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Welcome to Yale Cancer Center Answers with your hosts doctors Anees Chagpar, Susan Higgins and Steven Gore. Dr. Chagpar is Associate Professor of Surgical Oncology and Director of the Breast Center at Smilow Cancer Hospital at Yale, New Haven. Dr. Higgins is Professor of Therapeutic Radiology and of Obstetrics, Gynecology and Reproductive Sciences and Dr. Gore is Director of Hematological Malignancies at Smilow and an expert on Myelodysplastic Syndromes. Yale Cancer Center Answers features weekly conversations about the research diagnosis and treatment of cancer and if you would like to join the conversation, you can submit questions and comments to canceranswers@yale.edu or you can leave a voicemail message at 888-234-4YCC. This week it is a conversation about ophthalmic oncology with Dr. Flora Levin and Dr. Miguel Materin. Dr. Materin is Associate Professor of Medicine and of Ophthalmology and Visual Science and Director of Ophthalmic Oncology and Dr. Levin is Assistant Clinical Professor of Ophthalmology and Visual Science at Yale School of Medicine. Here is Dr. Steven Gore.

Gore Ophthalmic oncology, I have to say, this is something as an oncologist, I don’t think I know a lot about, what is it that the two of you do? Do you do the same thing?

Materin We deal with tumors, both benign and malignant, affecting the eye and tissues surrounding it including the eyelids, the eye, the surface of the eye and the orbit.

Gore How many different kinds of eye cancers are there?

Levin More than you can imagine, and more than one would think there are and I think that is something that our patients are always surprised by, and will say “I never thought I could get melanoma in my eye or skin cancer on my eyelids or tumors behind the eye.”

Gore We have heard about retinoblastoma for little kids, right?

Materin Yes. Every time we have interviews like these, it is not that it is happening every day.

Gore Well, I can imagine it should be.

Materin Something we would like to emphasize is this is not a common condition, so I do not want people who hear these conversation to think that there is a problem in their eye and the first thing they are going to be concerned about is a tumor, it is not that common. The thing is that because we specialize in that, we see more patients than the average ophthalmologist.

Gore How does somebody find out that they have an eye cancer? Do I need to be staring in my mirror every day when I am shaving and open up my eyelids and flash a light around?

Levin Our subspecialties divide a little bit in that I can speak to the external aspects, the periocular area.
Gore       Periocular, what does that mean?

Levin     The area around the eye, the eyebrows, the forehead, the upper cheek, the side of the nose, the outer temple, that is all in the realm of what I would look at.

Gore       It sounds like plastic surgery.

Levin     You are absolutely right. It is plastic surgery that concentrates in that area but also as an ophthalmologist, for me, I am educated and trained and very sensitive to conditions of the eye itself.

Gore       So are these mostly skin cancers that show up in those places?

Levin     For me, yes, the vast majority of the oncology that I deal with is skin cancers on the outside of the eye but also tumors behind the eyeball and eye socket or the orbit and those tumors can be either new tumors or metastatic lesions that have spread from somewhere else.

Gore       Tell us a little bit about what you do with these various tumors, I imagine that with these facial tumors, people self-identify, like you would anything on your face that gets diagnosed as cancer or no?

Levin     Sometimes and sometimes not because I think that people do not necessarily look for stuff or think of stuff on their eyelids, so often it gets referred from a general ophthalmologist who astutely recognized something while doing an exam or a dermatologist, especially in folks that have prior history of skin cancers, and then the vast majority of treatment is surgical and reconstructive but there are some nonsurgical options that we can offer as well.

Gore       And what about these tumors behind the eye, that sounds pretty scary.

Levin     A lot of them are benign. A lot of common things that we see will be benign and do not always require treatment, they can be followed. When they are not benign, a lot of times it is a multispecialty approach because even though I may be involved in getting the diagnosis by doing the biopsy, the treatment may not be surgical.

Gore       How does one biopsy a tumor behind the eye?
Levin There are ways.

Gore That is a trade secret that you are not going to give away.

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Levin I do not have to take the eyeball out, let us put it that way.

Gore I do not know how you are Susan, but eye surgery stuff just freaks me out and it does not sound very medical but it does.

Higgins As a radiation oncologist, I have been here since the day that we actually started the COMS project here with the plaques, so I actually participated in these cases almost 20 years ago with some of my colleagues and it really was fascinating to see exactly what you could do to gain exposure to that area and then put it all back together.

Gore You did not freak out.

Higgins It did bother me a little.

Materin Well that is an important point because people in general they think, who can have a tumor in the eye, but yes it does exist.

Gore I once had my ophthalmologist say that I have a nevus mole on my retina or wherever it is back there and all of a sudden that was kind of scary to have an ophthalmologist say, we have to follow this and take pictures every couple of years and make sure that is not melanoma, it was pretty scary.

Materin Actually that is what we do most of the time. Most of our patients are referred by other physicians because of the specialty.

Gore Miguel, you do not deal with these facial things and you do not deal behind the eyeball?

Materin The surface of the eye and the intraocular tumors inside the eye.

Gore So what kinds of cancers are those, are those metastatic or are they primary?
They can be primary, which means that they originate in the eye or they can come from other sites or other cancers like lung and breast, they are the most common ones when they spread to go into the eye and the primary cancers that originate from the eye in adults, the most common one is melanoma and in young kids, retinoblastoma.

Gore So when you talk about melanoma in the eye, it is not a metastatic lesion from the skin?

Materin Most of the time, it is not. It originates from the eye. The eye, actually, after the skin is the second most common place.

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Gore Are there melanocyte cells in the retina or in the eyeball somewhere?

Materin There is a structure behind the retina called a choroid. The choroid is a bed of blood that has melanocytes and that is where these melanomas can originate in the eye.

Gore I never really learned ophthalmic anatomy, I have to say. Choroid has always been very perplexing to me, and that is fascinating. Can these tumors be treated with curative intent?

Materin Yes, again we need to discuss that each tumor is different and each patient is different, so if we start talking about the retinoblastoma, the tumors that can affect young kinds, the good news is that it is one of the most curable tumors in the human body, so more than 90% of these kids can be cured from the cancer, at least in this county, which is not the same situation in several countries. That does not mean it is easy, there is a lot of work, it is a team effort because it is not only Dr. Levin and Dr. Materin, there is pediatric oncology involved, sometimes neuro-oncology involved, neurovascular surgeons, it is a whole team effort and I would like to include the nurses and our assistants because they need to talk to these patients and these families every week, so that is regarding the retinoblastoma. Regarding the melanoma, I know it is the same name of the melanoma of the skin, but the behavior is not like the one on the skin. As an example, when the melanoma from the skin spreads, most of the time, it goes to the lymph nodes first. When melanoma in the eye spreads, the most common place that it goes is the liver.

Gore Liver? I would have guessed maybe the brain because it would seem like it could creep right along the optic nerve.

Materin We really do not know why the liver, but that is the most common place for metastasis and the second is the lungs.
Gore It is a little off topic, I suppose, but are people studying the biology of these melanomas compared to skin melanomas?

Materin Yes, that is an excellent question because that is one of the reasons their behavior is different too, not every melanoma of the skin has the same gene mutations or gene alterations than when they are due to exposure to the sun. By the way, melanoma in the eye at least until today is not related to the sun exposure. Yes, there are specific mutations for melanomas inside the eye.

Gore And another question I wanted to ask you about that is we know that melanomas of the skin tend to be increased in fair skinned individuals and so on, is that also the case with melanoma of the eye or?

Materin Yes, it is, it is more common in white people.

Gore Gotcha.

Materin One point I would like to make also is that a diagnosis of intraocular tumor does not mean that we need to remove the eye, there are other methods and Susan, gladly she is here from radiation oncology because we work with them all the time, I can say every week.

Higgins We have used this team approach, radiation oncology and ophthalmic oncology, and I get some really good outcomes in these people and I was wondering if you could talk about the range of options for people with melanoma of the eye and basically where radiation fits into it and where other therapies fit in?

Materin Well as long as we can save the eye, we will try to use conservative methods, the main one is local radiation, and we do that in two surgeries. We put a small coin on the surface of the eye exactly where the tumor is, the patient stays in the hospital for four days and then we take the patient back to the operating room to remove the radiation device. When we have no chance to save the eye that is when we think about removing the eye and that is part of Dr. Levin’s work.

Higgins And even on the side of radiation, we have a whole team behind the scenes because these plaques are a very specialized type of instrument to treat this and we have a physicist, a radiation oncologist, and we actually come back from the OR and do all the calculations in terms of dose and
how long the plaque should be there and I think it is very gratifying for the radiation oncologists because we treat these patients and have some very good outcomes.

Gore  Where does the plaque sit, on top of the eye or inside the eye?

Materin  We localize where the tumor is and sometimes it is in the eye but in the posterior part of the eye and we do not remove the eye, we just rotate the eye.

Gore  He knows that I am going to freak out if he tells me that.

Materin  Yes, we localize and we are very, if I can use the term, compulsive about where the tumor is and actually once the plaque is placed, we use an ultrasound to be sure that the plaque is right behind the tumor. It is on the surface of the eye, it is on the eye wall.

Gore  I see, it is not inside the eye.

Materin  No it is not inside, we suture the plaque to the eye wall.

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Gore  And they stay in the hospital for four days?

Materin  Yes, it’s more of a precaution for other people, we do not want patients with radiation devices walking around.

Gore  You definitely do not want to walk through the sensors in the airport.

Materin  Absolutely not.

Higgins  We are going to take a short break for a medical minute. Please stay tuned to learn more information about ophthalmic oncology with Dr. Miguel Materin and Dr. Flora Levin.

Medical Minute  The American Cancer Society estimates that over 1500 people will be diagnosed with colorectal cancer in Connecticut alone this year. When detected early, colorectal cancer is easily treated and highly curable and as a result, it is recommended that men and women over the age of 50 have regular colonoscopies to screen for the disease. Clinical trials are currently underway at
federally designated comprehensive cancer centers, such as the one at Yale Cancer Center and at Smilow Cancer Hospital to test innovative treatments for colorectal cancer. Tumor gene analysis has helped to improve the management of the disease by identifying the patient’s most likely to benefit from chemotherapy and newer targeted agents resulting in a more patient-specific treatment. This has been a medical minute brought to you as a public service by Yale Cancer Center and Smilow Cancer Hospital at Yale-New Haven. More information is available at yalecancercenter.org. You are listening to WNPR, Connecticut’s Public Media Source for news and ideas.

Higgins Welcome back to Yale Cancer Center Answers. This is Dr. Susan Higgins along with my co-host Dr. Steven Gore. We are talking with our guests Dr. Miguel Materin and Dr. Flora Levin about ophthalmic oncology. Welcome back. So one of the issues that we discussed during our last session prior to the break was retinoblastoma, maybe you could tell our listeners what exactly retinoblastoma is and what the treatment approaches are and how you fit into that picture?

Materin Retinoblastoma is the most common intraocular primary tumor in young kids. It can affect one eye or it can affect both eyes. Also it can be a familial condition that different members of the same family can have, so there is a genetic component in some circumstances. One of the main points that we discuss with the parents and with the families is that the diagnosis of retinoblastoma does not mean removing the eyes. This does not mean that the kid is going to be blind. Yes, it is a cancer, but it is curable and our first call is to save the baby’s life. As I mentioned before, more than 90% of these kids can be saved from that. There are different methods to treat these patients and it depends on how many tumors the kid has, if one or both eyes are involved, etc., etc. The most recent treatment, and we do this treatment here at Yale, is what is called intra-arterial chemotherapy, so a pediatric vascular surgeon finds the femoral artery which is in the leg and places a catheter and it is done by the interventional neuroradiologist, Dr. Bulsara, and he puts the catheter right behind the eye and in the internal carotid artery and then they find the ophthalmic artery and that is where the chemotherapy is injected. Most of the time it requires more than one session once a month. That is I can say the number one treatment today. The second treatment is systemic chemotherapy, that is the chemotherapy that is provided to the entire body and then when we have no choice, Dr. Levin has to be involved and sometimes she needs to remove the eyes.

Higgins I find this really fascinating. Again, I was trained in the era as a radiation oncologist where the main state was radiation enucleation, we had only two choices and now we have a whole team of people as you just discussed. Could you fill us in on how your team works together and do you have tumor boards, how do you communicate?
Materin  Well most of the time the patients are referred by another physician, there is a phone call or an e-mail and that is when our assistant sends a communication to everybody that is going to be involved. Before we even know the patient, we know the patient is coming and everyone is aware that we are going to be seeing that kid, so we need to see the baby with general anesthesia and that is when we make the decision and then pediatric oncology will see the baby and will talk with the parents too and that is when the doctors who are involved are going to see the baby, so as I said, we know that it is coming before the baby comes.

Higgins  Then we rally the troupes and bring them in and then what?

Materin  Our goal is to have the baby treated within a week.

Higgins  That is amazing.

Materin  These babies need an MRI, so the imaging people are aware of this and they give this priority so we can have the babies treated within a week.

Gore  How old are these babies generally?

Materin  It can be from as young as a few days to within the first two or three years of life. I have seen it in all those kids and I would like the audience to know that there are only 250 new cases in the United States per year, so it is a very uncommon situation.

Higgins  One of the interesting things though, and this was recently in the news, there is a specific sign that a child with retinoblastoma could have that probably if you see it, should not be ignored, could you talk a little bit about that?

Materin  Of course, this cannot be ignored at all, it is a cancer.

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Higgins  In reflection in the eye.

Materin  Many times there is a wide reflex in one of the eyes or the parents say that the eye looks funny and they say there is some glare or there is a shift in the eye, so that is when at least they need to see the pediatrician and then the pediatric ophthalmologist, and they are going to do their exam and if it is needed, they are going to refer the patient to us.
That is great, just to digress into another area, we were talking about during the break, tumors around the eye and how those can be treated, again it is really a team approach and I was going to ask Dr. Levin if she can kind of outline what kind of tumors do we find around the eye and how does your team work to get the excellent outcome?

The most common tumor that we see of the skin around the eyes is a basal cell carcinoma which is the same as the most common tumor of the skin, in general, but we do see squamous cell carcinoma, we see melanoma and we also see tumors of the eyelids that are a little bit more prevalent and specific to the eyelids themselves that are much more rare, something called sebaceous cell carcinoma or Merkel cell carcinoma, and those can be difficult to diagnose because other things can masquerade or present themselves as benign or a sty, especially in an older person that does not go away with treatment, or comes back after treatment, is something that needs to be looked at carefully and often biopsied to exclude something that is more serious, although a sty is obviously much more common than a cancer. So the treatment is geared towards the specific lesion, obviously the first goal is to eliminate the lesion and a lot of these can be cured and then second is esthetics and function, so for the eye to function is very very important because it is not just how it looks, it is also how it protects the eyeball, covers the eyeball, lubricates the eyeball, so we want to reconstruct the eyelid in the best manner that it function and looks as well as it can and in the vast majority of cases, you would be surprised that even something that affects the entire eyelid, we are not talking about a lot of real estate, about 3 cm, but is something that can affect their whole upper or lower eyelid, can be reconstructed in a manner that is very pleasing both aesthetically and functionally. We still rely on surgery as the main state of treatment for most of these tumors and in certain circumstances in elderly patients or in patients in whom surgery is not the best option, we can use radiation, we can use certain topical agents or chemotherapy but surgery is still what we rely on the types of surgery and what I am talking about mainly is whether we use Mohs micrographic surgery or something called frozen section controlled excision, which is kind of similar but slightly different. It really depends for me where the lesion is, so the goal of the surgery is to spare as much healthy tissue as possible, obviously, especially talking about the eyelid where the real estate is so limited. Really, it is a decision of how much of the eyelid is affected and what the best method of reconstruction may be, so sometimes even though in theory with frozen section excision where the surgeon takes the tumor and sends it to pathology at the time of the surgery, the pathologist looks at the edges and tells the surgeon whether all of the tumor is gone or not, I may have to remove a little extra healthy tissue for reconstructive purposes, that may be the most efficient way of doing it whereas somewhere else that is not on the eyelid.
precisely, but maybe closer to the forehead or the cheek or the temple, a Mohs surgeon would be better equipped to spare as much healthy tissue as possible. Then the reconstructive methods are as vast as plastic surgery itself. We can use grafts, we can use flaps, we can move tissue around and generally the one thing that I think patients are surprised by is it takes time, you have to be patient, but the outcome is good, you just have to get yourself a team, we have to get you through the immediate postoperative period.

Gore So the reconstruction is not done at the time of the primary surgery?

Levin It depends, if I work with the Mohs surgeon, we can do it on the same day and the patient just goes from one place physically to another place but it does not have to be. There are days when we will separate it by a few days or a week and especially for larger lesions that is sometimes something you want to do so that you can plan accordingly. Obviously if the excision and the reconstruction are being done at the same time, then it is all one procedure done by the same person. For non skin cancer tumors, some of the treatments are not surgical. For instance, one of the more common malignancies in eye biopsy is lymphoma and I see it on the inside of the eyelids and we also see it on the eye socket and that can be in patients with a prior history of lymphoma or new lesions that get diagnosed as lymphoma and the treatment for lymphoma is radiation therapy most of the time, not surgery, so my role is to just get the diagnosis, get a piece of the tissue to establish the diagnosis and it is incredible how in the last few years we have been able to more and more precisely identify these tumors with genetic and cytology markers, etc., and again it is a team effort and then I refer the patients to radiation oncologists and get them treated in the most effective manner.

Higgins Having treated some of these patients in the past and having gone through the diagnostic procedures and work with the team, it is really important to have a pathologist who really knows how to look at a lymphoma and get the subtype because they are highly curable but the treatments have to be coordinated and targeted correctly and most of the tertiary care centers have a specific lymphoma pathologist and I think that is a really important member of our team. The public does not realize that there are people in pathology, they are not just general pathologists, and they do this as their main job and they help our team tremendously.

Levin Absolutely, as are ophthalmic pathologists. There are people within pathology who specialize within eye conditions and eye tumors, just as with dermatopathology, so absolutely you could not be more right and the one thing that for me is most disappointing fact which I am going to knock on wood which you can’t hear, but it has never happened to me, is to do a biopsy and not get a diagnosis, so we do everything we possibly can to make sure that we provide ample specimen and that we send it in the correct manner that it can be looked at and the patient can be given the right diagnosis in a timely fashion.
Higgins It is interesting about the pathology issue, because I work with the NCCN and we are actually incorporating this issue of getting expert pathologic diagnosis into the guidelines again because

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there are specific diseases like sarcoma, lymphoma, where it really takes someone who does many of these cases per year to do it well.

Gore Susan, I do not think our audience knows what the NCCN is, you might just want to mention.

Higgins The National Comprehensive Cancer Network is a group of institutions that are select institutions that are a part of a large network of cancer centers and the people who are involved in the NCCN, medical oncologists, radiation oncologists, surgical oncologists, we are working on guidelines that are really supposed to be the standard of care for all diseases and I was just on two conference calls last week and we spent quite a bit of time putting together these expert recommendations and we are now actually about to export some of these to other countries and we are thinking about resource based guidelines but really trying to lead the doctors and the public, there are guidelines geared toward the public also, and get them to follow some of these pathways and really know where to go for the best care and the most expertise.

Dr. Flora Levin is Assistant Clinical Professor of Ophthalmology and Visual Science at Yale School of Medicine and Dr. Miguel Materin is Associate Professor of Medicine and of Ophthalmology and Visual Science and Director of Ophthalmic Oncology. We invite you to share your questions and comments, you can send them to canceranswers@yale.edu or you can leave a voicemail message at 888-234-4YCC and as an additional resource, archived programs are available in both audio and written format at yalecancercenter.org. I am Bruce Barber hoping you will join us again next Sunday evening at 6:00 for another edition of Yale Cancer Center Answers here on WNPR, Connecticut's Public Media Source for news and ideas.