117777778

00:07:36.883 --> 00:07:39.339 Hypereosinophilic syndrome.

NOTE Confidence: 0.846271117777778

00:07:39.340 --> 00:07:41.314 Also of note and very interesting

NOTE Confidence: 0.846271117777778

00:07:41.314 --> 00:07:43.400 is that our modern definition,

NOTE Confidence: 0.846271117777778

00:07:43.400 --> 00:07:45.780 which I'll get to in a minute

NOTE Confidence: 0.846271117777778

00:07:45.780 --> 00:07:46.800 of Hypereosinophilic syndrome,

NOTE Confidence: 0.846271117777778

00:07:46.800 --> 00:07:50.478 is a vestige of their proposed

NOTE Confidence: 0.846271117777778

00:07:50.478 --> 00:07:52.710 diagnostic criteria in 1975,

NOTE Confidence: 0.846271117777778

00:07:52.710 --> 00:07:55.440 namely that you had to have an

NOTE Confidence: 0.846271117777778

00:07:55.440 --> 00:07:57.407 absolute acidophil count of greater

NOTE Confidence: 0.846271117777778

00:07:57.407 --> 00:08:00.716 than 1.5 * 10 to the 9th per liter.

NOTE Confidence: 0.846271117777778

00:08:00.720 --> 00:08:02.766 In their paper they had proposed

NOTE Confidence: 0.846271117777778

00:08:02.766 --> 00:08:05.075 that this was a persistent and

NOTE Confidence: 0.846271117777778

00:08:05.075 --> 00:08:07.685 sustained for at least six months.

NOTE Confidence: 0.846271117777778

00:08:07.690 --> 00:08:09.755 But we don't typically embrace

NOTE Confidence: 0.846271117777778

13

00:08:09.755 --> 00:08:12.450 the six month mark any longer,

NOTE Confidence: 0.846271117777778

00:08:12.450 --> 00:08:14.310 and that's for largely 2 reasons.

NOTE Confidence: 0.846271117777778

00:08:14.310 --> 00:08:15.046 One is,

NOTE Confidence: 0.846271117777778

00:08:15.046 --> 00:08:16.518 if patients have hypereosinophilia

NOTE Confidence: 0.846271117777778

00:08:16.518 --> 00:08:19.330 and we want to get them on treatment

NOTE Confidence: 0.846271117777778

00:08:19.330 --> 00:08:21.638 so that we can minimize any end

NOTE Confidence: 0.846271117777778

00:08:21.638 --> 00:08:23.690 organ damage that they may incur,

NOTE Confidence: 0.846271117777778

00:08:23.690 --> 00:08:25.895 and it's also because we have much

NOTE Confidence: 0.846271117777778

00:08:25.895 --> 00:08:27.575 more sophisticated tools to rapidly

NOTE Confidence: 0.846271117777778

00:08:27.575 --> 00:08:29.615 demonstrate that they are indeed clonal.

NOTE Confidence: 0.862994370384615

00:08:31.760 --> 00:08:34.469 So Fast forward to 2012 and this is our

NOTE Confidence: 0.862994370384615

00:08:34.469 --> 00:08:36.939 modern definition of hypereosinophilia.

NOTE Confidence: 0.862994370384615

00:08:36.940 --> 00:08:40.620 HE and Hypereosinophilic syndrome HES.

NOTE Confidence: 0.862994370384615

00:08:40.620 --> 00:08:43.014 Doctor Peter Violent and a group of

NOTE Confidence: 0.862994370384615

00:08:43.014 --> 00:08:45.007 experts in effect Affilia actually

NOTE Confidence: 0.862994370384615

00:08:45.007 --> 00:08:47.262 got together and they proposed

NOTE Confidence: 0.862994370384615

00:08:47.262 --> 00:08:49.120 common terminology and definitions

NOTE Confidence: 0.862994370384615

00:08:49.120 --> 00:08:51.718 for our US and affiliate disorders.

NOTE Confidence: 0.862994370384615

00:08:51.720 --> 00:08:55.185 Why so one of the major goals of this

NOTE Confidence: 0.862994370384615

00:08:55.185 --> 00:08:57.540 consensus paper was to enable us,

NOTE Confidence: 0.862994370384615

00:08:57.540 --> 00:08:59.724 as pathologists as clinicians,

NOTE Confidence: 0.862994370384615

00:08:59.724 --> 00:09:00.816 as laboratorians,

NOTE Confidence: 0.862994370384615

00:09:00.820 --> 00:09:03.244 to be able to communicate clearly

NOTE Confidence: 0.862994370384615

00:09:03.244 --> 00:09:06.126 across the board about what type of

NOTE Confidence: 0.862994370384615

00:09:06.126 --> 00:09:08.111 specific ES and affiliate disorder

NOTE Confidence: 0.862994370384615

00:09:08.111 --> 00:09:10.998 that an individual patient may have.

NOTE Confidence: 0.862994370384615

00:09:11.000 --> 00:09:13.448 In this consensus statement,

NOTE Confidence: 0.862994370384615

00:09:13.448 --> 00:09:15.896 HYPEREOSINOPHILIA was defined as

NOTE Confidence: 0.862994370384615

00:09:15.896 --> 00:09:17.628 persistent eosinophilia greater

NOTE Confidence: 0.862994370384615

00:09:17.628 --> 00:09:19.628 than 1.5 * 10 to the 9th per liter,

NOTE Confidence: 0.862994370384615

00:09:19.630 --> 00:09:20.630 and as I just mentioned,

NOTE Confidence: 0.862994370384615

00:09:20.630 --> 00:09:23.507 that's a vestige of the chosen paper.

NOTE Confidence: 0.862994370384615

00:09:23.510 --> 00:09:26.324 This has to be typically on two

NOTE Confidence: 0.862994370384615

00:09:26.324 --> 00:09:27.859 separate occasions separated by

NOTE Confidence: 0.862994370384615

00:09:27.859 --> 00:09:29.899 at least a month and or you have

NOTE Confidence: 0.862994370384615

00:09:29.899 --> 00:09:31.629 to have tissue hypereosinophilia

NOTE Confidence: 0.862994370384615

00:09:31.629 --> 00:09:33.974 which is greater than 20%.

NOTE Confidence: 0.862994370384615

00:09:33.980 --> 00:09:35.795 Eosinophils in the tissue of

NOTE Confidence: 0.862994370384615

00:09:35.795 --> 00:09:37.962 interest or bone marrow as defined

NOTE Confidence: 0.862994370384615

00:09:37.962 --> 00:09:40.098 by a pathologist or a marked

NOTE Confidence: 0.862994370384615

00:09:40.098 --> 00:09:42.094 deposition of use and affiliate

NOTE Confidence: 0.862994370384615

00:09:42.094 --> 00:09:44.512 granules and proteins in the tissue.

NOTE Confidence: 0.862994370384615

00:09:44.520 --> 00:09:45.398 Hypereosinophilic syndrome,

NOTE Confidence: 0.862994370384615

00:09:45.398 --> 00:09:48.032 obviously you need to meet the

NOTE Confidence: 0.862994370384615

00:09:48.032 --> 00:09:50.080 definition of hypereosinophilia,

NOTE Confidence: 0.862994370384615

00:09:50.080 --> 00:09:53.041 but in addition you have to have

NOTE Confidence: 0.862994370384615

00:09:53.041 --> 00:09:54.864 demonstrable end organ damage

16

NOTE Confidence: 0.862994370384615

00:09:54.864 --> 00:09:57.244 or dysfunction that is directly

NOTE Confidence: 0.862994370384615

00:09:57.244 --> 00:10:00.080 attributable to the SNF infiltrate,

NOTE Confidence: 0.862994370384615

00:10:00.080 --> 00:10:02.512 so it cannot be due to some other

NOTE Confidence: 0.862994370384615

00:10:02.512 --> 00:10:04.921 sort of disease process that has

NOTE Confidence: 0.862994370384615

00:10:04.921 --> 00:10:07.501 to be directly to the essentials.

NOTE Confidence: 0.862994370384615

00:10:07.510 --> 00:10:08.960 As shown in this table,

NOTE Confidence: 0.862994370384615

00:10:08.960 --> 00:10:10.815 the causes of ESPN affiliate

NOTE Confidence: 0.862994370384615

00:10:10.815 --> 00:10:12.670 are incredibly diverse and is,

NOTE Confidence: 0.862994370384615

00:10:12.670 --> 00:10:14.848 for me is one of the things I get

NOTE Confidence: 0.862994370384615

00:10:14.848 --> 00:10:16.959 nervous about when I see a casadia

NOTE Confidence: 0.862994370384615

00:10:16.959 --> 00:10:19.347 cinephilia because it is in fact so diverse.

NOTE Confidence: 0.862994370384615

00:10:19.350 --> 00:10:21.686 This may be due to a primary clonal

NOTE Confidence: 0.862994370384615

00:10:21.686 --> 00:10:24.005 state which you can see on the far left

NOTE Confidence: 0.862994370384615

00:10:24.010 --> 00:10:26.314 secondary to an underlying neoplasm in

NOTE Confidence: 0.862994370384615

00:10:26.314 --> 00:10:28.602 which the Essen affilia is actually

NOTE Confidence: 0.862994370384615

00:10:28.602 --> 00:10:30.648 reactive as shown in the center.

NOTE Confidence: 0.862994370384615

00:10:30.650 --> 00:10:33.758 Or it can be secondary to an

NOTE Confidence: 0.862994370384615

00:10:33.758 --> 00:10:36.040 entirely non neoplastic condition.

NOTE Confidence: 0.862994370384615

00:10:36.040 --> 00:10:37.687 In clinical practice,

NOTE Confidence: 0.862994370384615

00:10:37.687 --> 00:10:39.883 the overwhelming majority of

NOTE Confidence: 0.862994370384615

00:10:39.883 --> 00:10:42.357 hypereosinophilic states that we encounter

NOTE Confidence: 0.862994370384615

00:10:42.357 --> 00:10:45.373 are by far due to the secondary varieties.

NOTE Confidence: 0.862994370384615

00:10:45.380 --> 00:10:47.468 So in the case on the far right

NOTE Confidence: 0.862994370384615

00:10:47.468 --> 00:10:48.831 of entirely non neoplastic

NOTE Confidence: 0.862994370384615

00:10:48.831 --> 00:10:51.153 conditions this can be an infection,

NOTE Confidence: 0.862994370384615

00:10:51.160 --> 00:10:52.894 an allergic disorder,

NOTE Confidence: 0.862994370384615

00:10:52.894 --> 00:10:54.050 hypersensitivity reaction,

NOTE Confidence: 0.862994370384615

00:10:54.050 --> 00:10:55.126 drug reaction,

NOTE Confidence: 0.862994370384615

00:10:55.126 --> 00:10:56.740 a rheumatologic disease,

NOTE Confidence: 0.862994370384615

00:10:56.740 --> 00:10:57.835 and autoimmune phenomena.

NOTE Confidence: 0.862994370384615

00:10:57.835 --> 00:11:00.390 So there's a quite hefty number of

NOTE Confidence: 0.862994370384615

00:11:00.451 --> 00:11:02.486 underlying conditions that really need

NOTE Confidence: 0.862994370384615

00:11:02.486 --> 00:11:04.934 to be evaluated and excluded when

NOTE Confidence: 0.862994370384615

00:11:04.934 --> 00:11:07.016 presented with a case of essential.

NOTE Confidence: 0.862994370384615

00:11:07.020 --> 00:11:08.600 Earlier.

NOTE Confidence: 0.862994370384615

00:11:08.600 --> 00:11:10.592 In the cases that have an

NOTE Confidence: 0.862994370384615

00:11:10.592 --> 00:11:11.256 underlying neoplasm,

NOTE Confidence: 0.862994370384615

00:11:11.260 --> 00:11:13.000 whereby the is an affiliate,

NOTE Confidence: 0.862994370384615

00:11:13.000 --> 00:11:15.296 is reactive, as many of you know,

NOTE Confidence: 0.862994370384615

00:11:15.300 --> 00:11:18.036 we see this in cases of T cell lymphomas,

NOTE Confidence: 0.862994370384615

00:11:18.040 --> 00:11:19.093 classical Hodgkin lymphoma.

NOTE Confidence: 0.862994370384615

00:11:19.093 --> 00:11:22.756 For sure we can see it in a subset of

NOTE Confidence: 0.862994370384615

00:11:22.756 --> 00:11:25.024 carcinomas as well as the lymphocytic

NOTE Confidence: 0.862994370384615

00:11:25.024 --> 00:11:27.459 variant of Hypereosinophilic syndrome.

NOTE Confidence: 0.862994370384615

00:11:27.460 --> 00:11:30.526 As for the primary clonal Essen affiliates,

NOTE Confidence: 0.862994370384615

00:11:30.530 --> 00:11:32.756 these are of course less common,

NOTE Confidence: 0.862994370384615

00:11:32.760 --> 00:11:34.972 but as you can see from the

NOTE Confidence: 0.862994370384615

00:11:34.972 --> 00:11:36.978 less left side of the table,

NOTE Confidence: 0.862994370384615

00:11:36.980 --> 00:11:38.126 the diagnostic possibilities.

NOTE Confidence: 0.862994370384615

00:11:38.126 --> 00:11:40.800 Usually the one we consider first is

NOTE Confidence: 0.862994370384615

00:11:40.866 --> 00:11:42.786 chronically is cinephilic leukemia

NOTE Confidence: 0.862994370384615

00:11:42.786 --> 00:11:45.850 not otherwise specified and we have

NOTE Confidence: 0.862994370384615

00:11:45.850 --> 00:11:48.550 the new recently introduced WHO

NOTE Confidence: 0.862994370384615

00:11:48.550 --> 00:11:51.496 category of myeloid slash lymphoid

NOTE Confidence: 0.862994370384615

00:11:51.496 --> 00:11:55.619 neoplasms with ease and ophilia and a

NOTE Confidence: 0.781246922692308

00:11:55.720 --> 00:11:58.272 rearrangement of PDGFRA PDGFRB

NOTE Confidence: 0.781246922692308

00:11:58.272 --> 00:12:01.002 FGFR one and or Jack two.

NOTE Confidence: 0.781246922692308

00:12:01.002 --> 00:12:02.817 You can also see occasional

NOTE Confidence: 0.781246922692308

00:12:02.817 --> 00:12:04.940 cases of acute myeloid leukemia

NOTE Confidence: 0.781246922692308

00:12:04.940 --> 00:12:07.466 AML that can have Essen affilia,

NOTE Confidence: 0.781246922692308

00:12:07.470 --> 00:12:08.451 namely inversion 16.

NOTE Confidence: 0.781246922692308

00:12:08.451 --> 00:12:10.740 As well as a handful of other

NOTE Confidence: 0.781246922692308

00:12:10.815 --> 00:12:12.519 chronic myeloid disorders.

NOTE Confidence: 0.774982473846154

00:12:14.670 --> 00:12:16.812 So based on the diversity of causes

NOTE Confidence: 0.774982473846154

00:12:16.812 --> 00:12:18.968 of the oscillant theus and affiliate,

NOTE Confidence: 0.774982473846154

00:12:18.970 --> 00:12:21.730 this then naturally leads to a broad array.

NOTE Confidence: 0.774982473846154

00:12:21.730 --> 00:12:24.322 As I mentioned in the introduction

NOTE Confidence: 0.774982473846154

00:12:24.322 --> 00:12:26.050 of diagnostic testing options.

NOTE Confidence: 0.774982473846154

00:12:26.050 --> 00:12:27.506 As you can see on this slide,

NOTE Confidence: 0.774982473846154

00:12:27.510 --> 00:12:28.598 this is pretty chaotic,

NOTE Confidence: 0.774982473846154

00:12:28.598 --> 00:12:30.710 right that they are all over the map.

NOTE Confidence: 0.774982473846154

00:12:30.710 --> 00:12:33.054 They range from morphology

NOTE Confidence: 0.774982473846154

00:12:33.054 --> 00:12:34.226 to immunohistochemistry,

NOTE Confidence: 0.774982473846154

00:12:34.230 --> 00:12:37.718 to flow to cytogenetics to fish to next

NOTE Confidence: 0.774982473846154

00:12:37.718 --> 00:12:40.170 generation sequencing for myeloid disorder,

NOTE Confidence: 0.774982473846154

00:12:40.170 --> 00:12:41.715 associated genetic mutations.

NOTE Confidence: 0.774982473846154

00:12:41.715 --> 00:12:44.290 So the situation with the.

NOTE Confidence: 0.774982473846154

00:12:44.290 --> 00:12:46.242 Julia becomes very complicated,

NOTE Confidence: 0.774982473846154

00:12:46.242 --> 00:12:47.706 complicated and complex,

NOTE Confidence: 0.774982473846154

00:12:47.710 --> 00:12:49.960 pretty quick, and the question

NOTE Confidence: 0.774982473846154

00:12:49.960 --> 00:12:51.766 is what tests do we start with?

NOTE Confidence: 0.774982473846154

00:12:51.770 --> 00:12:54.639 Do I do them all or do I just do a subset?

NOTE Confidence: 0.925379948571429

00:12:57.160 --> 00:13:00.088 So as you can see from the number

NOTE Confidence: 0.925379948571429

00:13:00.088 --> 00:13:02.539 of references listed on this slide,

NOTE Confidence: 0.925379948571429

00:13:02.540 --> 00:13:04.716 many investigators advocate in

NOTE Confidence: 0.925379948571429

00:13:04.716 --> 00:13:07.436 2022 for a systematic approach

NOTE Confidence: 0.925379948571429

00:13:07.436 --> 00:13:10.357 to the work of ES and AFFILIA.

NOTE Confidence: 0.925379948571429

00:13:10.360 --> 00:13:12.472 Most will agree that this is

NOTE Confidence: 0.925379948571429

00:13:12.472 --> 00:13:13.880 a reasonable starting point.

NOTE Confidence: 0.925379948571429

00:13:13.880 --> 00:13:17.280 Step one, exclude secondary causes.

NOTE Confidence: 0.925379948571429

00:13:17.280 --> 00:13:18.540 And of course this is very,

NOTE Confidence: 0.925379948571429

00:13:18.540 --> 00:13:20.280 very difficult to do because

NOTE Confidence: 0.925379948571429

00:13:20.280 --> 00:13:22.609 it generally in invokes a lot

NOTE Confidence: 0.925379948571429

00:13:22.609 --> 00:13:24.157 of different subspecialties.

NOTE Confidence: 0.925379948571429

00:13:24.160 --> 00:13:25.695 A lot of different testing

NOTE Confidence: 0.925379948571429

00:13:25.695 --> 00:13:27.230 that has to be done.

NOTE Confidence: 0.925379948571429

00:13:27.230 --> 00:13:29.141 But this you want to try and

NOTE Confidence: 0.925379948571429

00:13:29.141 --> 00:13:31.088 do this because you don't want

NOTE Confidence: 0.925379948571429

00:13:31.088 --> 00:13:32.504 to unnecessarily subject your

NOTE Confidence: 0.925379948571429

00:13:32.504 --> 00:13:34.809 patient to a bone marrow biopsy.

NOTE Confidence: 0.925379948571429

00:13:34.810 --> 00:13:37.354 If the patient is deemed to

NOTE Confidence: 0.925379948571429

00:13:37.354 --> 00:13:39.050 not have a demonstrable,

NOTE Confidence: 0.925379948571429

00:13:39.050 --> 00:13:43.726 determined reactive cause for the SN affilia,

NOTE Confidence: 0.925379948571429

00:13:43.730 --> 00:13:46.114 then we move to Step 2 and this

NOTE Confidence: 0.925379948571429

00:13:46.114 --> 00:13:48.572 is where the clinician has deemed

NOTE Confidence: 0.925379948571429

00:13:48.572 --> 00:13:50.807 it necessary for the pathologist

NOTE Confidence: 0.925379948571429

00:13:50.807 --> 00:13:53.264 to exclude a primary peripheral

NOTE Confidence: 0.925379948571429

00:13:53.264 --> 00:13:55.684 blood and bone marrow clonal

NOTE Confidence: 0.925379948571429

00:13:55.684 --> 00:13:57.786 process for us as pathologist.

NOTE Confidence: 0.925379948571429

00:13:57.786 --> 00:13:59.806 This is an extremely important

NOTE Confidence: 0.925379948571429

00:13:59.806 --> 00:14:02.541 step in the process because the

NOTE Confidence: 0.925379948571429

00:14:02.541 --> 00:14:04.801 prognosis differ hugely between these.

NOTE Confidence: 0.925379948571429

00:14:04.810 --> 00:14:05.833 Entities and several.

NOTE Confidence: 0.925379948571429

00:14:05.833 --> 00:14:07.197 As you will hear,

NOTE Confidence: 0.925379948571429

00:14:07.200 --> 00:14:09.940 have very specific targeted therapies.

NOTE Confidence: 0.925379948571429

00:14:09.940 --> 00:14:10.918 For example,

NOTE Confidence: 0.925379948571429

00:14:10.918 --> 00:14:12.385 rearrangements that involve

NOTE Confidence: 0.925379948571429

00:14:12.385 --> 00:14:15.492 PDGFR alpha or PDGFR beta are

NOTE Confidence: 0.925379948571429

00:14:15.492 --> 00:14:17.828 exquisitely sensitive to tyrosine

NOTE Confidence: 0.925379948571429

00:14:17.828 --> 00:14:19.580 kinase inhibitor therapy,

NOTE Confidence: 0.925379948571429

00:14:19.580 --> 00:14:21.449 so we're not going to want to

NOTE Confidence: 0.925379948571429

00:14:21.449 --> 00:14:23.228 miss a lesion like that that

NOTE Confidence: 0.925379948571429

00:14:23.228 --> 00:14:25.052 maybe the patient does not have

NOTE Confidence: 0.925379948571429

00:14:25.052 --> 00:14:26.730 to undergo chemotherapy.

NOTE Confidence: 0.925379948571429

00:14:26.730 --> 00:14:29.383 Step #3 is you've ruled out all

NOTE Confidence: 0.925379948571429

00:14:29.383 --> 00:14:31.360 the primary clonal disorders.

NOTE Confidence: 0.925379948571429

00:14:31.360 --> 00:14:33.408 You don't see an underlying T cell lymphoma.

NOTE Confidence: 0.925379948571429

00:14:33.410 --> 00:14:36.506 Reactive cause is not readily discernible.

NOTE Confidence: 0.925379948571429

00:14:36.510 --> 00:14:39.450 The specific diagnosis can't be rendered in.

NOTE Confidence: 0.925379948571429

00:14:39.450 --> 00:14:40.221 In most situations,

NOTE Confidence: 0.925379948571429

00:14:40.221 --> 00:14:41.763 we're going to sign out the

NOTE Confidence: 0.925379948571429

00:14:41.763 --> 00:14:43.109 bone marrow descriptively,

NOTE Confidence: 0.925379948571429

00:14:43.110 --> 00:14:44.846 and specifically mention which

NOTE Confidence: 0.925379948571429

00:14:44.846 --> 00:14:47.450 diseases we were able to exclude.

NOTE Confidence: 0.849042092133333

00:14:50.080 --> 00:14:52.341 So this slide expands upon the quote

NOTE Confidence: 0.849042092133333

00:14:52.341 --> 00:14:54.265 three steps that I just talked

NOTE Confidence: 0.849042092133333

00:14:54.265 --> 00:14:56.351 about and shows a more granular and

NOTE Confidence: 0.849042092133333

00:14:56.418 --> 00:14:59.232 algorithmic approach to the work up of

NOTE Confidence: 0.849042092133333

00:14:59.232 --> 00:15:00.904 sustained unexplained Essen affilia.

NOTE Confidence: 0.849042092133333

25

00:15:00.904 --> 00:15:04.152 The entry point into this algorithm is

NOTE Confidence: 0.849042092133333

00:15:04.152 --> 00:15:07.720 after step one has theoretically been done.

NOTE Confidence: 0.849042092133333

00:15:07.720 --> 00:15:09.386 So again, that is going to be.

NOTE Confidence: 0.849042092133333

00:15:09.390 --> 00:15:10.954 Oftentimes it's a multidisciplinary

NOTE Confidence: 0.849042092133333

00:15:10.954 --> 00:15:13.711 set of clinicians they've done a lot

NOTE Confidence: 0.849042092133333

00:15:13.711 --> 00:15:15.436 of testing to exclude infection,

NOTE Confidence: 0.849042092133333

00:15:15.440 --> 00:15:19.352 drug autoimmune rheumatologic disorders,

NOTE Confidence: 0.849042092133333

00:15:19.352 --> 00:15:20.330 etcetera.

NOTE Confidence: 0.849042092133333

00:15:20.330 --> 00:15:22.220 If at this point the patient is

NOTE Confidence: 0.849042092133333

00:15:22.220 --> 00:15:24.356 clinically stable so they're not sick

NOTE Confidence: 0.849042092133333

00:15:24.356 --> 00:15:25.628 from Hypereosinophilic syndrome,

NOTE Confidence: 0.849042092133333

00:15:25.630 --> 00:15:27.760 many of us would advocate beginning

NOTE Confidence: 0.849042092133333

00:15:27.760 --> 00:15:29.579 by assessing the peripheral blood

NOTE Confidence: 0.849042092133333

00:15:29.579 --> 00:15:31.607 and bone marrow morphology for peak.

NOTE Confidence: 0.849042092133333

00:15:31.610 --> 00:15:34.538 For features that point us to a specific

NOTE Confidence: 0.849042092133333

00:15:34.538 --> 00:15:36.410 entity, as shown by the blue arrow.

NOTE Confidence: 0.849042092133333

00:15:36.410 --> 00:15:37.789 So what do I mean by that?

NOTE Confidence: 0.849042092133333

00:15:37.790 --> 00:15:39.204 So if you look in the bone

NOTE Confidence: 0.849042092133333

00:15:39.204 --> 00:15:40.730 marrow or the peripheral blood,

NOTE Confidence: 0.849042092133333

00:15:40.730 --> 00:15:41.830 and you see features, oh,

NOTE Confidence: 0.849042092133333

00:15:41.830 --> 00:15:43.098 this might be mastocytosis.

NOTE Confidence: 0.849042092133333

00:15:43.098 --> 00:15:46.178 Or this might be a specific type of myeloid

NOTE Confidence: 0.849042092133333

00:15:46.178 --> 00:15:48.410 neoplasm such as chronic myeloid leukemia,

NOTE Confidence: 0.849042092133333

00:15:48.410 --> 00:15:50.250 or you see lymphoma, then.

NOTE Confidence: 0.849042092133333

00:15:50.250 --> 00:15:51.470 If that's the case.

NOTE Confidence: 0.849042092133333

00:15:51.470 --> 00:15:54.009 Then we would start by doing a very

NOTE Confidence: 0.849042092133333

00:15:54.009 --> 00:15:56.235 targeted work up rather than the very

NOTE Confidence: 0.849042092133333

00:15:56.235 --> 00:15:58.570 broad and affilia type of approach.

NOTE Confidence: 0.906969326

00:16:00.610 --> 00:16:03.880 So here's an example of this in in real life.

NOTE Confidence: 0.906969326

00:16:03.880 --> 00:16:06.040 This patient was a 48 year old woman.

NOTE Confidence: 0.906969326

00:16:06.040 --> 00:16:08.086 She presented to her primary care

NOTE Confidence: 0.906969326

00:16:08.086 --> 00:16:10.320 physician with left Upper Quadrant Pain.

NOTE Confidence: 0.906969326

00:16:10.320 --> 00:16:12.800 They did a CBC and you can see those showed

NOTE Confidence: 0.906969326

00:16:12.862 --> 00:16:15.136 this whopping Leukocytosis with a greater

NOTE Confidence: 0.906969326

00:16:15.136 --> 00:16:17.730 than 100,000 white blood cell count.

NOTE Confidence: 0.906969326

00:16:17.730 --> 00:16:18.486 The peripheral blood,

NOTE Confidence: 0.906969326

00:16:18.486 --> 00:16:20.710 which I've shown you a snapshot on the left,

NOTE Confidence: 0.906969326

00:16:20.710 --> 00:16:22.234 definitely shows increased esena

NOTE Confidence: 0.906969326

00:16:22.234 --> 00:16:24.950 filters at least five in this field,

NOTE Confidence: 0.906969326

00:16:24.950 --> 00:16:27.326 and when you have a white count of 100,000,

NOTE Confidence: 0.906969326

00:16:27.330 --> 00:16:29.930 it's pretty obvious that you're going to meet

NOTE Confidence: 0.906969326

00:16:29.930 --> 00:16:32.269 the diagnostic criteria for Edison affiliate.

NOTE Confidence: 0.906969326

00:16:32.270 --> 00:16:35.090 However, in addition to the essentials,

NOTE Confidence: 0.906969326

00:16:35.090 --> 00:16:36.518 what do we see?

NOTE Confidence: 0.906969326

00:16:36.518 --> 00:16:39.200 We also see a granulocytic left shift.

NOTE Confidence: 0.906969326

00:16:39.200 --> 00:16:42.670 No dysplasia and increased basophils.

NOTE Confidence: 0.906969326

00:16:42.670 --> 00:16:44.574 When you look in the bone marrow aspirate

00:16:44.574 --> 00:16:46.126 smear which is shown in the center,

00:16:46.130 --> 00:16:47.288 what do we see? We see.

00:16:47.290 --> 00:16:48.174 It's hypercellular.

00:16:48.174 --> 00:16:49.942 There's a granulocytic predominance

00:16:49.942 --> 00:16:52.690 and look at those megakaryocytes.

00:16:52.690 --> 00:16:53.482 They're small.

00:16:53.482 --> 00:16:54.670 They're monologue eated.

00:16:54.670 --> 00:16:56.010 We have dwarf forms,

00:16:56.010 --> 00:16:58.020 so we're getting a little suspicious

00:16:58.084 --> 00:17:00.202 that we might be dealing with

00:17:00.202 --> 00:17:01.790 something specific on the far right

00:17:01.790 --> 00:17:03.510 you see the bone marrow core biopsy.

00:17:03.510 --> 00:17:06.730 It's basically packed 100% cellular

00:17:06.730 --> 00:17:08.018 granulocytic predominance.

00:17:08.020 --> 00:17:09.820 I mean the any ratio has got to

00:17:09.820 --> 00:17:11.488 be greater than 12:50 and you

NOTE Confidence: 0.906969326

00:17:11.488 --> 00:17:12.943 can see those small monologue.

NOTE Confidence: 0.906969326

00:17:12.950 --> 00:17:15.086 Get into dwarf megakaryocytes.

NOTE Confidence: 0.906969326

00:17:15.086 --> 00:17:17.756 So in this particular situation,

NOTE Confidence: 0.906969326

00:17:17.760 --> 00:17:19.360 do we have eosinophilia?

NOTE Confidence: 0.906969326

00:17:19.360 --> 00:17:19.760 Yes,

NOTE Confidence: 0.906969326

00:17:19.760 --> 00:17:22.496 but we have other features that might be

NOTE Confidence: 0.906969326

00:17:22.496 --> 00:17:24.272 suggesting what chronic myeloid leukemia.

NOTE Confidence: 0.906969326

00:17:24.272 --> 00:17:26.774 So rather than me doing all as

NOTE Confidence: 0.906969326

00:17:26.774 --> 00:17:28.520 I'm going to go through later,

NOTE Confidence: 0.906969326

00:17:28.520 --> 00:17:31.019 all the ES and affiliate related testing,

NOTE Confidence: 0.906969326

00:17:31.020 --> 00:17:33.435 we would probably start with a targeted

NOTE Confidence: 0.906969326

00:17:33.435 --> 00:17:35.341 work up looking for chromosomes

NOTE Confidence: 0.906969326

00:17:35.341 --> 00:17:36.949 at for Philadelphia chromosome

NOTE Confidence: 0.906969326

00:17:36.949 --> 00:17:39.293 and doing fish or molecular for

NOTE Confidence: 0.906969326

00:17:39.293 --> 00:17:41.315 the BCR ABL 1 fusion protein.

NOTE Confidence: 0.906969326

00:17:41.320 --> 00:17:43.732 And in fact that's what we did and we

NOTE Confidence: 0.906969326

00:17:43.732 --> 00:17:45.490 diagnosed this case as CML BCR ABL.

NOTE Confidence: 0.906969326

00:17:45.490 --> 00:17:47.270 And positive chronic phase.

NOTE Confidence: 0.906969326

00:17:47.270 --> 00:17:50.450 So in the context of this case,

NOTE Confidence: 0.906969326

00:17:50.450 --> 00:17:53.168 the ESCENA affiliate is technically present,

NOTE Confidence: 0.906969326

00:17:53.170 --> 00:17:55.739 but it exists merely because of the

NOTE Confidence: 0.906969326

00:17:55.739 --> 00:17:58.089 context of the overall disease.

NOTE Confidence: 0.906969326

00:17:58.090 --> 00:18:02.110 It's not its own distinct clonal

NOTE Confidence: 0.906969326

00:18:02.110 --> 00:18:03.450 theosophic disorder.

NOTE Confidence: 0.906969326

00:18:03.450 --> 00:18:03.641 OK,

NOTE Confidence: 0.906969326

00:18:03.641 --> 00:18:05.169 So what do we do in a situation

NOTE Confidence: 0.906969326

00:18:05.169 --> 00:18:06.863 where I don't see features that

NOTE Confidence: 0.906969326

00:18:06.863 --> 00:18:08.023 suggest a particular disorder?

NOTE Confidence: 0.906969326

00:18:08.030 --> 00:18:09.366 It's not mass cells.

NOTE Confidence: 0.906969326

00:18:09.366 --> 00:18:10.368 It's not lymphoma.

NOTE Confidence: 0.906969326

31

00:18:10.370 --> 00:18:12.795 Well based on the differential

NOTE Confidence: 0.906969326

00:18:12.795 --> 00:18:14.250 diagnostic possibilities that

NOTE Confidence: 0.906969326

00:18:14.250 --> 00:18:16.510 I mentioned mentioned back on.

NOTE Confidence: 0.906969326

00:18:16.510 --> 00:18:18.310 On the potential causes of

NOTE Confidence: 0.906969326

00:18:18.310 --> 00:18:19.750 primary colors and affilia,

NOTE Confidence: 0.906969326

00:18:19.750 --> 00:18:21.106 this could be mass cell disease.

NOTE Confidence: 0.906969326

00:18:21.110 --> 00:18:23.078 It could be chronic and Phillip

NOTE Confidence: 0.906969326

00:18:23.078 --> 00:18:24.390 leukemia not otherwise specified.

NOTE Confidence: 0.906969326

00:18:24.390 --> 00:18:26.903 Maybe it's one of those new myeloid

NOTE Confidence: 0.906969326

00:18:26.903 --> 00:18:29.195 slash lymphoid neoplasms with ease and

NOTE Confidence: 0.906969326

00:18:29.195 --> 00:18:31.505 affilia and a recurring genetic abnormality.

NOTE Confidence: 0.906969326

00:18:31.510 --> 00:18:34.110 Maybe it has a subtle T cell clone.

NOTE Confidence: 0.906969326

00:18:34.110 --> 00:18:35.965 So based on studies that

NOTE Confidence: 0.906969326

00:18:35.965 --> 00:18:37.449 are in the literature,

NOTE Confidence: 0.906969326

00:18:37.450 --> 00:18:38.480 peer reviewed,

NOTE Confidence: 0.906969326

00:18:38.480 --> 00:18:40.025 published literature reasonable

NOTE Confidence: 0.906969326

00:18:40.025 --> 00:18:41.570 up front testing,

NOTE Confidence: 0.906969326

00:18:41.570 --> 00:18:43.175 which is highlighted by the

NOTE Confidence: 0.906969326

00:18:43.175 --> 00:18:45.100 the boxes with the Blue Star

NOTE Confidence: 0.906969326

00:18:45.100 --> 00:18:47.492 immunohistochemistry for mast cells,

NOTE Confidence: 0.906969326

00:18:47.492 --> 00:18:50.200 T cell flow cytometry tree

NOTE Confidence: 0.906969326

00:18:50.200 --> 00:18:51.750 looking for subtle ibara clones.

NOTE Confidence: 0.906969326

00:18:51.750 --> 00:18:52.878 Kit D816V mutation,

NOTE Confidence: 0.906969326

00:18:52.878 --> 00:18:55.134 which is seen in the overwhelming

NOTE Confidence: 0.906969326

00:18:55.134 --> 00:18:57.207 majority cases of mass cell disease,

NOTE Confidence: 0.906969326

00:18:57.210 --> 00:18:58.594 want to do chromosomes,

NOTE Confidence: 0.906969326

00:18:58.594 --> 00:18:59.286 you know,

NOTE Confidence: 0.906969326

00:18:59.290 --> 00:19:00.874 just general karyotyping and

NOTE Confidence: 0.906969326

00:19:00.874 --> 00:19:03.250 you're going to want to do

NOTE Confidence: 0.802948320714286

00:19:03.322 --> 00:19:04.690 fish for the PDGFR.

NOTE Confidence: 0.802948320714286

00:19:04.690 --> 00:19:05.516 Offer rearrangement.

NOTE Confidence: 0.802948320714286

00:19:05.516 --> 00:19:07.994 I would also suggest considering given

NOTE Confidence: 0.802948320714286

00:19:07.994 --> 00:19:10.320 how the complexity of the Ascent

NOTE Confidence: 0.802948320714286

00:19:10.320 --> 00:19:12.840 affiliate is going to continue to grow.

NOTE Confidence: 0.802948320714286

00:19:12.840 --> 00:19:16.656 Consider doing DNA and RNA extract and hold.

NOTE Confidence: 0.802948320714286

00:19:16.660 --> 00:19:17.960 So you may be wondering,

NOTE Confidence: 0.802948320714286

00:19:17.960 --> 00:19:19.830 well why am I going to do fish for the

NOTE Confidence: 0.802948320714286

00:19:19.881 --> 00:19:21.771 PDGFR alpha when you mentioned that there

NOTE Confidence: 0.802948320714286

00:19:21.771 --> 00:19:23.919 are four that are recognized by The Who?

NOTE Confidence: 0.802948320714286

00:19:23.920 --> 00:19:26.701 So the reason for that is that the PDGFR

NOTE Confidence: 0.802948320714286

00:19:26.701 --> 00:19:29.436 alpha rearrangement in greater than 80 to

NOTE Confidence: 0.802948320714286

00:19:29.440 --> 00:19:32.140 85% of cases is cytogenetically cryptic,

NOTE Confidence: 0.802948320714286

00:19:32.140 --> 00:19:34.282 so you won't see it by a

NOTE Confidence: 0.802948320714286

00:19:34.282 --> 00:19:35.200 routine chromosomal study,

NOTE Confidence: 0.802948320714286

00:19:35.200 --> 00:19:36.810 so we don't want to miss this

NOTE Confidence: 0.802948320714286

00:19:36.810 --> 00:19:38.090 diagnosis number one because we

NOTE Confidence: 0.802948320714286

00:19:38.090 --> 00:19:39.440 won't see it with chromosomes,

NOTE Confidence: 0.802948320714286

00:19:39.440 --> 00:19:40.526 but number two.

NOTE Confidence: 0.802948320714286

00:19:40.526 --> 00:19:43.060 As I mentioned it is exquisitely sensitive

NOTE Confidence: 0.802948320714286

00:19:43.128 --> 00:19:45.438 to tyrosine kinase inhibitor therapy,

NOTE Confidence: 0.802948320714286

00:19:45.440 --> 00:19:46.658 so you really have to do.

NOTE Confidence: 0.802948320714286

00:19:46.660 --> 00:19:49.292 Because some laboratories would do it by

NOTE Confidence: 0.802948320714286

00:19:49.292 --> 00:19:51.828 molecular up front for this abnormality.

NOTE Confidence: 0.802948320714286

00:19:51.830 --> 00:19:54.746 Depending on what this aggregate of

NOTE Confidence: 0.802948320714286

00:19:54.746 --> 00:19:57.789 ancillary studies shows or doesn't show,

NOTE Confidence: 0.802948320714286

00:19:57.790 --> 00:19:59.995 this is going to help inform us

NOTE Confidence: 0.802948320714286

00:19:59.995 --> 00:20:02.650 as to whether we can move towards

NOTE Confidence: 0.802948320714286

00:20:02.650 --> 00:20:03.880 a specific diagnosis.

NOTE Confidence: 0.802948320714286

00:20:03.880 --> 00:20:06.157 So here's an example of of what I mean.

NOTE Confidence: 0.802948320714286

00:20:06.160 --> 00:20:09.132 So this this is a 59 year old woman.

NOTE Confidence: 0.802948320714286

00:20:09.132 --> 00:20:11.590 She hasn't been feeling well for 15 years.

NOTE Confidence: 0.802948320714286

00:20:11.590 --> 00:20:12.646 Can you imagine?

NOTE Confidence: 0.802948320714286

00:20:12.646 --> 00:20:14.054 15 years foggy brain.

NOTE Confidence: 0.802948320714286

00:20:14.060 --> 00:20:16.440 She has like spills occasionally.

NOTE Confidence: 0.802948320714286

00:20:16.440 --> 00:20:17.760 She has some abdominal pain,

NOTE Confidence: 0.802948320714286

00:20:17.760 --> 00:20:19.092 but it's not really.

NOTE Confidence: 0.802948320714286

00:20:19.092 --> 00:20:20.740 You know, chronologically reproducible.

NOTE Confidence: 0.802948320714286

00:20:20.740 --> 00:20:24.660 No itching and then she has these occasional

NOTE Confidence: 0.802948320714286

00:20:24.734 --> 00:20:27.520 small red freckles on her bilateral shins.

NOTE Confidence: 0.802948320714286

00:20:27.520 --> 00:20:28.880 So of course you know she's going to

NOTE Confidence: 0.802948320714286

00:20:28.880 --> 00:20:30.439 go in through her primary care doc.

NOTE Confidence: 0.802948320714286

00:20:30.440 --> 00:20:32.252 She gets extensive testing.

NOTE Confidence: 0.802948320714286

00:20:32.252 --> 00:20:33.808 Infectious disease, autoimmune.

NOTE Confidence: 0.802948320714286

00:20:33.808 --> 00:20:36.400 Rheumatology, you know etcetera.

NOTE Confidence: 0.802948320714286

00:20:36.400 --> 00:20:37.564 Drugs medications.

NOTE Confidence: 0.802948320714286

00:20:37.564 --> 00:20:39.310 Everything is negative,

NOTE Confidence: 0.802948320714286

00:20:39.310 --> 00:20:41.310 so they do a CBC and you can see here.

NOTE Confidence: 0.802948320714286

00:20:41.310 --> 00:20:42.522 It's basically unremarkable.

NOTE Confidence: 0.802948320714286

00:20:42.522 --> 00:20:44.946 All the counts are normal except

NOTE Confidence: 0.802948320714286

00:20:44.946 --> 00:20:46.879 the absolute east and a field

NOTE Confidence: 0.802948320714286

00:20:46.879 --> 00:20:48.968 count is 580 which is just over

NOTE Confidence: 0.802948320714286

00:20:48.968 --> 00:20:51.208 our upper range of normal of a 500.

NOTE Confidence: 0.802948320714286

00:20:51.210 --> 00:20:53.370 So we look at our peripheral blood smear

NOTE Confidence: 0.802948320714286

00:20:53.370 --> 00:20:55.547 and see if we see anything basically

NOTE Confidence: 0.802948320714286

00:20:55.547 --> 00:20:58.889 compatible with the CBC differential matches.

NOTE Confidence: 0.802948320714286

00:20:58.890 --> 00:21:00.390 There's a few mature EO,

NOTE Confidence: 0.802948320714286

00:21:00.390 --> 00:21:02.226 a few scattered monos and neutrophils.

NOTE Confidence: 0.802948320714286

00:21:02.230 --> 00:21:04.938 So pretty much boring.

NOTE Confidence: 0.802948320714286

00:21:04.940 --> 00:21:07.058 Bone marrow aspirate was also performed.

NOTE Confidence: 0.802948320714286

00:21:07.060 --> 00:21:08.080 Relatively unremarkable.

NOTE Confidence: 0.802948320714286

00:21:08.080 --> 00:21:11.140 There's intact trial and intimate voices.

NOTE Confidence: 0.802948320714286

00:21:11.140 --> 00:21:12.336 We have progressive maturation.

NOTE Confidence: 0.802948320714286

00:21:12.336 --> 00:21:14.530 We don't have an increase in blasts.

NOTE Confidence: 0.802948320714286

00:21:14.530 --> 00:21:15.700 We don't have lymphoma cells.

00:21:15.700 --> 00:21:17.009 We don't have an increase in monos.

00:21:17.010 --> 00:21:18.346 We have no dysplasia.

00:21:18.346 --> 00:21:20.759 We have no basophils and we have

00:21:20.759 --> 00:21:22.732 about 4% epinephelus and uphill.

00:21:22.732 --> 00:21:25.180 So you know not that impressive.

00:21:25.180 --> 00:21:25.590 We did.

00:21:25.590 --> 00:21:26.000 Also note,

00:21:26.000 --> 00:21:27.230 you know every now and then

00:21:27.280 --> 00:21:28.710 there were scattered mast cells,

00:21:28.710 --> 00:21:30.327 but you really had to hunt for

00:21:30.327 --> 00:21:32.315 them and for the most part they

00:21:32.315 --> 00:21:33.865 were round and relatively mature.

00:21:33.870 --> 00:21:35.170 But occasionally there was a.

00:21:35.170 --> 00:21:39.074 Single form. Bone marrow core biopsy.

00:21:39.074 --> 00:21:40.480 Again, completely unremarkable.

NOTE Confidence: 0.802948320714286

00:21:40.480 --> 00:21:43.510 Normal cellular for her age progressive

NOTE Confidence: 0.802948320714286

00:21:43.510 --> 00:21:46.210 intact normal trilineage hematopoiesis.

NOTE Confidence: 0.802948320714286

00:21:46.210 --> 00:21:48.880 No obvious bone abnormalities or no

NOTE Confidence: 0.802948320714286

00:21:48.880 --> 00:21:52.639 infiltrates, no granulomas etcetera.

NOTE Confidence: 0.802948320714286

00:21:52.640 --> 00:21:54.956 But because of the subtle increase

NOTE Confidence: 0.802948320714286

00:21:54.956 --> 00:21:57.304 in her peripheral eyes and ophilia

NOTE Confidence: 0.802948320714286

00:21:57.304 --> 00:21:59.500 and the history that the clinician

NOTE Confidence: 0.802948320714286

00:21:59.500 --> 00:22:02.031 told us of spells and these red

NOTE Confidence: 0.802948320714286

00:22:02.031 --> 00:22:03.415 freckles on her shins,

NOTE Confidence: 0.822355347777778

00:22:03.420 --> 00:22:06.297 we did deploy the algorithmic approach for

NOTE Confidence: 0.822355347777778

00:22:06.297 --> 00:22:08.788 eastern Affilia, which, as I mentioned,

NOTE Confidence: 0.822355347777778

00:22:08.788 --> 00:22:10.873 includes immunohistochemistry for mast cells.

NOTE Confidence: 0.822355347777778

00:22:10.880 --> 00:22:12.916 And as you can see here, I've shown

NOTE Confidence: 0.822355347777778

00:22:12.916 --> 00:22:14.706 it at two different magnifications.

NOTE Confidence: 0.822355347777778

00:22:14.710 --> 00:22:16.850 The tryptase stains highlight no.

NOTE Confidence: 0.822355347777778

00:22:16.850 --> 00:22:18.677 I don't know. It's a normal number.

00:22:18.680 --> 00:22:21.396 Maybe a slight increase in mass cells,

00:22:21.400 --> 00:22:24.488 but as you can appreciate a good proportion

00:22:24.488 --> 00:22:27.389 of them appear distinctly spindled.

00:22:27.390 --> 00:22:29.946 And while there's no focal compact

00:22:29.946 --> 00:22:32.028 dense aggregate formation which we

00:22:32.028 --> 00:22:34.508 would need according to The Who to meet

00:22:34.508 --> 00:22:36.948 major criterion for mass cell disease,

00:22:36.950 --> 00:22:39.547 there is this sort of subtle perivascular

00:22:39.547 --> 00:22:41.479 collection in the right image,

00:22:41.480 --> 00:22:43.226 as indicated by the blue arrow.

00:22:43.230 --> 00:22:45.082 So we are seeing a little, you know,

00:22:45.082 --> 00:22:46.828 while most of them are interstitial

00:22:46.828 --> 00:22:48.030 and individually distributed,

00:22:48.030 --> 00:22:50.442 there might be a subtle collection

00:22:50.442 --> 00:22:52.850 around the vessel as part of the workout.

NOTE Confidence: 0.822355347777778

00:22:52.850 --> 00:22:54.640 We also do a CD-25,

NOTE Confidence: 0.822355347777778

00:22:54.640 --> 00:22:57.330 and as you can see here on quite high power.

NOTE Confidence: 0.822355347777778

00:22:57.330 --> 00:23:00.030 There is aberrant positivity on

NOTE Confidence: 0.822355347777778

00:23:00.030 --> 00:23:01.650 the mast cells.

NOTE Confidence: 0.822355347777778

00:23:01.650 --> 00:23:02.143 Importantly,

NOTE Confidence: 0.822355347777778

00:23:02.143 --> 00:23:04.608 this aberrant expression can be

NOTE Confidence: 0.822355347777778

00:23:04.608 --> 00:23:07.390 difficult to assess on low power,

NOTE Confidence: 0.822355347777778

00:23:07.390 --> 00:23:08.675 so it's really imperative when

NOTE Confidence: 0.822355347777778

00:23:08.675 --> 00:23:10.270 you have a case like this,

NOTE Confidence: 0.822355347777778

00:23:10.270 --> 00:23:13.154 go to higher power to either appreciate

NOTE Confidence: 0.822355347777778

00:23:13.154 --> 00:23:15.080 positive or negative staining.

NOTE Confidence: 0.822355347777778

00:23:15.080 --> 00:23:15.418 Similarly,

NOTE Confidence: 0.822355347777778

00:23:15.418 --> 00:23:17.446 as in a case like this,

NOTE Confidence: 0.822355347777778

00:23:17.450 --> 00:23:20.054 given that the mast cells are

NOTE Confidence: 0.822355347777778

00:23:20.054 --> 00:23:21.356 interstitial and individually

NOTE Confidence: 0.822355347777778

00:23:21.356 --> 00:23:23.019 distributed without aggregates,

NOTE Confidence: 0.822355347777778

00:23:23.020 --> 00:23:24.917 it can be really hard to actually

NOTE Confidence: 0.822355347777778

00:23:24.917 --> 00:23:27.155 find the mast cells and be confident

NOTE Confidence: 0.822355347777778

00:23:27.155 --> 00:23:28.855 that they are indeed negative,

NOTE Confidence: 0.822355347777778

00:23:28.860 --> 00:23:31.070 and that makes the interpretation

NOTE Confidence: 0.822355347777778

00:23:31.070 --> 00:23:31.954 even trickier.

NOTE Confidence: 0.822355347777778

00:23:31.960 --> 00:23:34.736 So at this point in our patient we

NOTE Confidence: 0.822355347777778

00:23:34.736 --> 00:23:36.765 have abnormal spindled mast cells

NOTE Confidence: 0.822355347777778

00:23:36.765 --> 00:23:39.273 which Co Express aberrant CD 25,

NOTE Confidence: 0.822355347777778

00:23:39.280 --> 00:23:42.904 so we have two of the four minor

NOTE Confidence: 0.822355347777778

00:23:42.904 --> 00:23:45.418 criteria for SM for The Who.

NOTE Confidence: 0.822355347777778

00:23:45.420 --> 00:23:46.916 So as I mentioned,

NOTE Confidence: 0.822355347777778

00:23:46.916 --> 00:23:48.786 another part of the eosinophilia

NOTE Confidence: 0.822355347777778

00:23:48.786 --> 00:23:50.445 workup is to perform testing

NOTE Confidence: 0.822355347777778

00:23:50.445 --> 00:23:52.162 for the kit D816B mutation,

NOTE Confidence: 0.822355347777778

00:23:52.162 --> 00:23:55.370 and here in our institution we do an

NOTE Confidence: 0.822355347777778

00:23:55.454 --> 00:23:58.370 allele specific PCR assay that has

NOTE Confidence: 0.822355347777778

00:23:58.370 --> 00:24:00.695 an incredible sensitivity of 0.01%.

NOTE Confidence: 0.822355347777778

00:24:00.695 --> 00:24:03.320 So if we have a decent cellular,

NOTE Confidence: 0.822355347777778

00:24:03.320 --> 00:24:04.708 non hemo dilute aspirate,

NOTE Confidence: 0.822355347777778

00:24:04.708 --> 00:24:07.196 it is very likely that with the

NOTE Confidence: 0.822355347777778

00:24:07.196 --> 00:24:09.236 if the mutation is present that

NOTE Confidence: 0.822355347777778

00:24:09.236 --> 00:24:11.230 we will actually detect it even

NOTE Confidence: 0.822355347777778

00:24:11.230 --> 00:24:13.337 if we have very few mast cells.

NOTE Confidence: 0.822355347777778

00:24:13.340 --> 00:24:15.420 So we did the testing in this particular.

NOTE Confidence: 0.822355347777778

00:24:15.420 --> 00:24:17.856 Patient and you can see the positive

NOTE Confidence: 0.822355347777778

00:24:17.856 --> 00:24:20.630 signal for the presence of a kit D816.

NOTE Confidence: 0.822355347777778

00:24:20.630 --> 00:24:23.630 The mutation in the top image.

NOTE Confidence: 0.822355347777778

00:24:23.630 --> 00:24:26.010 If the mutation were absent,

NOTE Confidence: 0.822355347777778

00:24:26.010 --> 00:24:27.738 the top image would be devoid

NOTE Confidence: 0.822355347777778

00:24:27.738 --> 00:24:29.977 of a signal and the the signal

NOTE Confidence: 0.822355347777778

00:24:29.977 --> 00:24:32.011 that you're seeing on the bottom

NOTE Confidence: 0.822355347777778

00:24:32.011 --> 00:24:34.088 image is actually the wild type.

NOTE Confidence: 0.822355347777778

00:24:34.090 --> 00:24:36.162 In her particular case.

NOTE Confidence: 0.822355347777778

00:24:36.162 --> 00:24:38.234 So with this finding,

NOTE Confidence: 0.822355347777778

00:24:38.240 --> 00:24:41.775 we now have 3 minor criteria according

NOTE Confidence: 0.822355347777778

00:24:41.775 --> 00:24:45.608 to The Who we have aberrant CD 25

NOTE Confidence: 0.822355347777778

00:24:45.608 --> 00:24:48.088 expression we have spindled mast

NOTE Confidence: 0.822355347777778

00:24:48.088 --> 00:24:50.835 cells and we have a kit D8160.

NOTE Confidence: 0.822355347777778

00:24:50.835 --> 00:24:53.921 So in this particular case the

NOTE Confidence: 0.822355347777778

00:24:53.921 --> 00:24:56.226 the use and affiliate algorithm

NOTE Confidence: 0.822355347777778

00:24:56.226 --> 00:24:58.673 was important to deploy because

NOTE Confidence: 0.822355347777778

00:24:58.673 --> 00:25:01.278 as I hopefully have illustrated,

NOTE Confidence: 0.822355347777778

00:25:01.280 --> 00:25:03.805 massel infiltrates can be morphologically

NOTE Confidence: 0.822355347777778

00:25:03.805 --> 00:25:05.320 occult and inconspicuous,

NOTE Confidence: 0.822355347777778

00:25:05.320 --> 00:25:06.958 and you have to use your clinical.

NOTE Confidence: 0.822355347777778

00:25:06.960 --> 00:25:08.875 History to help you discern

NOTE Confidence: 0.822355347777778

00:25:08.875 --> 00:25:10.407 these types of cases,

NOTE Confidence: 0.822355347777778

00:25:10.410 --> 00:25:11.890 and importantly in this case,

NOTE Confidence: 0.822355347777778

00:25:11.890 --> 00:25:14.179 we were able to make a diagnosis

NOTE Confidence: 0.822355347777778

00:25:14.179 --> 00:25:15.160 that explained this.

NOTE Confidence: 0.870910466363636

00:25:15.160 --> 00:25:16.536 Patient's spells, foggy brain

NOTE Confidence: 0.870910466363636

00:25:16.536 --> 00:25:19.060 that she had had for 15 years.

NOTE Confidence: 0.7771988675

00:25:21.720 --> 00:25:23.576 So if the mass cell workup is negative,

NOTE Confidence: 0.7771988675

00:25:23.580 --> 00:25:24.712 which it oftentimes is,

NOTE Confidence: 0.7771988675

00:25:24.712 --> 00:25:27.176 you're going to rely on the results of

NOTE Confidence: 0.7771988675

00:25:27.176 --> 00:25:29.300 your cytogenetics and your fish testing.

NOTE Confidence: 0.7771988675

00:25:29.300 --> 00:25:30.600 Depending on these results,

NOTE Confidence: 0.7771988675

00:25:30.600 --> 00:25:32.800 the case is going to end up,

NOTE Confidence: 0.7771988675

00:25:32.800 --> 00:25:37.287 typically in one of three diagnostic buckets.

NOTE Confidence: 0.7771988675

00:25:37.290 --> 00:25:39.240 If there is positivity by chromosomes

NOTE Confidence: 0.7771988675

00:25:39.240 --> 00:25:42.227 and or fish for one of The Who

NOTE Confidence: 0.7771988675

00:25:42.227 --> 00:25:43.442 recurring genetic abnormalities

NOTE Confidence: 0.7771988675

00:25:43.442 --> 00:25:45.889 associated with the existing affiliate,

NOTE Confidence: 0.7771988675

00:25:45.890 --> 00:25:52.856 namely PDGFRA, PDGFRB FGFR One or Jack 2,

NOTE Confidence: 0.7771988675

00:25:52.856 --> 00:25:55.366 then we would diagnose those

NOTE Confidence: 0.7771988675

00:25:55.366 --> 00:25:56.370 neoplasms accordingly.

NOTE Confidence: 0.7771988675

00:25:56.370 --> 00:25:59.550 Importantly, given that most cases

NOTE Confidence: 0.7771988675

00:25:59.550 --> 00:26:02.730 of the non PDGFRA rearrangements

NOTE Confidence: 0.7771988675

00:26:02.826 --> 00:26:06.472 are cytogenetically evident if you

NOTE Confidence: 0.7771988675

00:26:06.472 --> 00:26:09.177 do get a chromosomal abnormality,

NOTE Confidence: 0.7771988675

00:26:09.180 --> 00:26:12.280 AT-5232 or 8P11 that suggests ohh, PDGFR,

NOTE Confidence: 0.7771988675

00:26:12.280 --> 00:26:15.290 beta or FGFR, one might be involved.

NOTE Confidence: 0.7771988675

00:26:15.290 --> 00:26:17.789 You absolutely have to do fish or

NOTE Confidence: 0.7771988675

00:26:17.789 --> 00:26:19.807 some other type of confirmatory

NOTE Confidence: 0.7771988675

00:26:19.807 --> 00:26:22.429 testing to document that in that

NOTE Confidence: 0.7771988675

00:26:22.429 --> 00:26:24.690 indeed that particular genetic

NOTE Confidence: 0.7771988675

00:26:24.690 --> 00:26:26.730 locus is in fact rearranged.

NOTE Confidence: 0.7771988675

00:26:26.730 --> 00:26:28.698 And the reason for this is not only

NOTE Confidence: 0.7771988675

00:26:28.698 --> 00:26:30.639 because it's making the right diagnosis,

NOTE Confidence: 0.7771988675

00:26:30.640 --> 00:26:33.682 but it also may dictate appropriate

NOTE Confidence: 0.7771988675

00:26:33.682 --> 00:26:35.203 downstream therapeutic management.

NOTE Confidence: 0.86859606

00:26:37.700 --> 00:26:40.180 If the chromosome results demonstrate

NOTE Confidence: 0.86859606

00:26:40.180 --> 00:26:42.660 a myeloid disorder associated clonal

NOTE Confidence: 0.86859606

00:26:42.734 --> 00:26:44.888 abnormality, this would of course

NOTE Confidence: 0.86859606

00:26:44.888 --> 00:26:47.990 exclude trisomy 8 - y and deletion 20 Q.

NOTE Confidence: 0.86859606

00:26:47.990 --> 00:26:50.758 Then this could be used in the appropriate

NOTE Confidence: 0.86859606

00:26:50.758 --> 00:26:53.802 context as a diagnostic criterion to support

NOTE Confidence: 0.86859606

00:26:53.802 --> 00:26:56.087 a diagnosis of chronic geoscientific

NOTE Confidence: 0.86859606

00:26:56.155 --> 00:26:58.307 leukemia not otherwise specified.

NOTE Confidence: 0.86859606

00:26:58.310 --> 00:27:01.802 And finally, if you come up empty with fish,

NOTE Confidence: 0.86859606

00:27:01.810 --> 00:27:03.430 you come up empty with chromosomes,

NOTE Confidence: 0.86859606

00:27:03.430 --> 00:27:05.008 they're all normal.

NOTE Confidence: 0.86859606

00:27:05.008 --> 00:27:07.638 This indicates one of three

NOTE Confidence: 0.86859606

00:27:07.638 --> 00:27:08.690 diagnostic possibilities.

NOTE Confidence: 0.86859606

00:27:08.690 --> 00:27:10.646 Probably the most likely is it's

NOTE Confidence: 0.86859606

00:27:10.646 --> 00:27:12.630 a reactive heist and affiliate,

NOTE Confidence: 0.86859606

00:27:12.630 --> 00:27:14.542 for which we just haven't been able to

NOTE Confidence: 0.86859606

00:27:14.542 --> 00:27:16.690 figure out what the underlying cause is yet.

NOTE Confidence: 0.86859606

00:27:16.690 --> 00:27:19.298 It's possible it could be a case of

NOTE Confidence: 0.86859606

00:27:19.298 --> 00:27:21.170 true idiopathic hypereosinophilia,

NOTE Confidence: 0.86859606

00:27:21.170 --> 00:27:25.154 which I would say those are becoming less.

NOTE Confidence: 0.86859606

00:27:25.160 --> 00:27:27.914 Less common because we are now

NOTE Confidence: 0.86859606

00:27:27.914 --> 00:27:29.750 finding the genetic underpinnings

NOTE Confidence: 0.86859606

00:27:29.828 --> 00:27:31.908 of those particular entities.

NOTE Confidence: 0.86859606

00:27:31.910 --> 00:27:32.376 Or lastly,

NOTE Confidence: 0.86859606

00:27:32.376 --> 00:27:34.240 it could be a clonal ES and affiliate

NOTE Confidence: 0.86859606

00:27:34.291 --> 00:27:36.133 for which we haven't yet detected

NOTE Confidence: 0.86859606

00:27:36.133 --> 00:27:37.377 the genetic alteration, right?

NOTE Confidence: 0.86859606

00:27:37.377 --> 00:27:39.596 So if you're only doing you know

NOTE Confidence: 0.86859606

00:27:39.596 --> 00:27:41.712 fishing chromosomes and maybe a limited

NOTE Confidence: 0.86859606

00:27:41.712 --> 00:27:43.136 next generation sequencing panel,

NOTE Confidence: 0.86859606

00:27:43.140 --> 00:27:45.216 there's obviously still a whole host

NOTE Confidence: 0.86859606

00:27:45.216 --> 00:27:47.668 of the genome that may be abnormal.

NOTE Confidence: 0.86859606

00:27:47.670 --> 00:27:48.510 In my opinion,

NOTE Confidence: 0.86859606

00:27:48.510 --> 00:27:49.910 this is my personal opinion

NOTE Confidence: 0.86859606

00:27:49.910 --> 00:27:51.680 in these particular scenarios.

NOTE Confidence: 0.86859606

00:27:51.680 --> 00:27:53.591 I think it's really important to go

NOTE Confidence: 0.86859606

00:27:53.591 --> 00:27:55.356 back and do a global reassessment

NOTE Confidence: 0.86859606

00:27:55.356 --> 00:27:57.428 of all the facts in the case,

NOTE Confidence: 0.86859606

00:27:57.430 --> 00:27:59.320 how worried is my clinician that I'm

NOTE Confidence: 0.86859606

00:27:59.320 --> 00:28:01.570 dealing with a malignant disease process?

NOTE Confidence: 0.86859606

00:28:01.570 --> 00:28:03.250 Is it behaving in the patient

NOTE Confidence: 0.86859606

00:28:03.250 --> 00:28:05.090 as a as a neoplasm?

NOTE Confidence: 0.86859606

00:28:05.090 --> 00:28:07.295 How worried am I as a pathologist

NOTE Confidence: 0.86859606

00:28:07.295 --> 00:28:09.050 based on what I'm seeing?

NOTE Confidence: 0.86859606

00:28:09.050 --> 00:28:11.570 So part of us evolving our strategy in

NOTE Confidence: 0.86859606

00:28:11.570 --> 00:28:14.002 these cases is learning when we should

NOTE Confidence: 0.86859606

00:28:14.002 --> 00:28:16.620 continue to move forward and push forward.

NOTE Confidence: 0.86859606

00:28:16.620 --> 00:28:18.420 This genetic testing or RAC,

NOTE Confidence: 0.86859606

00:28:18.420 --> 00:28:20.195 whatever it happens to be

NOTE Confidence: 0.86859606

00:28:20.195 --> 00:28:21.970 and when we should hold.

NOTE Confidence: 0.86859606

00:28:21.970 --> 00:28:25.225 If there is sufficient clinical and or

NOTE Confidence: 0.86859606

00:28:25.225 --> 00:28:28.029 pathologic suspicion for a clonal disorder,

NOTE Confidence: 0.86859606

00:28:28.030 --> 00:28:30.380 additional testing either through next

NOTE Confidence: 0.86859606

00:28:30.380 --> 00:28:33.313 generation sequencing or RNA C should

NOTE Confidence: 0.86859606

00:28:33.313 --> 00:28:35.868 be considered as clinically indicated.

NOTE Confidence: 0.86859606

00:28:35.870 --> 00:28:36.582 Also importantly,

NOTE Confidence: 0.86859606

00:28:36.582 --> 00:28:37.650 at this step,

NOTE Confidence: 0.86859606

00:28:37.650 --> 00:28:40.121 if you're very worried as a clinician

NOTE Confidence: 0.86859606

00:28:40.121 --> 00:28:42.378 or pathologist and you've only done

NOTE Confidence: 0.86859606

00:28:42.378 --> 00:28:44.268 chromosomes to look for PDGFRB,

NOTE Confidence: 0.86859606

00:28:44.270 --> 00:28:45.038 FGFR, one,

NOTE Confidence: 0.86859606

00:28:45.038 --> 00:28:45.422 etcetera,

NOTE Confidence: 0.86859606

00:28:45.422 --> 00:28:48.517 I would actually consider doing fish at that

NOTE Confidence: 0.86859606

00:28:48.517 --> 00:28:51.245 point because we now know that even though,

NOTE Confidence: 0.86859606

00:28:51.250 --> 00:28:52.158 albeit small,

NOTE Confidence: 0.86859606

00:28:52.158 --> 00:28:53.520 number of cases.

NOTE Confidence: 0.86859606

00:28:53.520 --> 00:28:55.330 There are those cases that

NOTE Confidence: 0.86859606

00:28:55.330 --> 00:28:56.416 are cytogenetically cryptic,

NOTE Confidence: 0.86859606

00:28:56.420 --> 00:28:57.010 so again,

NOTE Confidence: 0.86859606

00:28:57.010 --> 00:28:58.190 as I mentioned before,

NOTE Confidence: 0.86859606

00:28:58.190 --> 00:29:00.222 because of prognostic and

NOTE Confidence: 0.86859606

00:29:00.222 --> 00:29:01.238 therapeutic implications,

NOTE Confidence: 0.86859606

00:29:01.240 --> 00:29:03.452 we would want to make sure we

NOTE Confidence: 0.86859606

00:29:03.452 --> 00:29:04.400 were definitively including

NOTE Confidence: 0.86859606

00:29:04.460 --> 00:29:06.068 or excluding those diagnoses.

NOTE Confidence: 0.75865975

00:29:08.350 --> 00:29:10.282 So I've mentioned a little bit

NOTE Confidence: 0.75865975

00:29:10.282 --> 00:29:12.143 about the myeloid slash lymphoid

NOTE Confidence: 0.75865975

00:29:12.143 --> 00:29:14.693 neoplasms with eosinophilia and the

NOTE Confidence: 0.75865975

00:29:14.693 --> 00:29:16.223 recurring genetic abnormalities,

NOTE Confidence: 0.75865975

00:29:16.230 --> 00:29:20.646 namely PDGFRA B, FGFR one and Jack two.

NOTE Confidence: 0.75865975

00:29:20.650 --> 00:29:23.746 As those are currently recognized by The Who.

NOTE Confidence: 0.75865975

00:29:23.750 --> 00:29:25.150 As you can see in this table,

NOTE Confidence: 0.75865975

00:29:25.150 --> 00:29:27.334 I've listed those four genes in that

NOTE Confidence: 0.75865975

00:29:27.334 --> 00:29:29.060 order along with their chromosomal

NOTE Confidence: 0.75865975

00:29:29.060 --> 00:29:31.250 location just for ease of reference

NOTE Confidence: 0.75865975

00:29:31.250 --> 00:29:33.499 and some of the translocation partners

NOTE Confidence: 0.75865975

00:29:33.499 --> 00:29:35.689 that have been reported to date.

NOTE Confidence: 0.75865975

00:29:35.690 --> 00:29:37.766 As you can appreciate these genes.

NOTE Confidence: 0.75865975

00:29:37.770 --> 00:29:40.085 And translocate with a variety

NOTE Confidence: 0.75865975

00:29:40.085 --> 00:29:41.474 of different partners.

NOTE Confidence: 0.75865975

00:29:41.480 --> 00:29:42.164 Indeed more.

NOTE Confidence: 0.75865975

00:29:42.164 --> 00:29:44.216 There's more than 30 partners that

NOTE Confidence: 0.75865975

00:29:44.216 --> 00:29:46.640 have been described to date for PDGFR,

NOTE Confidence: 0.75865975

00:29:46.640 --> 00:29:51.136 beta and more than 15 for FGFR one.

NOTE Confidence: 0.75865975

00:29:51.140 --> 00:29:53.342 I've also listed the most common

NOTE Confidence: 0.75865975

00:29:53.342 --> 00:29:55.384 translocation partners in front of the

NOTE Confidence: 0.75865975

00:29:55.384 --> 00:29:57.180 semi colon, just for ease of reference.

NOTE Confidence: 0.75865975

00:29:57.180 --> 00:29:58.188 So for example,

NOTE Confidence: 0.75865975

00:29:58.188 --> 00:30:01.048 FIP 1L1 is by far the most common

NOTE Confidence: 0.75865975

00:30:01.048 --> 00:30:03.592 partner with PDGFRA and I mentioned

NOTE Confidence: 0.75865975

00:30:03.592 --> 00:30:06.390 that 80 to 85% of those cases are

NOTE Confidence: 0.75865975

00:30:06.390 --> 00:30:08.390 cytogenetically cryptic and that is because.

NOTE Confidence: 0.75865975

00:30:08.390 --> 00:30:12.016 Partner FIP 1L1 is actually on 4212 as

NOTE Confidence: 0.75865975

00:30:12.016 --> 00:30:14.350 we'll see in see here in a little bit.

53

NOTE Confidence: 0.75865975

00:30:14.350 --> 00:30:18.040 Also you can see that ETV six is the

NOTE Confidence: 0.75865975

00:30:18.040 --> 00:30:21.650 most common partner with PDGFR beta.

NOTE Confidence: 0.75865975

00:30:21.650 --> 00:30:23.225 You'll also notice that after

NOTE Confidence: 0.75865975

00:30:23.225 --> 00:30:24.485 the Jack 2 Gene,

NOTE Confidence: 0.75865975

00:30:24.490 --> 00:30:26.258 I've also inserted two

NOTE Confidence: 0.75865975

00:30:26.258 --> 00:30:27.584 additional tyrosine kinases,

NOTE Confidence: 0.75865975

00:30:27.590 --> 00:30:29.630 FLIP 3 and Abel one,

NOTE Confidence: 0.75865975

00:30:29.630 --> 00:30:31.790 and the reason I've included these

NOTE Confidence: 0.75865975

00:30:31.790 --> 00:30:34.107 here is although they're not currently

NOTE Confidence: 0.75865975

00:30:34.107 --> 00:30:36.555 recognized by The Who as distinct

NOTE Confidence: 0.75865975

00:30:36.555 --> 00:30:37.990 clinical pathologic entities.

NOTE Confidence: 0.75865975

00:30:37.990 --> 00:30:40.072 They are emerging in the published

NOTE Confidence: 0.75865975

00:30:40.072 --> 00:30:41.924 literature as being associated with

NOTE Confidence: 0.75865975

00:30:41.924 --> 00:30:43.969 the cinephilia and having these

NOTE Confidence: 0.75865975

00:30:43.969 --> 00:30:45.196 recurring genetic abnormalities.

NOTE Confidence: 0.75865975

00:30:45.200 --> 00:30:47.741 So I think it's important to note

NOTE Confidence: 0.75865975

00:30:47.741 --> 00:30:50.075 that this list of genetics is

NOTE Confidence: 0.75865975

00:30:50.075 --> 00:30:52.397 only going to continue to grow.

NOTE Confidence: 0.75865975

00:30:52.400 --> 00:30:53.076 And lastly,

NOTE Confidence: 0.75865975

00:30:53.076 --> 00:30:55.442 on the very bottom there's also a

NOTE Confidence: 0.75865975

00:30:55.442 --> 00:30:57.533 handful of other non translocation

NOTE Confidence: 0.75865975

00:30:57.533 --> 00:30:59.638 events that have been reported

NOTE Confidence: 0.75865975

00:30:59.638 --> 00:31:01.533 recently that do associate as

NOTE Confidence: 0.75865975

00:31:01.533 --> 00:31:02.937 well with ESPN Ophilia.

NOTE Confidence: 0.75865975

00:31:02.940 --> 00:31:04.236 These include insertion,

NOTE Confidence: 0.75865975

00:31:04.236 --> 00:31:07.480 deletion events and Exxon 13 of Jack 2.

NOTE Confidence: 0.75865975

00:31:07.480 --> 00:31:08.230 The stat

NOTE Confidence: 0.894272401428571

00:31:10.460 --> 00:31:12.184 5BN642H mutation and then,

NOTE Confidence: 0.894272401428571

00:31:12.184 --> 00:31:13.477 although not specific,

NOTE Confidence: 0.894272401428571

00:31:13.480 --> 00:31:16.080 a whole host of mutations

NOTE Confidence: 0.894272401428571

00:31:16.080 --> 00:31:18.796 in genes such as ASX 1 TET,

NOTE Confidence: 0.894272401428571

00:31:18.800 --> 00:31:21.200 2 easy H2 and others.

NOTE Confidence: 0.894272401428571

00:31:21.200 --> 00:31:22.468 So again this list.

NOTE Confidence: 0.894272401428571

00:31:22.468 --> 00:31:24.053 The genetic findings in clonal

NOTE Confidence: 0.894272401428571

00:31:24.053 --> 00:31:25.709 east and affiliates just continues

NOTE Confidence: 0.894272401428571

00:31:25.709 --> 00:31:28.068 to grow and I would argue it's

NOTE Confidence: 0.894272401428571

00:31:28.068 --> 00:31:29.926 getting even more complicated and

NOTE Confidence: 0.894272401428571

00:31:29.926 --> 00:31:31.642 a consequence of this is that

NOTE Confidence: 0.894272401428571

00:31:31.642 --> 00:31:33.764 it forces us in somewhat of a

NOTE Confidence: 0.894272401428571

00:31:33.764 --> 00:31:35.558 good way to evolve our strategy

NOTE Confidence: 0.894272401428571

00:31:35.620 --> 00:31:37.713 with respect to how are we going

NOTE Confidence: 0.894272401428571

00:31:37.713 --> 00:31:39.822 to approach and work up these

NOTE Confidence: 0.894272401428571

00:31:39.822 --> 00:31:41.922 cases in 2022 and beyond with

NOTE Confidence: 0.894272401428571

00:31:41.922 --> 00:31:43.860 the ultimate goal of getting the

NOTE Confidence: 0.894272401428571

00:31:43.922 --> 00:31:45.777 right diagnosis but doing the

NOTE Confidence: 0.894272401428571

00:31:45.777 --> 00:31:47.632 right testing for our patients.

NOTE Confidence: 0.916227138461538

00:31:49.960 --> 00:31:51.572 Recognition of these recurring

NOTE Confidence: 0.916227138461538

00:31:51.572 --> 00:31:53.184 genetic abnormalities is important

NOTE Confidence: 0.916227138461538

00:31:53.184 --> 00:31:55.546 for a couple of reasons, and again,

NOTE Confidence: 0.916227138461538

00:31:55.546 --> 00:31:57.177 as I mentioned on the last slide,

NOTE Confidence: 0.916227138461538

00:31:57.180 --> 00:31:58.386 although rearrangements of

NOTE Confidence: 0.916227138461538

00:31:58.386 --> 00:32:00.396 flip three and able one,

NOTE Confidence: 0.916227138461538

00:32:00.400 --> 00:32:02.338 I've listed them out separately here.

NOTE Confidence: 0.916227138461538

00:32:02.340 --> 00:32:04.170 That's just, that's merely because that

NOTE Confidence: 0.916227138461538

00:32:04.170 --> 00:32:05.820 they're not recognized by The Who,

NOTE Confidence: 0.916227138461538

00:32:05.820 --> 00:32:07.480 but I've included them here

NOTE Confidence: 0.916227138461538

00:32:07.480 --> 00:32:08.476 because they share,

NOTE Confidence: 0.916227138461538

00:32:08.480 --> 00:32:09.420 as I will show you,

NOTE Confidence: 0.916227138461538

00:32:09.420 --> 00:32:12.370 many of the amazingly similar

NOTE Confidence: 0.916227138461538

00:32:12.370 --> 00:32:14.730 characteristics to the currently

NOTE Confidence: 0.916227138461538

00:32:14.730 --> 00:32:16.831 recognized WHO entities first,

NOTE Confidence: 0.916227138461538

00:32:16.831 --> 00:32:19.988 as you might expect based on the.

NOTE Confidence: 0.916227138461538

00:32:19.990 --> 00:32:21.589 WHO naming convention,

NOTE Confidence: 0.916227138461538

00:32:21.589 --> 00:32:24.254 these genetic alterations are typically

NOTE Confidence: 0.916227138461538

00:32:24.254 --> 00:32:26.687 associated with the US and OPHILIA.

NOTE Confidence: 0.916227138461538

00:32:26.690 --> 00:32:28.574 That's good for us as pathologist

NOTE Confidence: 0.916227138461538

00:32:28.574 --> 00:32:31.382 because it helps us be able to identify

NOTE Confidence: 0.916227138461538

00:32:31.382 --> 00:32:33.710 them and do the appropriate testing.

NOTE Confidence: 0.916227138461538

00:32:33.710 --> 00:32:34.188 Second,

NOTE Confidence: 0.916227138461538

00:32:34.188 --> 00:32:36.100 translocations involving these genes

NOTE Confidence: 0.916227138461538

00:32:36.100 --> 00:32:39.878 are notorious as I'll show you on the

NOTE Confidence: 0.916227138461538

00:32:39.878 --> 00:32:42.068 next slides for Multilineage involvement,

NOTE Confidence: 0.916227138461538

00:32:42.070 --> 00:32:44.093 so this can include a whole variety

NOTE Confidence: 0.916227138461538

00:32:44.093 --> 00:32:45.560 of chronic myeloid disorders.

NOTE Confidence: 0.916227138461538

00:32:45.560 --> 00:32:47.228 They may manifest as chronic yeast,

NOTE Confidence: 0.916227138461538

00:32:47.230 --> 00:32:49.288 and I feel like leukemia and OS.

NOTE Confidence: 0.916227138461538

00:32:49.290 --> 00:32:51.342 They may look like.

NOTE Confidence: 0.916227138461538

00:32:51.342 --> 00:32:52.368 Myelodysplastic myeloproliferative

NOTE Confidence: 0.916227138461538

00:32:52.368 --> 00:32:53.394 overlap syndrome.

NOTE Confidence: 0.916227138461538

00:32:53.400 --> 00:32:55.175 They may also present as

NOTE Confidence: 0.916227138461538

00:32:55.175 --> 00:32:56.595 an acute myeloid leukemia.

NOTE Confidence: 0.916227138461538

00:32:56.600 --> 00:32:58.796 They can also present as B&amp;T

NOTE Confidence: 0.916227138461538

00:32:58.796 --> 00:32:59.804 cell lymphoblastic leukemia,

NOTE Confidence: 0.916227138461538

00:32:59.804 --> 00:33:02.319 so it's pretty much all over the map,

NOTE Confidence: 0.916227138461538

00:33:02.320 --> 00:33:04.147 but if they have the S and

NOTE Confidence: 0.916227138461538

00:33:04.147 --> 00:33:04.930 affilia accompanying them,

NOTE Confidence: 0.916227138461538

00:33:04.930 --> 00:33:08.938 they can help us recognize them more readily.

NOTE Confidence: 0.916227138461538

00:33:08.940 --> 00:33:09.613 Third,

NOTE Confidence: 0.916227138461538

00:33:09.613 --> 00:33:11.632 there are significant

NOTE Confidence: 0.916227138461538

00:33:11.632 --> 00:33:12.978 therapeutic implications,

NOTE Confidence: 0.916227138461538

00:33:12.980 --> 00:33:14.048 depending on which of

NOTE Confidence: 0.916227138461538

00:33:14.048 --> 00:33:15.116 these genes are rearranged,

NOTE Confidence: 0.916227138461538

00:33:15.120 --> 00:33:16.542 as I've mentioned.

NOTE Confidence: 0.916227138461538

00:33:16.542 --> 00:33:18.438 Rearrangements of PDGFRA and

NOTE Confidence: 0.916227138461538

00:33:18.438 --> 00:33:21.107 B are exquisitely sensitive to

NOTE Confidence: 0.916227138461538

00:33:21.107 --> 00:33:22.859 tyrosine kinase inhibitors.

NOTE Confidence: 0.916227138461538

00:33:22.860 --> 00:33:23.334 However,

NOTE Confidence: 0.916227138461538

00:33:23.334 --> 00:33:25.704 rearrangements of FGFR one and

NOTE Confidence: 0.916227138461538

00:33:25.704 --> 00:33:27.600 Jack two are not.

NOTE Confidence: 0.916227138461538

00:33:27.600 --> 00:33:28.011 Therefore,

NOTE Confidence: 0.916227138461538

00:33:28.011 --> 00:33:30.477 in those situations that opens up

NOTE Confidence: 0.916227138461538

00:33:30.477 --> 00:33:32.326 the possibility for alternative

NOTE Confidence: 0.916227138461538

00:33:32.326 --> 00:33:35.056 therapies in those particular patients.

NOTE Confidence: 0.916227138461538

00:33:35.060 --> 00:33:36.110 Jack 2 inhibitors.

NOTE Confidence: 0.916227138461538

00:33:36.110 --> 00:33:37.860 Maybe a flip 3 inhibitor,

NOTE Confidence: 0.916227138461538

00:33:37.860 --> 00:33:40.996 maybe a small molecule you know

NOTE Confidence: 0.916227138461538

00:33:40.996 --> 00:33:43.152 that has that has a clinical trial,

NOTE Confidence: 0.916227138461538

00:33:43.160 --> 00:33:45.335 so this information is important

NOTE Confidence: 0.916227138461538

00:33:45.335 --> 00:33:47.075 for your clinical folks.

NOTE Confidence: 0.916227138461538

00:33:47.080 --> 00:33:48.448 Because they know how to treat

NOTE Confidence: 0.916227138461538

00:33:48.448 --> 00:33:49.768 the patients and whether to try

NOTE Confidence: 0.916227138461538

00:33:49.768 --> 00:33:51.028 to get them on a clinical trial.

NOTE Confidence: 0.911577364

00:33:53.880 --> 00:33:55.300 So this slide is busy,

NOTE Confidence: 0.911577364

00:33:55.300 --> 00:33:58.116 but I like it because it summarizes many

NOTE Confidence: 0.911577364

00:33:58.116 --> 00:34:00.516 of the clinical pathologic features

NOTE Confidence: 0.911577364

00:34:00.516 --> 00:34:03.750 of the four WHO recognized myeloid

NOTE Confidence: 0.911577364

00:34:03.750 --> 00:34:06.842 lymphoid neoplasms with ES and OPHILIA

NOTE Confidence: 0.911577364

00:34:06.842 --> 00:34:09.312 and a recurring genetic abnormality.

NOTE Confidence: 0.911577364

00:34:09.320 --> 00:34:11.994 I'm going to show you this same

NOTE Confidence: 0.911577364

00:34:11.994 --> 00:34:14.086 display of information for Flip 3

NOTE Confidence: 0.911577364

00:34:14.086 --> 00:34:16.403 and Abel one on the next slide so

NOTE Confidence: 0.911577364

00:34:16.403 --> 00:34:18.384 the genes are listed across the top

NOTE Confidence: 0.911577364

00:34:18.384 --> 00:34:21.162 in the first row of each column and

NOTE Confidence: 0.911577364

00:34:21.162 --> 00:34:23.173 the disease presentation the extra

NOTE Confidence: 0.911577364

00:34:23.173 --> 00:34:25.718 medullary tissue involvement and the

NOTE Confidence: 0.911577364

00:34:25.718 --> 00:34:27.245 association with hypereosinophilia

NOTE Confidence: 0.911577364

00:34:27.245 --> 00:34:29.758 are shown in the far left column.

NOTE Confidence: 0.911577364

00:34:29.760 --> 00:34:32.034 So helicopter view as you look

NOTE Confidence: 0.911577364

00:34:32.034 --> 00:34:34.460 across all of these four genes,

NOTE Confidence: 0.911577364

00:34:34.460 --> 00:34:37.382 you can appreciate that a heterogeneous

NOTE Confidence: 0.911577364

00:34:37.382 --> 00:34:39.760 presentation is very typical as I.

NOTE Confidence: 0.911577364

00:34:39.760 --> 00:34:42.050 You had mentioned previously the

NOTE Confidence: 0.911577364

00:34:42.050 --> 00:34:44.759 disease presentations and this can vary

NOTE Confidence: 0.911577364

00:34:44.759 --> 00:34:47.153 to some extent depending on what the

NOTE Confidence: 0.911577364

00:34:47.153 --> 00:34:50.170 what the recurring genetic abnormality is.

NOTE Confidence: 0.911577364

00:34:50.170 --> 00:34:52.134 Chronic isn't affiliate leukemia.

NOTE Confidence: 0.911577364

00:34:52.134 --> 00:34:53.607 Chronic myelomonocytic leukemia.

NOTE Confidence: 0.911577364

00:34:53.610 --> 00:34:55.014 Acute myeloid leukemia

NOTE Confidence: 0.911577364

00:34:55.014 --> 00:34:55.950 lymphoblastic leukemia,

NOTE Confidence: 0.911577364

00:34:55.950 --> 00:34:58.330 mass cell disease, and others.

NOTE Confidence: 0.911577364

00:34:58.330 --> 00:35:01.750 The plus signs that are next to the disease

NOTE Confidence: 0.911577364

00:35:01.750 --> 00:35:04.151 represents the relative proportion of

NOTE Confidence: 0.911577364

00:35:04.151 --> 00:35:06.581 cases within that diagnostic category

NOTE Confidence: 0.911577364

00:35:06.581 --> 00:35:09.816 that reportedly present as that particular.

NOTE Confidence: 0.911577364

00:35:09.820 --> 00:35:10.993 Type of disorder.

NOTE Confidence: 0.911577364

00:35:10.993 --> 00:35:12.166 So for example,

NOTE Confidence: 0.911577364

00:35:12.170 --> 00:35:15.754 the majority of cases with the PDGFR

NOTE Confidence: 0.911577364

00:35:15.754 --> 00:35:17.930 alpha rearrangement present as CEO,

NOTE Confidence: 0.911577364

00:35:17.930 --> 00:35:19.710 chronic use and affiliate leukemia.

NOTE Confidence: 0.911577364

00:35:19.710 --> 00:35:20.914 In contrast,

NOTE Confidence: 0.911577364

00:35:20.914 --> 00:35:23.924 most cases of PDGFR beta

NOTE Confidence: 0.911577364

00:35:23.924 --> 00:35:27.313 rearrangement present as a chronic

NOTE Confidence: 0.911577364

00:35:27.313 --> 00:35:29.530 myelomonocytic like picture.

NOTE Confidence: 0.911577364

00:35:29.530 --> 00:35:31.804 Another key take away from this

NOTE Confidence: 0.911577364

00:35:31.804 --> 00:35:34.098 table is the association with

NOTE Confidence: 0.911577364

00:35:34.098 --> 00:35:36.228 Extramedullary disease presentations.

NOTE Confidence: 0.911577364

00:35:36.230 --> 00:35:39.835 This is particularly true for FGFR 1.

NOTE Confidence: 0.911577364

00:35:39.840 --> 00:35:42.008 Rearranged cases in fact,

NOTE Confidence: 0.911577364

00:35:42.008 --> 00:35:44.718 FGFR 1 rearranged cases are

NOTE Confidence: 0.911577364

00:35:44.718 --> 00:35:47.678 notorious for a complex presentation.

NOTE Confidence: 0.911577364

00:35:47.680 --> 00:35:49.899 What do I mean by complex presentation?

NOTE Confidence: 0.911577364

00:35:49.900 --> 00:35:52.525 That basically means that the case will

NOTE Confidence: 0.911577364

00:35:52.525 --> 00:35:55.529 present as a chronic myeloid neoplasm,

NOTE Confidence: 0.911577364

00:35:55.530 --> 00:35:57.275 possibly with eosinophilia in the

NOTE Confidence: 0.911577364

00:35:57.275 --> 00:35:59.020 peripheral blood or bone marrow.

NOTE Confidence: 0.911577364

00:35:59.020 --> 00:36:01.155 But then it will have a lymphoblastic

NOTE Confidence: 0.911577364

00:36:01.155 --> 00:36:02.872 lymphoma or a myeloid sarcoma

NOTE Confidence: 0.911577364

00:36:02.872 --> 00:36:04.348 or a mixed phenotype.

NOTE Confidence: 0.911577364

00:36:04.350 --> 00:36:06.294 Acute chemia presentation

NOTE Confidence: 0.911577364

00:36:06.294 --> 00:36:08.886 in an extramedullary site.

NOTE Confidence: 0.911577364

00:36:08.890 --> 00:36:10.370 This is important because as

NOTE Confidence: 0.911577364

00:36:10.370 --> 00:36:12.395 you can see with the association

NOTE Confidence: 0.911577364

00:36:12.395 --> 00:36:14.327 percent with ESPN affiliate,

NOTE Confidence: 0.911577364

00:36:14.330 --> 00:36:16.759 it's only about 80% of cases that

NOTE Confidence: 0.911577364

00:36:16.759 --> 00:36:18.410 have these genetic rearrangements

NOTE Confidence: 0.911577364

00:36:18.410 --> 00:36:20.550 that have ESPN affiliate.

NOTE Confidence: 0.911577364

00:36:20.550 --> 00:36:22.222 So how am I going to diagnose it

NOTE Confidence: 0.911577364

00:36:22.222 --> 00:36:23.795 in the other 20% that don't have

NOTE Confidence: 0.911577364

00:36:23.795 --> 00:36:24.615 any S and affiliate,

NOTE Confidence: 0.911577364

00:36:24.620 --> 00:36:26.545 and that's where it really becomes tricky.

NOTE Confidence: 0.911577364

00:36:26.550 --> 00:36:28.750 So knowledge about these heterogeneous

NOTE Confidence: 0.911577364

00:36:28.750 --> 00:36:31.393 disease presentations as well as the

NOTE Confidence: 0.911577364

00:36:31.393 --> 00:36:33.283 complex presentations can really aid

NOTE Confidence: 0.911577364

00:36:33.283 --> 00:36:35.790 you as a pathologist to be thinking.

NOTE Confidence: 0.911577364

00:36:35.790 --> 00:36:36.062 Ooh,

NOTE Confidence: 0.911577364

00:36:36.062 --> 00:36:38.900 even though I've got a Tal and a lymph node.

NOTE Confidence: 0.911577364

00:36:38.900 --> 00:36:40.370 You know there's no use in affiliate,

NOTE Confidence: 0.911577364

00:36:40.370 --> 00:36:42.113 but I've got maybe a chronic myeloid

NOTE Confidence: 0.911577364

00:36:42.113 --> 00:36:44.223 in the bone marrow would prompt you

NOTE Confidence: 0.911577364

00:36:44.223 --> 00:36:45.858 to potentially consider testing for

NOTE Confidence: 0.911577364

00:36:45.858 --> 00:36:47.848 one of these genetic abnormalities.

NOTE Confidence: 0.924656755555555

00:36:50.140 --> 00:36:52.300 So just as I mentioned on the last slide,

NOTE Confidence: 0.924656755555555

00:36:52.300 --> 00:36:54.376 I think Eason I feel like

NOTE Confidence: 0.924656755555555

00:36:54.376 --> 00:36:55.760 disorders with recurrent genetic

NOTE Confidence: 0.924656755555555

00:36:55.827 --> 00:36:57.737 abnormalities is a is expanding.

NOTE Confidence: 0.924656755555555

00:36:57.740 --> 00:36:58.751 This includes rearrangements

NOTE Confidence: 0.924656755555555

00:36:58.751 --> 00:37:00.773 of foot three and Abel one.

NOTE Confidence: 0.924656755555555

00:37:00.780 --> 00:37:03.364 And as you can see they are amazingly

NOTE Confidence: 0.924656755555555

00:37:03.364 --> 00:37:05.582 similar to the ones that are

NOTE Confidence: 0.924656755555555

00:37:05.582 --> 00:37:07.452 currently recognized by The Who.

NOTE Confidence: 0.924656755555555

00:37:07.460 --> 00:37:09.930 They can have a heterogeneous

NOTE Confidence: 0.924656755555555

00:37:09.930 --> 00:37:10.918 disease presentation.

NOTE Confidence: 0.924656755555555

00:37:10.920 --> 00:37:13.314 They have a frequent but not 100%

NOTE Confidence: 0.924656755555555

00:37:13.320 --> 00:37:15.558 association with the US and AFFILIA,

NOTE Confidence: 0.924656755555555

00:37:15.560 --> 00:37:18.035 and they can have extramedullary

NOTE Confidence: 0.924656755555555

00:37:18.035 --> 00:37:19.025 disease involvement.

NOTE Confidence: 0.924656755555555

00:37:19.030 --> 00:37:21.082 Foot three rearranged cases.

NOTE Confidence: 0.924656755555555

00:37:21.082 --> 00:37:22.108 In particular,

NOTE Confidence: 0.924656755555555

00:37:22.110 --> 00:37:23.646 it's kind of easy to remember

NOTE Confidence: 0.924656755555555

00:37:23.646 --> 00:37:25.270 because it starts with F and FGFR.

NOTE Confidence: 0.924656755555555

00:37:25.270 --> 00:37:26.418 One starts with F.

NOTE Confidence: 0.924656755555555

00:37:26.418 --> 00:37:28.932 They are very similar in that they tend

NOTE Confidence: 0.924656755555555

00:37:28.932 --> 00:37:31.128 to present with a complex presentation,

NOTE Confidence: 0.924656755555555

00:37:31.130 --> 00:37:33.194 which again includes CEO or CEO

NOTE Confidence: 0.924656755555555

00:37:33.194 --> 00:37:35.527 like picture in the peripheral blood

NOTE Confidence: 0.924656755555555

00:37:35.527 --> 00:37:37.752 and T lymphoblastic lymphoma or

NOTE Confidence: 0.924656755555555

00:37:37.752 --> 00:37:40.098 a myeloid sarcoma in the tissue.

NOTE Confidence: 0.924656755555555

00:37:40.100 --> 00:37:41.340 Able one, rearranged cases,

NOTE Confidence: 0.924656755555555

00:37:41.340 --> 00:37:42.580 on the other hand,

NOTE Confidence: 0.924656755555555

00:37:42.580 --> 00:37:44.965 have much less of an

NOTE Confidence: 0.924656755555555

00:37:44.965 --> 00:37:45.919 extramedullary presentation,

NOTE Confidence: 0.924656755555555

00:37:45.920 --> 00:37:47.500 and the overwhelming majority present

NOTE Confidence: 0.924656755555555

00:37:47.500 --> 00:37:49.080 as a chronic myeloid disease.

NOTE Confidence: 0.924656755555555

00:37:49.080 --> 00:37:52.240 Typically CE L excuse me or an overlap.

NOTE Confidence: 0.924656755555555

00:37:52.240 --> 00:37:53.390 MDSM PN.

NOTE Confidence: 0.90648889

00:37:55.470 --> 00:37:56.850 So what do these cases

NOTE Confidence: 0.90648889

00:37:56.850 --> 00:37:58.230 look like in real life?

NOTE Confidence: 0.90648889

00:37:58.230 --> 00:37:59.982 Well, this case is classic and

NOTE Confidence: 0.90648889

00:37:59.982 --> 00:38:02.386 it's a nice one to see if you

NOTE Confidence: 0.90648889

00:38:02.386 --> 00:38:04.138 haven't had one come across your

NOTE Confidence: 0.90648889

00:38:04.206 --> 00:38:06.046 desk in in clinical practice,

NOTE Confidence: 0.90648889

00:38:06.050 --> 00:38:08.624 so this was a 35 year old male who

NOTE Confidence: 0.90648889

00:38:08.624 --> 00:38:10.859 presented with constitutional symptoms.

NOTE Confidence: 0.90648889

00:38:10.860 --> 00:38:13.690 CBC was done and it was noted that he had

NOTE Confidence: 0.90648889

00:38:13.760 --> 00:38:16.296 an absolutely essential count of 4500,

NOTE Confidence: 0.90648889

00:38:16.296 --> 00:38:18.240 so greater than the 1.5 times

NOTE Confidence: 0.90648889

00:38:18.240 --> 00:38:19.840 into the nine per liter.

NOTE Confidence: 0.90648889

00:38:19.840 --> 00:38:22.128 I've shown you a high power image of

NOTE Confidence: 0.90648889

00:38:22.128 --> 00:38:23.648 the peripheral blood and basically

NOTE Confidence: 0.90648889

00:38:23.648 --> 00:38:25.430 the majority of his ES NFL's

NOTE Confidence: 0.90648889

00:38:25.430 --> 00:38:27.300 were cytologically unremarkable.

NOTE Confidence: 0.90648889

00:38:27.300 --> 00:38:28.440 The bone marrow aspirates

NOTE Confidence: 0.90648889

00:38:28.440 --> 00:38:29.580 were specular and cellular.

NOTE Confidence: 0.90648889

00:38:29.580 --> 00:38:31.396 There was a lot to look at and

NOTE Confidence: 0.90648889

00:38:31.396 --> 00:38:32.810 basically we saw predominance.

NOTE Confidence: 0.90648889

00:38:32.810 --> 00:38:35.846 Escena Phils and Escena Phillip precursors.

NOTE Confidence: 0.90648889

00:38:35.850 --> 00:38:38.550 The core biopsy was markedly hypercellular,

NOTE Confidence: 0.90648889

00:38:38.550 --> 00:38:40.315 basically due to the increased

69

NOTE Confidence: 0.90648889

00:38:40.315 --> 00:38:41.727 via syphilis and precursors,

NOTE Confidence: 0.90648889

00:38:41.730 --> 00:38:44.474 and I wasn't able to appreciate any obvious.

NOTE Confidence: 0.90648889

00:38:44.480 --> 00:38:46.466 You know, mass selling fill trades,

NOTE Confidence: 0.90648889

00:38:46.470 --> 00:38:48.514 no lymphoma. There was no increased blast.

NOTE Confidence: 0.90648889

00:38:48.520 --> 00:38:51.300 The legs were predominantly unremarkable.

NOTE Confidence: 0.90648889

00:38:51.300 --> 00:38:52.740 But because it's a work up

NOTE Confidence: 0.90648889

00:38:52.740 --> 00:38:53.460 for ESPN affiliate,

NOTE Confidence: 0.90648889

00:38:53.460 --> 00:38:56.036 we did the IMMUNOSTAINS for mast cells

NOTE Confidence: 0.90648889

00:38:56.040 --> 00:38:58.336 and you can see here with the tryptase.

NOTE Confidence: 0.90648889

00:38:58.340 --> 00:39:00.635 We have very similar to what we saw before,

NOTE Confidence: 0.90648889

00:39:00.640 --> 00:39:01.968 but perhaps an increased

NOTE Confidence: 0.90648889

00:39:01.968 --> 00:39:04.073 number of mast cells increased,

NOTE Confidence: 0.90648889

00:39:04.073 --> 00:39:05.619 interstitially distributed

NOTE Confidence: 0.90648889

00:39:05.619 --> 00:39:09.335 spindly mast cells and they showed

NOTE Confidence: 0.90648889

00:39:09.335 --> 00:39:11.195 aberrant CD 25 expression.

NOTE Confidence: 0.90648889

00:39:11.200 --> 00:39:13.990 As you can see in the lower right image.

NOTE Confidence: 0.90648889

00:39:13.990 --> 00:39:15.342 This is very typical,

NOTE Confidence: 0.90648889

00:39:15.342 --> 00:39:17.370 but it's not exclusive of this

NOTE Confidence: 0.90648889

00:39:17.442 --> 00:39:19.626 disorder is the lack of a

NOTE Confidence: 0.90648889

00:39:19.626 --> 00:39:21.082 mass cell aggregate formation.

NOTE Confidence: 0.90648889

00:39:21.090 --> 00:39:21.960 In rare cases,

NOTE Confidence: 0.90648889

00:39:21.960 --> 00:39:23.410 it can actually form aggregates,

NOTE Confidence: 0.90648889

00:39:23.410 --> 00:39:25.391 but this type of pattern would be

NOTE Confidence: 0.90648889

00:39:25.391 --> 00:39:28.008 a clue that you might be dealing

NOTE Confidence: 0.90648889

00:39:28.008 --> 00:39:29.708 with this particular abnormality.

NOTE Confidence: 0.90648889

00:39:29.710 --> 00:39:32.194 We did do kit molecular testing

NOTE Confidence: 0.90648889

00:39:32.194 --> 00:39:34.470 for DNA 16B and it was negative,

NOTE Confidence: 0.90648889

00:39:34.470 --> 00:39:37.186 so that would essentially exclude not always,

NOTE Confidence: 0.90648889

00:39:37.190 --> 00:39:41.258 but essentially excludes mass cell disease.

NOTE Confidence: 0.90648889

00:39:41.260 --> 00:39:43.627 We also did as part of our algorithm fish

NOTE Confidence: 0.90648889

00:39:43.627 --> 00:39:45.880 for a PDGFR alpha gene rearrangement.

NOTE Confidence: 0.90648889

00:39:45.880 --> 00:39:47.880 Again, as I mentioned,

NOTE Confidence: 0.90648889

00:39:47.880 --> 00:39:49.880 because these are cytogenetically

NOTE Confidence: 0.90648889

00:39:49.880 --> 00:39:52.660 cryptic and 80% of those cases are

NOTE Confidence: 0.90648889

00:39:52.660 --> 00:39:55.852 because of the FIP 1L1 gene which is

NOTE Confidence: 0.90648889

00:39:55.852 --> 00:39:58.972 colocalized on 4Q12 with PDGFR alpha.

NOTE Confidence: 0.90648889

00:39:58.972 --> 00:40:02.922 So the 5th 1L1 PDGFR Alpha fusion is

NOTE Confidence: 0.90648889

00:40:02.922 --> 00:40:05.717 the consequence of an interstitial

NOTE Confidence: 0.90648889

00:40:05.717 --> 00:40:09.442 deletion on chromosome 4 Q 1/2 and

NOTE Confidence: 0.90648889

00:40:09.442 --> 00:40:11.380 a key component of this fusion

NOTE Confidence: 0.90648889

00:40:11.462 --> 00:40:13.846 is the loss of the chip 2 gene,

NOTE Confidence: 0.90648889

00:40:13.850 --> 00:40:16.730 which sits in between FIP one

NOTE Confidence: 0.90648889

00:40:16.730 --> 00:40:18.170 and PDGFR alpha,

NOTE Confidence: 0.90648889

00:40:18.170 --> 00:40:19.950 and I'm only mentioning this

NOTE Confidence: 0.90648889

00:40:19.950 --> 00:40:22.091 because on occasion you may hear

NOTE Confidence: 0.90648889

00:40:22.091 --> 00:40:24.177 this fish Pro panel referred to as

NOTE Confidence: 0.90648889

00:40:24.177 --> 00:40:26.369 to fish or chip 2 deletion fish.

NOTE Confidence: 0.90648889

00:40:26.370 --> 00:40:28.736 So just be aware that chip two

NOTE Confidence: 0.90648889

00:40:28.736 --> 00:40:30.580 really has nothing to do with.

NOTE Confidence: 0.90648889

00:40:30.580 --> 00:40:33.009 But it's just by default what people

NOTE Confidence: 0.90648889

00:40:33.009 --> 00:40:35.912 refer to this as in this particular assay,

NOTE Confidence: 0.90648889

00:40:35.912 --> 00:40:36.738 the normal.

NOTE Confidence: 0.90648889

00:40:36.740 --> 00:40:37.830 So like you and me,

NOTE Confidence: 0.90648889

00:40:37.830 --> 00:40:39.734 hopefully normal fish pattern

NOTE Confidence: 0.90648889

00:40:39.734 --> 00:40:42.114 is 2 fused triple signals,

NOTE Confidence: 0.90648889

00:40:42.120 --> 00:40:45.000 meaning the red Aqua in the green are

NOTE Confidence: 0.90648889

00:40:45.000 --> 00:40:46.897 all colocalized because they're all

NOTE Confidence: 0.90648889

00:40:46.897 --> 00:40:49.880 sitting right at that band on four Q 12.

NOTE Confidence: 0.90648889

00:40:49.880 --> 00:40:51.888 So as you can see on the chromosome

NOTE Confidence: 0.90648889

00:40:51.888 --> 00:40:54.156 image on the far right flip one is FIP,

NOTE Confidence: 0.90648889

00:40:54.160 --> 00:40:55.188 1L1 is green chip,

NOTE Confidence: 0.90648889

00:40:55.188 --> 00:40:55.959 two is red,

NOTE Confidence: 0.788285506

00:40:55.960 --> 00:40:59.040 and PDGFR alpha is blue.

NOTE Confidence: 0.788285506

00:40:59.040 --> 00:41:01.406 So if you have an. Abnormal fip 1L1.

NOTE Confidence: 0.788285506

00:41:01.406 --> 00:41:04.118 PDGFR Alpha fusion the red probe

NOTE Confidence: 0.788285506

00:41:04.118 --> 00:41:06.443 is going to be lost, right?

NOTE Confidence: 0.788285506

00:41:06.443 --> 00:41:07.775 You have the interstitial

NOTE Confidence: 0.788285506

00:41:07.775 --> 00:41:09.107 deletion of chip two.

NOTE Confidence: 0.788285506

00:41:09.110 --> 00:41:11.294 And as you can see in this particular

NOTE Confidence: 0.788285506

00:41:11.294 --> 00:41:13.586 patient I've shown highlighted by the arrow,

NOTE Confidence: 0.788285506

00:41:13.590 --> 00:41:17.302 the fish assay is positive for a chip

NOTE Confidence: 0.788285506

00:41:17.302 --> 00:41:20.540 to deletion, AKA loss of the red signal.

NOTE Confidence: 0.788285506

00:41:20.540 --> 00:41:23.928 So the surrogate of that is that

NOTE Confidence: 0.788285506

00:41:23.928 --> 00:41:26.650 this manifests as a fifth one.

NOTE Confidence: 0.788285506

00:41:26.650 --> 00:41:28.534 L1 PDGFR alpha fusion.

NOTE Confidence: 0.788285506

00:41:28.534 --> 00:41:30.889 So in this particular case.

NOTE Confidence: 0.788285506

00:41:30.890 --> 00:41:33.165 You're actually able to make a diagnosis.

NOTE Confidence: 0.788285506

00:41:33.170 --> 00:41:34.798 This was our diagnosis.

NOTE Confidence: 0.788285506

00:41:34.798 --> 00:41:37.751 It's a chronic myeloid neoplasm with theists

NOTE Confidence: 0.788285506

00:41:37.751 --> 00:41:40.838 and affilia and a PDGFR alpha rearrangement,

NOTE Confidence: 0.788285506

00:41:40.840 --> 00:41:42.960 and the partners FIP 1L1.

NOTE Confidence: 0.788285506

00:41:42.960 --> 00:41:45.264 Typical features of this are just

NOTE Confidence: 0.788285506

00:41:45.264 --> 00:41:47.509 very nicely exemplified by this case.

NOTE Confidence: 0.788285506

00:41:47.510 --> 00:41:49.766 Almost all the patients are male.

NOTE Confidence: 0.788285506

00:41:49.770 --> 00:41:51.786 They actually present at a younger age,

NOTE Confidence: 0.788285506

00:41:51.790 --> 00:41:54.247 so in the 30s or 40s is not uncommon.

NOTE Confidence: 0.788285506

00:41:54.250 --> 00:41:55.770 They typically have peripherally

NOTE Confidence: 0.788285506

00:41:55.770 --> 00:41:56.910 as an affiliate,

NOTE Confidence: 0.788285506

00:41:56.910 --> 00:41:59.227 and they have those abnormal mass cells,

NOTE Confidence: 0.788285506

00:41:59.230 --> 00:42:00.649 those interstitial individually.

NOTE Confidence: 0.788285506

00:42:00.649 --> 00:42:03.316 Distributed mass cells that express CD-25,

NOTE Confidence: 0.788285506

00:42:03.316 --> 00:42:04.500 and they typically don't

NOTE Confidence: 0.788285506

00:42:04.500 --> 00:42:05.980 have an increase in blast.

NOTE Confidence: 0.788285506

00:42:05.980 --> 00:42:07.480 They don't have dysplasia, etcetera,

NOTE Confidence: 0.788285506

00:42:07.480 --> 00:42:09.940 so it's very typical presentation.

NOTE Confidence: 0.788285506

00:42:09.940 --> 00:42:10.455 Importantly,

NOTE Confidence: 0.788285506

00:42:10.455 --> 00:42:12.515 this fusion has significant

NOTE Confidence: 0.788285506

00:42:12.515 --> 00:42:14.060 not only diagnostic,

NOTE Confidence: 0.788285506

00:42:14.060 --> 00:42:15.434 but therapeutic implications.

NOTE Confidence: 0.788285506

00:42:15.434 --> 00:42:18.182 Because this is a target for

NOTE Confidence: 0.788285506

00:42:18.182 --> 00:42:19.939 tyrosine kinase inhibitors.

NOTE Confidence: 0.832716715758621

00:42:22.110 --> 00:42:24.526 OK, so with this next case I'm going

NOTE Confidence: 0.832716715758621

00:42:24.526 --> 00:42:27.218 to shift gears and I'm going to talk

NOTE Confidence: 0.832716715758621

00:42:27.218 --> 00:42:29.272 about the interface of idiopathic

NOTE Confidence: 0.832716715758621

00:42:29.272 --> 00:42:31.840 hypereosinophilia and chronic lymphocytic

NOTE Confidence: 0.832716715758621

00:42:31.840 --> 00:42:34.408 leukemia not otherwise specified.

NOTE Confidence: 0.832716715758621

00:42:34.410 --> 00:42:36.587 So this is a very interesting case.

NOTE Confidence: 0.832716715758621

00:42:36.590 --> 00:42:38.622 It came across my desk a couple of

NOTE Confidence: 0.832716715758621

00:42:38.622 --> 00:42:40.373 years ago and our institution patient

NOTE Confidence: 0.832716715758621

00:42:40.373 --> 00:42:42.847 was 61 years old and he was actually

NOTE Confidence: 0.832716715758621

00:42:42.847 --> 00:42:44.785 hospitalized because he was going to

NOTE Confidence: 0.832716715758621

00:42:44.785 --> 00:42:47.116 have a whipple for a tubulovillous

NOTE Confidence: 0.832716715758621

00:42:47.116 --> 00:42:50.410 adenoma in the head of the pancreas.

NOTE Confidence: 0.832716715758621

00:42:50.410 --> 00:42:52.678 So you know, obviously part of Presurgical

NOTE Confidence: 0.832716715758621

00:42:52.678 --> 00:42:55.781 workup was to do a CDC and they found this

NOTE Confidence: 0.832716715758621

00:42:55.781 --> 00:42:57.950 whopping absolutely as an affiliate account.

NOTE Confidence: 0.832716715758621

00:42:57.950 --> 00:42:59.063 20,000 was absolutely

NOTE Confidence: 0.832716715758621

00:42:59.063 --> 00:43:00.547 as an affiliate account,

NOTE Confidence: 0.832716715758621

00:43:00.550 --> 00:43:01.480 so the surgeons you know

NOTE Confidence: 0.832716715758621

00:43:01.480 --> 00:43:02.410 they kind of go well.

NOTE Confidence: 0.832716715758621

00:43:02.410 --> 00:43:03.366 That's kind of weird,

NOTE Confidence: 0.832716715758621

00:43:03.366 --> 00:43:05.109 and so then they decided to get

NOTE Confidence: 0.832716715758621

00:43:05.109 --> 00:43:06.633 a hematology consult just to see

NOTE Confidence: 0.832716715758621

00:43:06.633 --> 00:43:08.463 what that means or what they should

00:43:08.463 --> 00:43:09.987 do before the doing the whipple,

00:43:09.990 --> 00:43:12.000 so the hematologist determined that

00:43:12.000 --> 00:43:15.478 they needed to do a bone marrow biopsy.

00:43:15.480 --> 00:43:17.671 And along with that comes peripheral blood

00:43:17.671 --> 00:43:20.130 smear review so the peripheral blood smear,

00:43:20.130 --> 00:43:21.870 which I've shown here.

00:43:21.870 --> 00:43:24.045 The slide corroborated the massively

00:43:24.045 --> 00:43:26.760 increased and expanded number of eosinophils,

00:43:26.760 --> 00:43:29.154 and for the most part they were

00:43:29.154 --> 00:43:30.180 actually morphologically unremarkable.

00:43:30.180 --> 00:43:31.812 Some of them might have had

00:43:31.812 --> 00:43:32.900 a few cytoplasmic vacuoles,

00:43:32.900 --> 00:43:35.180 but they weren't distinctly hypo granular.

00:43:35.180 --> 00:43:36.215 They weren't hypersegmented.

00:43:36.215 --> 00:43:39.480 They were pretty boring, honestly.

00:43:39.480 --> 00:43:41.244 But here's the bone marrow aspirate

NOTE Confidence: 0.832716715758621

00:43:41.244 --> 00:43:42.420 definitely showed increased yeast

NOTE Confidence: 0.832716715758621

00:43:42.463 --> 00:43:43.060 in the fields.

NOTE Confidence: 0.832716715758621

00:43:43.060 --> 00:43:46.259 It was about 40% of nucleated cells.

NOTE Confidence: 0.832716715758621

00:43:46.260 --> 00:43:48.584 There was background intact,

NOTE Confidence: 0.832716715758621

00:43:48.584 --> 00:43:50.327 erythropoiesis background intact,

NOTE Confidence: 0.832716715758621

00:43:50.330 --> 00:43:51.662 ranial choices, no dysplasia,

NOTE Confidence: 0.832716715758621

00:43:51.662 --> 00:43:52.994 no increase in blast,

NOTE Confidence: 0.832716715758621

00:43:53.000 --> 00:43:55.358 no lymphoma, no increase in monos,

NOTE Confidence: 0.832716715758621

00:43:55.360 --> 00:43:57.180 but the megs which I'm showing you

NOTE Confidence: 0.832716715758621

00:43:57.180 --> 00:43:59.428 here with a couple of arrows they told

NOTE Confidence: 0.832716715758621

00:43:59.428 --> 00:44:01.919 to me they were telling a different story.

NOTE Confidence: 0.832716715758621

00:44:01.920 --> 00:44:03.720 I thought they were pretty abnormal,

NOTE Confidence: 0.832716715758621

00:44:03.720 --> 00:44:06.856 some of them were really small with

NOTE Confidence: 0.832716715758621

00:44:06.856 --> 00:44:09.112 these hyperchromatic condensed nuclei and

NOTE Confidence: 0.832716715758621

00:44:09.112 --> 00:44:12.066 others were very clearly small and monologue.

00:44:12.070 --> 00:44:13.570 So I was thinking about,

00:44:13.570 --> 00:44:15.005 you know what testing should I do?

00:44:15.010 --> 00:44:17.096 I know I have to follow the

00:44:17.096 --> 00:44:17.990 ESPN affiliate algorithm,

00:44:17.990 --> 00:44:20.111 but I was also really worried about

00:44:20.111 --> 00:44:21.590 other potential myeloid disorders.

00:44:21.590 --> 00:44:24.200 So I kind of broke from the S and

00:44:24.200 --> 00:44:26.190 AFFILIA algorithm a little bit.

00:44:26.190 --> 00:44:27.990 And this is what I ordered.

00:44:27.990 --> 00:44:30.349 I did carry a typing. It was normal.

00:44:30.349 --> 00:44:33.008 I did BCR ABL 1 fish and I did

00:44:33.008 --> 00:44:34.016 inversion 16 fish,

00:44:34.020 --> 00:44:36.858 which is the CBF beta MH 11.

00:44:36.858 --> 00:44:40.036 I looked for a rearrangement by fish

00:44:40.036 --> 00:44:44.364 for PDGFR alpha beta FGFR one and Jack two.

00:44:44.370 --> 00:44:47.130 I also looked for a myeloproliferative

NOTE Confidence: 0.832716715758621

00:44:47.130 --> 00:44:48.510 neoplasm driver mutation,

NOTE Confidence: 0.832716715758621

00:44:48.510 --> 00:44:50.795 so like Jack to ****** color.

NOTE Confidence: 0.832716715758621

00:44:50.795 --> 00:44:52.620 I did kit of course,

NOTE Confidence: 0.832716715758621

00:44:52.620 --> 00:44:54.468 just because that's part of the algorithm.

NOTE Confidence: 0.832716715758621

00:44:54.470 --> 00:44:56.460 Everything was normal flow cytometry.

NOTE Confidence: 0.832716715758621

00:44:56.460 --> 00:44:58.378 Is normal and I had no abnormal

NOTE Confidence: 0.832716715758621

00:44:58.378 --> 00:45:00.550 mast cells by immunohistochemistry,

NOTE Confidence: 0.832716715758621

00:45:00.550 --> 00:45:04.270 so it's not CML, it's not inversion 16.

NOTE Confidence: 0.832716715758621

00:45:04.270 --> 00:45:05.932 I'm not really getting a recurring

NOTE Confidence: 0.832716715758621

00:45:05.932 --> 00:45:06.486 genetic abnormality,

NOTE Confidence: 0.832716715758621

00:45:06.490 --> 00:45:08.604 so it's probably not one of those.

NOTE Confidence: 0.832716715758621

00:45:08.610 --> 00:45:09.950 I can't really call.

NOTE Confidence: 0.832716715758621

00:45:09.950 --> 00:45:11.290 Is it hydropathic hypereosinophilic?

NOTE Confidence: 0.832716715758621

00:45:11.290 --> 00:45:12.163 What is it?

NOTE Confidence: 0.832716715758621

00:45:12.163 --> 00:45:13.327 Is it CL Nos?

00:45:13.330 --> 00:45:15.634 Or am I just barking up the wrong

00:45:15.634 --> 00:45:18.133 tree and this is just an odd

00:45:18.133 --> 00:45:19.983 reaction to this underlying tubulo

00:45:20.061 --> 00:45:21.159 villous adenoma?

00:45:21.160 --> 00:45:23.944 So for me to make a diagnosis of

00:45:23.944 --> 00:45:24.640 idiopathic hypereosinophilia,

00:45:24.640 --> 00:45:26.920 basically that's a diagnosis of exclusion,

00:45:26.920 --> 00:45:29.174 so I'd have to exclude everything else.

00:45:29.180 --> 00:45:31.860 What about CEL and OS?

00:45:31.860 --> 00:45:33.960 So here are The Who criteria.

00:45:33.960 --> 00:45:35.400 There are five of them.

00:45:35.400 --> 00:45:36.600 The first four we had

00:45:36.600 --> 00:45:37.560 already checked the boxes.

00:45:37.560 --> 00:45:39.760 OK, so we have used an affiliate of

00:45:39.760 --> 00:45:42.100 excluded all these other myeloid disorders.

00:45:42.100 --> 00:45:43.610 I don't have a rearrangement

NOTE Confidence: 0.866765784545454

00:45:43.610 --> 00:45:44.214 that's recurring,

NOTE Confidence: 0.866765784545454

00:45:44.220 --> 00:45:46.290 and I know that my blasts are less than

NOTE Confidence: 0.866765784545454

00:45:46.290 --> 00:45:49.005 20% and I don't have inversion 16 or 822,

NOTE Confidence: 0.866765784545454

00:45:49.005 --> 00:45:52.155 but I didn't have criterion #5.

NOTE Confidence: 0.866765784545454

00:45:52.160 --> 00:45:53.852 I did not have a Colonel

NOTE Confidence: 0.866765784545454

00:45:53.852 --> 00:45:54.416 cytogenetic abnormality,

NOTE Confidence: 0.866765784545454

00:45:54.420 --> 00:45:55.590 and I did not have more

NOTE Confidence: 0.866765784545454

00:45:55.590 --> 00:45:56.931 than 2% blasts in blood,

NOTE Confidence: 0.866765784545454

00:45:56.931 --> 00:46:00.080 or more than 5% in the bone marrow.

NOTE Confidence: 0.866765784545454

00:46:00.080 --> 00:46:02.270 Even though I had hyperius and

NOTE Confidence: 0.866765784545454

00:46:02.270 --> 00:46:04.166 affiliate and abnormal appearing legs

NOTE Confidence: 0.866765784545454

00:46:04.166 --> 00:46:06.046 couldn't quite make the diagnosis.

NOTE Confidence: 0.866765784545454

00:46:06.050 --> 00:46:08.570 If I followed The Who strictly.

NOTE Confidence: 0.866765784545454

00:46:08.570 --> 00:46:11.394 So there is a reference in the 2017

NOTE Confidence: 0.866765784545454

00:46:11.394 --> 00:46:14.951 Blue book that you can use a molecular

00:46:14.951 --> 00:46:17.670 genetic abnormality to support clonality,

00:46:17.670 --> 00:46:20.134 but those in those cases you have to

00:46:20.134 --> 00:46:22.005 absolutely exclude that you're not

00:46:22.005 --> 00:46:23.995 dealing with chip clonal hematopoiesis

00:46:23.995 --> 00:46:25.410 of indeterminate potential.

00:46:25.410 --> 00:46:27.839 So for example if I had done

00:46:27.839 --> 00:46:29.541 next generation sequencing and I

00:46:29.541 --> 00:46:31.335 picked up a single mutation and.

00:46:31.340 --> 00:46:33.780 SX1 or Ted two or DNMT 3A.

00:46:33.780 --> 00:46:35.810 So the classic culprits of chip and

00:46:35.810 --> 00:46:37.935 it's at a reasonably low variant

00:46:37.935 --> 00:46:40.008 allele frequency that I wouldn't be

00:46:40.008 --> 00:46:42.132 able to use that as a as a diagnostic

00:46:42.140 --> 00:46:44.516 slam dunk criterion for clonal abnormality.

00:46:44.520 --> 00:46:46.914 So just exercise caution if you're going

00:46:46.914 --> 00:46:50.277 to go the next generation sequencing route.

NOTE Confidence: 0.866765784545454

00:46:50.280 --> 00:46:52.226 So what do we know about NGS

NOTE Confidence: 0.866765784545454

00:46:52.226 --> 00:46:53.660 in this particular scenario?

NOTE Confidence: 0.866765784545454

00:46:53.660 --> 00:46:55.484 So I tried to summarize on the literature

NOTE Confidence: 0.866765784545454

00:46:55.484 --> 00:46:57.471 that I was able to find about NGS

NOTE Confidence: 0.866765784545454

00:46:57.471 --> 00:46:59.219 and the ascent affiliates pretty limited.

NOTE Confidence: 0.866765784545454

00:46:59.220 --> 00:47:00.780 As you can see,

NOTE Confidence: 0.866765784545454

00:47:00.780 --> 00:47:02.892 but we knew know that from

NOTE Confidence: 0.866765784545454

00:47:02.892 --> 00:47:03.996 several of these studies,

NOTE Confidence: 0.866765784545454

00:47:04.000 --> 00:47:05.820 myeloid disorder associated gene

NOTE Confidence: 0.866765784545454

00:47:05.820 --> 00:47:08.550 mutations can be identified as in

NOTE Confidence: 0.866765784545454

00:47:08.624 --> 00:47:11.074 the small fraction of idiopathic

NOTE Confidence: 0.866765784545454

00:47:11.074 --> 00:47:13.034 hypereosinophilia or IHS cases,

NOTE Confidence: 0.866765784545454

00:47:13.040 --> 00:47:14.916 but they do appear to be present,

NOTE Confidence: 0.866765784545454

00:47:14.920 --> 00:47:18.308 and they may be sensitive in helping

NOTE Confidence: 0.866765784545454

00:47:18.308 --> 00:47:20.120 prove clonality in the study.

00:47:20.120 --> 00:47:21.800 Down by saw Wang at all,

00:47:21.800 --> 00:47:24.170 they found that in cases of

00:47:24.170 --> 00:47:25.355 Hypereosinophilic syndrome that

00:47:25.355 --> 00:47:27.168 were actually NGS positive,

00:47:27.170 --> 00:47:29.570 meaning they detected an abnormality.

00:47:29.570 --> 00:47:31.645 Those actually shared clinical and

00:47:31.645 --> 00:47:33.720 bone marrow finding overlap with

00:47:33.791 --> 00:47:36.146 chronic yeast anopheline leukemia Nos.

00:47:36.150 --> 00:47:37.692 So they really made the argument

00:47:37.692 --> 00:47:39.465 that if you find these genetic

00:47:39.465 --> 00:47:41.190 abnormalities and it's not chip,

00:47:41.190 --> 00:47:43.205 it's probably going to behave

00:47:43.205 --> 00:47:44.734 more like a CELNOS.

00:47:44.734 --> 00:47:47.246 So it can be useful to help it,

00:47:47.250 --> 00:47:48.858 you know, diagnose clonality

00:47:48.858 --> 00:47:50.466 in those particular situations.

NOTE Confidence: 0.866765784545454

00:47:50.470 --> 00:47:51.360 But again,

NOTE Confidence: 0.866765784545454

00:47:51.360 --> 00:47:53.585 remember you gotta exclude chip,

NOTE Confidence: 0.866765784545454

00:47:53.590 --> 00:47:56.005 and even though these studies are limited,

NOTE Confidence: 0.866765784545454

00:47:56.010 --> 00:47:58.306 I think this is pretty powerful in,

NOTE Confidence: 0.866765784545454

00:47:58.310 --> 00:48:00.596 you know information because it does

NOTE Confidence: 0.866765784545454

00:48:00.596 --> 00:48:03.258 indicate that NGSS is going to probably

NOTE Confidence: 0.866765784545454

00:48:03.258 --> 00:48:05.388 play a much more significant role

NOTE Confidence: 0.866765784545454

00:48:05.388 --> 00:48:08.950 in our diagnosis of these disorders.

NOTE Confidence: 0.866765784545454

00:48:08.950 --> 00:48:11.662 So next generation sequencing can be

NOTE Confidence: 0.866765784545454

00:48:11.662 --> 00:48:14.962 helpful in the border between IH E&amp;CEL,

NOTE Confidence: 0.866765784545454

00:48:14.962 --> 00:48:16.686 but what about morphology?

NOTE Confidence: 0.866765784545454

00:48:16.690 --> 00:48:18.958 So in another very interesting study,

NOTE Confidence: 0.866765784545454

00:48:18.960 --> 00:48:20.748 Doctor Sawang and and a bunch

NOTE Confidence: 0.866765784545454

00:48:20.748 --> 00:48:21.940 of her bone marrow

NOTE Confidence: 0.852077069166667

00:48:22.003 --> 00:48:23.639 pathology colleagues looked at

NOTE Confidence: 0.852077069166667

00:48:23.639 --> 00:48:25.684 exactly this question and what

NOTE Confidence: 0.852077069166667

00:48:25.684 --> 00:48:27.528 they found was bone marrow.

NOTE Confidence: 0.852077069166667

00:48:27.530 --> 00:48:28.468 Morphology matters,

NOTE Confidence: 0.852077069166667

00:48:28.468 --> 00:48:30.813 so if you have abnormalities

NOTE Confidence: 0.852077069166667

00:48:30.813 --> 00:48:33.610 such as Mark Hypercellularity,

NOTE Confidence: 0.852077069166667

00:48:33.610 --> 00:48:35.074 you have dysplastic features.

NOTE Confidence: 0.852077069166667

00:48:35.074 --> 00:48:37.270 You have increased blasts which would

NOTE Confidence: 0.852077069166667

00:48:37.326 --> 00:48:39.126 make sense or abnormal appearing.

NOTE Confidence: 0.852077069166667

00:48:39.130 --> 00:48:41.580 Gets in a field that really served

NOTE Confidence: 0.852077069166667

00:48:41.580 --> 00:48:44.026 to support a diagnosis more in

NOTE Confidence: 0.852077069166667

00:48:44.026 --> 00:48:46.216 keeping with a malignancy IE.

NOTE Confidence: 0.852077069166667

00:48:46.220 --> 00:48:48.565 Chronic eczema philic leukemia Nos

NOTE Confidence: 0.852077069166667

00:48:48.565 --> 00:48:51.520 rather than a reactive eosinophilic product.

NOTE Confidence: 0.852077069166667

00:48:51.520 --> 00:48:54.341 You know process so to me this

NOTE Confidence: 0.852077069166667

00:48:54.341 --> 00:48:56.422 provides support that in addition

NOTE Confidence: 0.852077069166667

00:48:56.422 --> 00:48:58.792 to our current WHO criteria it

NOTE Confidence: 0.852077069166667

00:48:58.792 --> 00:49:01.877 might be possible for us to include

NOTE Confidence: 0.852077069166667

00:49:01.877 --> 00:49:04.449 morphology in our diagnosis of CELNOS.

NOTE Confidence: 0.852077069166667

00:49:04.449 --> 00:49:07.680 OK, so let's return back to to my case.

NOTE Confidence: 0.852077069166667

00:49:07.680 --> 00:49:09.390 So I had actually ordered.

NOTE Confidence: 0.852077069166667

00:49:09.390 --> 00:49:10.305 Next generation sequencing.

NOTE Confidence: 0.852077069166667

00:49:10.305 --> 00:49:12.135 Because I was really that worried

NOTE Confidence: 0.852077069166667

00:49:12.135 --> 00:49:13.861 but it was cancelled by the

NOTE Confidence: 0.852077069166667

00:49:13.861 --> 00:49:15.226 clinical team because they thought

NOTE Confidence: 0.852077069166667

00:49:15.274 --> 00:49:16.999 the hypereosinophilia was due to

NOTE Confidence: 0.852077069166667

00:49:16.999 --> 00:49:18.379 the underlying pancreatic lesion.

NOTE Confidence: 0.852077069166667

00:49:18.380 --> 00:49:20.788 Plus we did not have any prior

NOTE Confidence: 0.852077069166667

00:49:20.788 --> 00:49:22.503 information or knowledge about CBC

NOTE Confidence: 0.852077069166667

00:49:22.503 --> 00:49:24.345 that would have shown that the

NOTE Confidence: 0.852077069166667

00:49:24.345 --> 00:49:26.871 that the hybrid is an affiliate

NOTE Confidence: 0.852077069166667

00:49:26.871 --> 00:49:28.719 predated this tubulovillous adenoma.

NOTE Confidence: 0.852077069166667

00:49:28.720 --> 00:49:30.485 But because of the persistent

NOTE Confidence: 0.852077069166667

00:49:30.485 --> 00:49:31.897 unexplained ES and affiliate,

NOTE Confidence: 0.852077069166667

00:49:31.900 --> 00:49:33.839 the patient had two subsequent bone marrows,

NOTE Confidence: 0.852077069166667

00:49:33.840 --> 00:49:36.072 one at 8 months and one at 14 months

NOTE Confidence: 0.852077069166667

00:49:36.072 --> 00:49:37.960 from the original presentation.

NOTE Confidence: 0.852077069166667

00:49:37.960 --> 00:49:39.280 They all looked identical.

NOTE Confidence: 0.852077069166667

00:49:39.280 --> 00:49:39.610 OK,

NOTE Confidence: 0.852077069166667

00:49:39.610 --> 00:49:42.460 so they had ESPN affiliate morphologically

NOTE Confidence: 0.852077069166667

00:49:42.460 --> 00:49:44.360 unremarkable hypercellular and scattered.

NOTE Confidence: 0.852077069166667

00:49:44.360 --> 00:49:45.248 You know,

NOTE Confidence: 0.852077069166667

00:49:45.248 --> 00:49:47.468 atypical or dysplastic clicking next.

NOTE Confidence: 0.852077069166667

00:49:47.470 --> 00:49:47.776 However,

NOTE Confidence: 0.852077069166667

00:49:47.776 --> 00:49:49.000 the third bone marrow,

NOTE Confidence: 0.852077069166667

00:49:49.000 --> 00:49:50.365 as you can see on the slide,

NOTE Confidence: 0.852077069166667

00:49:50.370 --> 00:49:52.210 showed a cytogenetic abnormality

NOTE Confidence: 0.852077069166667

00:49:52.210 --> 00:49:54.970 and basically 19 of 20 metaphyses.

NOTE Confidence: 0.852077069166667

00:49:54.970 --> 00:49:57.490 So this now enables us to confirm a

NOTE Confidence: 0.852077069166667

00:49:57.490 --> 00:50:00.230 diagnosis of chronic use in a physical

NOTE Confidence: 0.852077069166667

00:50:00.230 --> 00:50:01.862 tenia not otherwise specified.

NOTE Confidence: 0.852077069166667

00:50:01.870 --> 00:50:02.268 Similarly,

NOTE Confidence: 0.852077069166667

00:50:02.268 --> 00:50:05.452 at the 14 month bone marrow they also

NOTE Confidence: 0.852077069166667

00:50:05.452 --> 00:50:07.212 undertook next generation sequencing

NOTE Confidence: 0.852077069166667

00:50:07.212 --> 00:50:09.780 and we were able to identify.

NOTE Confidence: 0.852077069166667

00:50:09.780 --> 00:50:11.796 2 genetic alterations,

NOTE Confidence: 0.852077069166667

00:50:11.796 --> 00:50:14.778 1 in ASX 01 and the other an SRS of two,

NOTE Confidence: 0.852077069166667

00:50:14.780 --> 00:50:16.412 both of which are pretty common

NOTE Confidence: 0.852077069166667

00:50:16.412 --> 00:50:16.956 chip mutations.

NOTE Confidence: 0.852077069166667

00:50:16.960 --> 00:50:18.760 But the fact that there were two of

NOTE Confidence: 0.852077069166667

00:50:18.760 --> 00:50:20.773 them and not just one and the fact

NOTE Confidence: 0.852077069166667

00:50:20.773 --> 00:50:22.138 that the variant allele frequencies

NOTE Confidence: 0.852077069166667

00:50:22.138 --> 00:50:24.594 were in the high 40s really supports that.

00:50:24.600 --> 00:50:27.239 This was in fact a clonal process,

00:50:27.240 --> 00:50:28.504 so with this information,

00:50:28.504 --> 00:50:31.300 just as a research you know investigation,

00:50:31.300 --> 00:50:33.288 I actually went back to my original

00:50:33.288 --> 00:50:35.296 DNA extract and hold and we were

00:50:35.296 --> 00:50:36.934 able to document that those same

00:50:36.996 --> 00:50:38.830 2 mutations at the same high V

00:50:38.830 --> 00:50:40.386 AF were actually present.

00:50:40.386 --> 00:50:44.216 The initial bone marrow biopsy

00:50:44.220 --> 00:50:46.796 So I think this case has several

00:50:46.796 --> 00:50:49.640 key messages as we sort of evolve

00:50:49.640 --> 00:50:51.320 our strategy in diagnosing

00:50:51.320 --> 00:50:52.520 hypereosinophilic conditions.

00:50:52.520 --> 00:50:53.193 First,

00:50:53.193 --> 00:50:55.212 morphology matters the

00:50:55.212 --> 00:50:56.558 marked hypercellularity,

NOTE Confidence: 0.852077069166667

00:50:56.560 --> 00:50:58.570 and those abnormal megas really were

NOTE Confidence: 0.852077069166667

00:50:58.570 --> 00:51:01.653 a clue that we were dealing to a

NOTE Confidence: 0.852077069166667

00:51:01.653 --> 00:51:03.738 primary clonal ESPN affiliate disorder.

NOTE Confidence: 0.852077069166667

00:51:03.740 --> 00:51:04.660 Second patients,

NOTE Confidence: 0.852077069166667

00:51:04.660 --> 00:51:07.697 they can have ticks and fleas, right?

NOTE Confidence: 0.852077069166667

00:51:07.697 --> 00:51:09.913 So this guy actually had two separate things.

NOTE Confidence: 0.852077069166667

00:51:09.920 --> 00:51:11.220 If there's so to me,

NOTE Confidence: 0.852077069166667

00:51:11.220 --> 00:51:12.852 if there's sufficient clinical

NOTE Confidence: 0.852077069166667

00:51:12.852 --> 00:51:14.076 or pathologic suspicion,

NOTE Confidence: 0.852077069166667

00:51:14.080 --> 00:51:16.606 we probably should be pushing those

NOTE Confidence: 0.852077069166667

00:51:16.606 --> 00:51:18.668 boundaries and really confirming whether

NOTE Confidence: 0.852077069166667

00:51:18.668 --> 00:51:21.196 a clonal process is or is not present.

NOTE Confidence: 0.852077069166667

00:51:21.200 --> 00:51:22.037 I think DNA,

NOTE Confidence: 0.852077069166667

00:51:22.037 --> 00:51:23.153 even RNA extracted and

NOTE Confidence: 0.852077069166667

00:51:23.153 --> 00:51:24.830 hold is not unreasonable.

NOTE Confidence: 0.852077069166667

00:51:24.830 --> 00:51:26.321 We don't see a ton of years

NOTE Confidence: 0.852077069166667

00:51:26.321 --> 00:51:26.960 in affiliate cases,

NOTE Confidence: 0.939893661538462

00:51:26.960 --> 00:51:29.410 so it's not like a huge burden on our system

NOTE Confidence: 0.939893661538462

00:51:29.469 --> 00:51:31.688 to process the specimens because you can

NOTE Confidence: 0.939893661538462

00:51:31.688 --> 00:51:33.927 always come back to it at a later date.

NOTE Confidence: 0.939893661538462

00:51:33.930 --> 00:51:35.810 You don't have to go and procure another

NOTE Confidence: 0.939893661538462

00:51:35.810 --> 00:51:37.280 bone marrow, but you can say OK,

NOTE Confidence: 0.939893661538462

00:51:37.280 --> 00:51:39.920 now we really need to do some RNA

NOTE Confidence: 0.939893661538462

00:51:39.920 --> 00:51:42.699 sequencing or you know XYZ type of testing.

NOTE Confidence: 0.939893661538462

00:51:42.700 --> 00:51:44.440 Third, I thought it was reasonable

NOTE Confidence: 0.939893661538462

00:51:44.440 --> 00:51:45.980 this patient was clinically stable.

NOTE Confidence: 0.939893661538462

00:51:45.980 --> 00:51:48.095 We knew he was having a whipple and they

NOTE Confidence: 0.939893661538462

00:51:48.095 --> 00:51:50.317 can always get him through that surgery.

NOTE Confidence: 0.939893661538462

00:51:50.320 --> 00:51:52.315 Get him recovered. And recheck the CDC,

NOTE Confidence: 0.939893661538462

00:51:52.320 --> 00:51:55.336 and if it's still persistent then we could

NOTE Confidence: 0.939893661538462

00:51:55.336 --> 00:51:58.560 have done the DNA evaluation at that point.

NOTE Confidence: 0.939893661538462

00:51:58.560 --> 00:52:00.150 So here's my final diagnosis.

NOTE Confidence: 0.939893661538462

00:52:00.150 --> 00:52:02.320 In this case, took us a while to get there,

NOTE Confidence: 0.939893661538462

00:52:02.320 --> 00:52:05.344 but I think it is the right one.

NOTE Confidence: 0.939893661538462

00:52:05.350 --> 00:52:07.366 So in summary, I hope I've convinced

NOTE Confidence: 0.939893661538462

00:52:07.366 --> 00:52:09.258 you that he is an affiliate,

NOTE Confidence: 0.939893661538462

00:52:09.260 --> 00:52:11.230 is not a straightforward disorder,

NOTE Confidence: 0.939893661538462

00:52:11.230 --> 00:52:13.036 and it can be quite complicated

NOTE Confidence: 0.939893661538462

00:52:13.036 --> 00:52:15.309 to work up in many instances.

NOTE Confidence: 0.939893661538462

00:52:15.310 --> 00:52:17.478 In fact, because Hypereosinophilia

NOTE Confidence: 0.939893661538462

00:52:17.478 --> 00:52:19.646 is relatively rarely encountered

NOTE Confidence: 0.939893661538462

00:52:19.646 --> 00:52:22.049 in routine clinical practice,

NOTE Confidence: 0.939893661538462

00:52:22.050 --> 00:52:24.930 and because it has a whole host of

NOTE Confidence: 0.939893661538462

00:52:24.930 --> 00:52:27.338 neoplastic and non neoplastic causes.

NOTE Confidence: 0.939893661538462

00:52:27.340 --> 00:52:29.968 I would advocate for a systematic

NOTE Confidence: 0.939893661538462

00:52:29.968 --> 00:52:32.265 yet comprehensive approach to the

NOTE Confidence: 0.939893661538462

00:52:32.265 --> 00:52:34.640 evaluation of these particular cases.

NOTE Confidence: 0.939893661538462

00:52:34.640 --> 00:52:36.365 Obviously your approach should be

NOTE Confidence: 0.939893661538462

00:52:36.365 --> 00:52:38.660 evidence based, and it should in all,

NOTE Confidence: 0.939893661538462

00:52:38.660 --> 00:52:40.790 in almost all likelihood continue to

NOTE Confidence: 0.939893661538462

00:52:40.790 --> 00:52:43.660 evolve as we gain additional knowledge,

NOTE Confidence: 0.939893661538462

00:52:43.660 --> 00:52:45.492 particularly from the genetic

NOTE Confidence: 0.939893661538462

00:52:45.492 --> 00:52:47.324 perspective about the molecular

NOTE Confidence: 0.939893661538462

00:52:47.324 --> 00:52:49.240 underpinnings of these disorders.

NOTE Confidence: 0.939893661538462

00:52:49.240 --> 00:52:50.072 Whenever possible,

NOTE Confidence: 0.939893661538462

00:52:50.072 --> 00:52:52.984 try and adhere and render diagnosis utilizing

NOTE Confidence: 0.939893661538462

00:52:52.984 --> 00:52:55.579 your most current classification system.

NOTE Confidence: 0.939893661538462

00:52:55.580 --> 00:52:58.094 Another important aspect that I emphasized

NOTE Confidence: 0.939893661538462

00:52:58.094 --> 00:53:01.487 earlier on is be astute at recognizing

NOTE Confidence: 0.939893661538462

00:53:01.487 --> 00:53:03.128 the heterogeneous heterogeneous

NOTE Confidence: 0.939893661538462

00:53:03.128 --> 00:53:05.960 ways these entities may present,

NOTE Confidence: 0.939893661538462

00:53:05.960 --> 00:53:09.194 including having a high index of suspicion.

NOTE Confidence: 0.939893661538462

00:53:09.200 --> 00:53:11.712 If you have a T lymphoblastic lymphoma in

NOTE Confidence: 0.939893661538462

00:53:11.712 --> 00:53:14.519 a lymph node or in the skin or something.

NOTE Confidence: 0.939893661538462

00:53:14.520 --> 00:53:16.690 Just be thinking about that if the

NOTE Confidence: 0.939893661538462

00:53:16.690 --> 00:53:18.618 S and affiliate is not present,

NOTE Confidence: 0.939893661538462

00:53:18.620 --> 00:53:20.940 and then in the words of Doctor Lebaron

NOTE Confidence: 0.939893661538462

00:53:20.940 --> 00:53:22.629 Washington he's a hematopathologist.

NOTE Confidence: 0.939893661538462

00:53:22.630 --> 00:53:25.518 He practices in Houston, he was a hematoma.

NOTE Confidence: 0.939893661538462

00:53:25.520 --> 00:53:27.932 Pathology fellow a couple of years

NOTE Confidence: 0.939893661538462

00:53:27.932 --> 00:53:29.138 ahead of me.

NOTE Confidence: 0.939893661538462

00:53:29.140 --> 00:53:30.940 I really appreciate this quote

NOTE Confidence: 0.939893661538462

00:53:30.940 --> 00:53:32.740 if it does not fit,

NOTE Confidence: 0.939893661538462

00:53:32.740 --> 00:53:34.936 you must not quit and this is so true

NOTE Confidence: 0.939893661538462

00:53:34.936 --> 00:53:36.948 and pathology it's true in clinical

NOTE Confidence: 0.939893661538462

00:53:36.948 --> 00:53:39.043 medicine and it's true in these

NOTE Confidence: 0.939893661538462

00:53:39.043 --> 00:53:41.035 sneaky cases of bias and affilia.

NOTE Confidence: 0.939893661538462

00:53:41.040 --> 00:53:43.544 So if your case doesn't make sense or

NOTE Confidence: 0.939893661538462

00:53:43.544 --> 00:53:46.659 something isn't adding up, don't give up.

NOTE Confidence: 0.939893661538462

00:53:46.659 --> 00:53:48.498 Continue your investigation.

NOTE Confidence: 0.939893661538462

00:53:48.500 --> 00:53:49.247 And with that,

NOTE Confidence: 0.939893661538462

00:53:49.247 --> 00:53:51.600 I thank you very much for your attention,

NOTE Confidence: 0.939893661538462

00:53:51.600 --> 00:53:53.896 and I'd be happy to take any questions.

NOTE Confidence: 0.824112487894737

00:53:58.030 --> 00:53:59.418 Thank you so much.

NOTE Confidence: 0.824112487894737

00:53:59.418 --> 00:54:02.141 I think that was the most clear

NOTE Confidence: 0.824112487894737

00:54:02.141 --> 00:54:04.353 presentation and walk through

NOTE Confidence: 0.824112487894737

00:54:04.353 --> 00:54:06.565 of esena Phillip disorders.

NOTE Confidence: 0.824112487894737

00:54:06.570 --> 00:54:09.154 Just want to see if anybody has questions.

NOTE Confidence: 0.824112487894737

00:54:09.160 --> 00:54:10.492 They want to just.

NOTE Confidence: 0.824112487894737

00:54:10.492 --> 00:54:12.980 Pop in or throw in the chat.

NOTE Confidence: 0.755343238833333

00:54:24.800 --> 00:54:27.860 OK Manji, you have an announcement.

NOTE Confidence: 0.755343238833333

00:54:27.860 --> 00:54:30.530 First of all I want to congratulate

NOTE Confidence: 0.755343238833333

00:54:30.530 --> 00:54:34.172 Doctor Richard for such a fantastic

NOTE Confidence: 0.755343238833333

00:54:34.172 --> 00:54:37.620 presentation on hypereosinophilic syndromes

NOTE Confidence: 0.755343238833333

00:54:37.620 --> 00:54:41.470 and this is so fitting because this is

NOTE Confidence: 0.886466445

00:54:41.480 --> 00:54:45.380 the last grand round of our academic year.

NOTE Confidence: 0.886466445

00:54:45.380 --> 00:54:48.810 So it's ending on a very high dot.

NOTE Confidence: 0.886466445

00:54:48.810 --> 00:54:51.790 If it does not fit, do not quit.

NOTE Confidence: 0.886466445

00:54:51.790 --> 00:54:53.670 I love that. Thank you.

NOTE Confidence: 0.895815633333333

00:54:55.710 --> 00:54:58.356 I actually have a question on you

NOTE Confidence: 0.895815633333333

00:54:58.356 --> 00:55:00.648 know we we have quite a few of these.

NOTE Confidence: 0.895815633333333

00:55:00.650 --> 00:55:03.106 Mastocytosis mast cell hyperplasia.

NOTE Confidence: 0.895815633333333

00:55:03.106 --> 00:55:06.790 Sometimes in the context of PDGFRA,

NOTE Confidence: 0.895815633333333

00:55:06.790 --> 00:55:10.814 PDGFRB rearranged tumors and,

NOTE Confidence: 0.895815633333333

00:55:10.814 --> 00:55:14.675 you know, without seeing how it rolls

NOTE Confidence: 0.895815633333333

00:55:14.675 --> 00:55:16.520 out genetically when you're trying

NOTE Confidence: 0.895815633333333

00:55:16.583 --> 00:55:18.485 to make that diagnosis at first,

NOTE Confidence: 0.895815633333333

00:55:18.490 --> 00:55:21.310 it can be very difficult.

NOTE Confidence: 0.895815633333333

00:55:21.310 --> 00:55:24.045 Whether you're going to actually

NOTE Confidence: 0.895815633333333

00:55:24.045 --> 00:55:26.233 call it SMTHN and.

NOTE Confidence: 0.895815633333333

00:55:26.240 --> 00:55:28.688 I wonder sometimes when you get

NOTE Confidence: 0.895815633333333

00:55:28.688 --> 00:55:30.532 everything back and you know.

NOTE Confidence: 0.895815633333333

00:55:30.532 --> 00:55:32.320 Of course you still mentioned

NOTE Confidence: 0.895815633333333

00:55:32.320 --> 00:55:33.800 that there is mastocytosis,

NOTE Confidence: 0.895815633333333

00:55:33.800 --> 00:55:36.956 but now it's PDGFRA or PDGFRB,

NOTE Confidence: 0.895815633333333

00:55:36.960 --> 00:55:38.780 really driving the whole process,

NOTE Confidence: 0.895815633333333

00:55:38.780 --> 00:55:41.620 especially without the KIT mutation,

NOTE Confidence: 0.895815633333333

00:55:41.620 --> 00:55:43.920 would you say that those patients

NOTE Confidence: 0.895815633333333

00:55:43.920 --> 00:55:47.520 really do not have a clinical

NOTE Confidence: 0.895815633333333

00:55:47.520 --> 00:55:50.370 behavior fitting with SM, or even

NOTE Confidence: 0.821843752857143

00:55:51.340 --> 00:55:52.999 yeah, so that is a great question.

NOTE Confidence: 0.821843752857143

00:55:53.000 --> 00:55:56.358 So this is me speaking, you know,

NOTE Confidence: 0.821843752857143

00:55:56.358 --> 00:55:58.153 just as me terminology is

NOTE Confidence: 0.821843752857143

00:55:58.153 --> 00:55:59.730 absolutely critical in a case.

NOTE Confidence: 0.821843752857143

00:55:59.730 --> 00:56:02.808 Those are not systemic mastocytosis cases.

NOTE Confidence: 0.821843752857143

00:56:02.810 --> 00:56:04.938 We have seen cases that present just

NOTE Confidence: 0.821843752857143

00:56:04.938 --> 00:56:07.133 the whole bone marrows we faced

NOTE Confidence: 0.821843752857143

00:56:07.133 --> 00:56:08.765 by spindled aggregated massels,

NOTE Confidence: 0.821843752857143

00:56:08.770 --> 00:56:12.558 but they have a PDGFRA not call those SM.

NOTE Confidence: 0.821843752857143

00:56:12.558 --> 00:56:13.806 Those are not SM.

NOTE Confidence: 0.821843752857143

00:56:13.810 --> 00:56:15.736 They do not need to be on my to

NOTE Confidence: 0.821843752857143

00:56:15.736 --> 00:56:17.669 store and they I mean they they they

NOTE Confidence: 0.821843752857143

00:56:17.669 --> 00:56:19.829 need to go a totally different way.

NOTE Confidence: 0.821843752857143

00:56:19.830 --> 00:56:22.044 So the way you know we had that SH

NOTE Confidence: 0.821843752857143

00:56:22.044 --> 00:56:24.469 EA HP Workshop a couple years ago

NOTE Confidence: 0.821843752857143

00:56:24.469 --> 00:56:26.680 and we actually talked about what?

NOTE Confidence: 0.821843752857143

00:56:26.680 --> 00:56:28.306 The terminology should be because The

NOTE Confidence: 0.821843752857143

00:56:28.306 --> 00:56:30.619 Who is not very helpful in this regard,

NOTE Confidence: 0.821843752857143

00:56:30.620 --> 00:56:32.678 and they actually say you know most

NOTE Confidence: 0.821843752857143

00:56:32.678 --> 00:56:34.745 cases of PDGFRA present as chronic

NOTE Confidence: 0.821843752857143

00:56:34.745 --> 00:56:36.620 chest and affiliate leukemia Nos.

NOTE Confidence: 0.821843752857143

00:56:36.620 --> 00:56:38.055 Please do not call it that either,

NOTE Confidence: 0.821843752857143

00:56:38.060 --> 00:56:39.326 because that's not what it is.

NOTE Confidence: 0.821843752857143

00:56:39.330 --> 00:56:41.115 That's a death sentence for the patient,

NOTE Confidence: 0.821843752857143

00:56:41.120 --> 00:56:41.447 right?

NOTE Confidence: 0.821843752857143

00:56:41.447 --> 00:56:43.736 So I think I would advocate the

NOTE Confidence: 0.821843752857143

00:56:43.736 --> 00:56:46.137 best way to sign these cases out.

NOTE Confidence: 0.821843752857143

00:56:46.140 --> 00:56:47.804 You saw the way I did the one

NOTE Confidence: 0.821843752857143

00:56:47.804 --> 00:56:48.874 with the 5th 1L1.

NOTE Confidence: 0.821843752857143

00:56:48.874 --> 00:56:50.509 I call it chronic myeloid

NOTE Confidence: 0.821843752857143

00:56:50.509 --> 00:56:52.139 neoplasm because it's not wrong.

NOTE Confidence: 0.821843752857143

00:56:52.140 --> 00:56:54.142 It has its own affilia and I

NOTE Confidence: 0.821843752857143

00:56:54.142 --> 00:56:55.662 specifically state with the genetic

NOTE Confidence: 0.821843752857143

00:56:55.662 --> 00:56:57.474 alteration is and I actually do.

NOTE Confidence: 0.821843752857143

00:56:57.480 --> 00:57:00.580 Not further subcategorize it because.

NOTE Confidence: 0.821843752857143

00:57:00.580 --> 00:57:03.871 In our current thinking of The Who you know,

NOTE Confidence: 0.821843752857143

00:57:03.871 --> 00:57:05.856 CML is its own thing.

NOTE Confidence: 0.821843752857143

00:57:05.860 --> 00:57:07.360 It has a triple hit genetics.

NOTE Confidence: 0.821843752857143

00:57:07.360 --> 00:57:09.649 It is not PDGFR beta rearranged so

NOTE Confidence: 0.821843752857143

00:57:09.649 --> 00:57:12.652 please do not call that CML with EOS

NOTE Confidence: 0.821843752857143

00:57:12.652 --> 00:57:14.597 and that PDGFR beta rearrangement.

NOTE Confidence: 0.821843752857143

00:57:14.600 --> 00:57:16.778 So I think you bring up a very very

NOTE Confidence: 0.821843752857143

00:57:16.778 --> 00:57:18.695 good point that while the terminology

NOTE Confidence: 0.821843752857143

00:57:18.695 --> 00:57:21.278 we have right now is kind of clunky,

NOTE Confidence: 0.821843752857143

00:57:21.280 --> 00:57:23.260 it it works because it conveys.

NOTE Confidence: 0.821843752857143

00:57:23.260 --> 00:57:25.024 Is it chronic or is it acute?

NOTE Confidence: 0.821843752857143

00:57:25.030 --> 00:57:26.774 You know which abnormality

NOTE Confidence: 0.821843752857143

00:57:26.774 --> 00:57:28.518 abnormality does it have,

NOTE Confidence: 0.821843752857143

00:57:28.520 --> 00:57:30.984 but you don't want to give the patient.

NOTE Confidence: 0.821843752857143

00:57:30.990 --> 00:57:32.007 For the clinician,

NOTE Confidence: 0.821843752857143

00:57:32.007 --> 00:57:33.702 the impression that it's going

NOTE Confidence: 0.821843752857143

00:57:33.702 --> 00:57:35.079 to behave like an SM,

NOTE Confidence: 0.821843752857143

00:57:35.080 --> 00:57:36.394 when in fact it has nothing

NOTE Confidence: 0.821843752857143

00:57:36.394 --> 00:57:37.700 to do with SM at all.

NOTE Confidence: 0.821843752857143

00:57:37.700 --> 00:57:40.550 So very very good point.

NOTE Confidence: 0.821843752857143

00:57:40.550 --> 00:57:41.064 And actually,

NOTE Confidence: 0.821843752857143

00:57:41.064 --> 00:57:43.520 if you see a case that you think is

NOTE Confidence: 0.821843752857143

00:57:43.520 --> 00:57:45.536 SM or has perivascular aggregates or

NOTE Confidence: 0.821843752857143

00:57:45.536 --> 00:57:47.500 peritubular and your kit is negative.

NOTE Confidence: 0.821843752857143

00:57:47.500 --> 00:57:49.024 And you've only activated the mass

NOTE Confidence: 0.821843752857143

00:57:49.024 --> 00:57:50.743 cell side of the pathway because

NOTE Confidence: 0.821843752857143

00:57:50.743 --> 00:57:52.378 you don't have ESPN affiliate,

NOTE Confidence: 0.821843752857143

00:57:52.380 --> 00:57:53.122 for example.

NOTE Confidence: 0.821843752857143

00:57:53.122 --> 00:57:55.348 Don't forget to do PDGFR alpha

NOTE Confidence: 0.821843752857143

00:57:55.348 --> 00:57:56.910 because you may prized.

NOTE Confidence: 0.8043536775

00:57:58.810 --> 00:58:00.903 Yeah, one thing that I I'm sure

NOTE Confidence: 0.8043536775

00:58:00.903 --> 00:58:03.063 you just didn't have time to get

NOTE Confidence: 0.8043536775

00:58:03.063 --> 00:58:05.210 to is a lymphocytic variant of HHS

NOTE Confidence: 0.8043536775

00:58:05.210 --> 00:58:07.314 which you know that work up for.

NOTE Confidence: 0.8043536775

00:58:07.314 --> 00:58:10.520 US at least has been. Mainly, you know,

NOTE Confidence: 0.8043536775

00:58:10.520 --> 00:58:13.270 instigated on the clinical side.

NOTE Confidence: 0.8043536775

00:58:13.270 --> 00:58:16.742 I wonder how much have you guys just

NOTE Confidence: 0.8043536775

00:58:16.742 --> 00:58:19.789 initiated the work up for LVHS versus,

NOTE Confidence: 0.8043536775

00:58:19.790 --> 00:58:21.370 you know, getting the flow

NOTE Confidence: 0.8043536775

00:58:21.370 --> 00:58:23.310 request and then doing the rest?

NOTE Confidence: 0.784812512727273

00:58:23.500 --> 00:58:24.172 Yeah, so we.

NOTE Confidence: 0.784812512727273

00:58:24.172 --> 00:58:26.030 I mean we to be honest with you.

NOTE Confidence: 0.784812512727273

00:58:26.030 --> 00:58:27.689 I mean I think maybe over 20

NOTE Confidence: 0.784812512727273

00:58:27.689 --> 00:58:29.139 years we've seen like 8 or 10.

NOTE Confidence: 0.784812512727273

00:58:29.140 --> 00:58:31.700 These cases that we actually think are LBHS.

NOTE Confidence: 0.784812512727273

00:58:31.700 --> 00:58:33.068 They're not like emerging

NOTE Confidence: 0.784812512727273

00:58:33.068 --> 00:58:34.778 PTCL or something like that,

NOTE Confidence: 0.784812512727273

00:58:34.780 --> 00:58:36.970 but because they exist and because

NOTE Confidence: 0.784812512727273

00:58:36.970 --> 00:58:39.723 you know the largest study was out of

NOTE Confidence: 0.784812512727273

00:58:39.723 --> 00:58:41.997 the NIH in terms of treatment since

NOTE Confidence: 0.784812512727273

00:58:41.997 --> 00:58:44.217 they respond so well to steroids,

NOTE Confidence: 0.784812512727273

00:58:44.220 --> 00:58:45.165 we actually do.

NOTE Confidence: 0.784812512727273

00:58:45.165 --> 00:58:47.055 Do we usually do peripheral blood

NOTE Confidence: 0.784812512727273

00:58:47.055 --> 00:58:49.072 flow for the aberrant T cell phones

NOTE Confidence: 0.784812512727273

00:58:49.072 --> 00:58:51.288 in every case of the US and affiliate

NOTE Confidence: 0.784812512727273

00:58:51.288 --> 00:58:54.111 just to get that out as a dot.

NOTE Confidence: 0.784812512727273

00:58:54.111 --> 00:58:56.836 Basically as a diagnosis so you

NOTE Confidence: 0.784812512727273

00:58:56.836 --> 00:58:58.488 know every now and then we get

NOTE Confidence: 0.784812512727273

00:58:58.488 --> 00:58:59.929 surprised when we get an abnormal.

NOTE Confidence: 0.784812512727273

00:58:59.930 --> 00:59:00.779 The cell clone,

NOTE Confidence: 0.784812512727273

00:59:00.779 --> 00:59:02.760 but almost all cases I would say

NOTE Confidence: 0.784812512727273

00:59:02.820 --> 00:59:05.160 upwards of 99% of the cases with

NOTE Confidence: 0.784812512727273

00:59:05.160 --> 00:59:06.910 ease and affiliate are negative

NOTE Confidence: 0.784812512727273

00:59:06.978 --> 00:59:09.938 by I think you know flow in most

NOTE Confidence: 0.784812512727273

00:59:09.938 --> 00:59:12.050 instances isn't that expensive,

NOTE Confidence: 0.784812512727273

00:59:12.050 --> 00:59:14.395 so I think you know again because

NOTE Confidence: 0.784812512727273

00:59:14.395 --> 00:59:16.170 it impacts the diagnosis,

NOTE Confidence: 0.784812512727273

00:59:16.170 --> 00:59:17.568 but it also impacts how this

NOTE Confidence: 0.784812512727273

00:59:17.568 --> 00:59:18.930 patient's going to be treated.

NOTE Confidence: 0.784812512727273

00:59:18.930 --> 00:59:19.524 I mean,

NOTE Confidence: 0.784812512727273

00:59:19.524 --> 00:59:21.306 it's just it's a totally different

NOTE Confidence: 0.784812512727273

00:59:21.306 --> 00:59:23.746 deal when it's LVHS versus it's a

NOTE Confidence: 0.784812512727273

00:59:23.746 --> 00:59:25.151 reactive Austin affiliate, right?

NOTE Confidence: 0.784812512727273

00:59:25.151 --> 00:59:27.799 Or a mass cell process the the will

NOTE Confidence: 0.784812512727273

00:59:27.799 --> 00:59:30.339 do something entirely different.

NOTE Confidence: 0.787123338888889

00:59:31.300 --> 00:59:33.487 Yeah, the flow for T cell panel is done,

NOTE Confidence: 0.787123338888889

00:59:33.490 --> 00:59:36.490 but I I think you know sometimes they're

NOTE Confidence: 0.787123338888889

00:59:36.490 --> 00:59:39.439 not thinking about that entity specifically

NOTE Confidence: 0.864694529230769

00:59:39.980 --> 00:59:41.268 and that's why we have it as part

NOTE Confidence: 0.864694529230769

00:59:41.268 --> 00:59:42.479 of our algorithm number one.

NOTE Confidence: 0.864694529230769

00:59:42.480 --> 00:59:43.896 I don't forget to do it,

NOTE Confidence: 0.864694529230769

00:59:43.900 --> 00:59:46.884 but I also you know it gets covered.

NOTE Confidence: 0.864694529230769

00:59:46.890 --> 00:59:49.669 Yeah. Yeah, no great question.

NOTE Confidence: 0.927273177777778

00:59:53.960 --> 00:59:55.300 All right, I think we're

NOTE Confidence: 0.927273177777778

00:59:55.300 --> 00:59:56.372 actually on the hour.

NOTE Confidence: 0.927273177777778

00:59:56.380 --> 00:59:58.920 If nobody has other questions,

NOTE Confidence: 0.927273177777778

00:59:58.920 --> 01:00:00.678 I just really want to thank

NOTE Confidence: 0.927273177777778

01:00:00.678 --> 01:00:02.214 Doctor Weikart for coming today

NOTE Confidence: 0.927273177777778

01:00:02.214 --> 01:00:04.020 and speaking to us and visiting.

NOTE Confidence: 0.927273177777778

01:00:04.020 --> 01:00:05.819 I hope that I'll be able to

NOTE Confidence: 0.927273177777778

01:00:05.819 --> 01:00:07.773 get you to physically come in

NOTE Confidence: 0.927273177777778

01:00:07.773 --> 01:00:09.987 and have some New Haven pizza.

NOTE Confidence: 0.768954052

01:00:10.540 --> 01:00:11.920 Yeah, that would be great.

NOTE Confidence: 0.768954052

01:00:11.920 --> 01:00:13.070 Yeah, thank you very much

NOTE Confidence: 0.768954052

01:00:13.070 --> 01:00:13.990 again for the opportunity.

NOTE Confidence: 0.768954052

01:00:13.990 --> 01:00:15.490 It was an absolute pleasure and

NOTE Confidence: 0.768954052

01:00:15.490 --> 01:00:17.199 I love meeting the people I did.

NOTE Confidence: 0.768954052

01:00:17.200 --> 01:00:18.244 And yeah, it was.

NOTE Confidence: 0.768954052

01:00:18.244 --> 01:00:19.549 It was a great day.

NOTE Confidence: 0.768954052

01:00:19.550 --> 01:00:20.530 Thank you so much.

NOTE Confidence: 0.586536735

01:00:22.170 --> 01:00:22.850 Mind you.