

Unique Challenges of Ocular Oncology

WITH J. WILLIAM HARBOUR, MD

Treating patients with eye cancer is a specialized area of retina care. Certainly the challenges faced are of a different nature than those of a more typical retina practice. Retina Today spoke with J. William Harbour, MD, of the Bascom Palmer Eye Institute in Miami, about some of the differences, and how he approaches them. Figures 1-5 in this article are representative of some examples of diagnostics and imaging for ocular oncology.

Retina Today: From an overall view, how does specializing in ocular oncology make your job different from that of a retina specialist who treats the usual spectrum of retinal problems?

J. William Harbour, MD: One of the major differences is that my patients have potentially fatal diseases, so they and their families come to me afraid and confused. This situation is even further intensified when the patient is a child with eye cancer. So, a major part of my job is to create a bond of trust with the patient and family and to reassure them that I have the expertise that they need and that I will do everything I can to help them. I have to limit the number of patients I see in a day so that I can be sure that each patient receives the time and attention they require and that all their questions are answered. Also, I have to consider the whole patient, not just the eye, and to be knowledgeable of systemic issues related to the cancer patient such as chemotherapeutic agents, radiation therapy, imaging, lab testing and systemic manifestations of their disease. Because most of the conditions that I see are rare, I don't assume that the primary care physician will know how to monitor the patient, so I work closely with the patient's other doctors and personally oversee the systemic testing and imaging. It's a little extra work for me,



Figure 1. Intraoperative ultrasound for plaque localization.

but I believe that it's the right thing to do.

RT: When a patient with uveal melanoma first comes to you, what kind of testing do you recommend to determine the extent of the cancer, and how do you proceed after screening?

Dr. Harbour: I obtain a baseline CT scan of the chest, abdomen and pelvis and a blood test for three liver enzymes. Most of the time, we don't find metastatic cancer at baseline, but many patients will later develop metastasis despite successful treatment of the ocular tumor. We can accurately predict which patients are later going to develop metastasis by obtaining a gene expression profile, which is a molecular prognostic test that renders a result of class 1 if the patient is at low risk or class 2 if the patient is at high risk of metastasis. That allows us to individualize patient care so that the high-risk patients

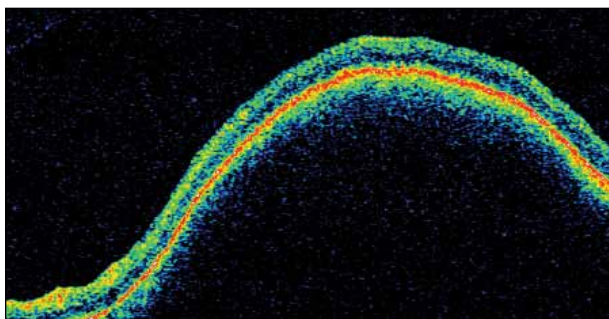


Figure 2. OCT of a choroidal melanoma.

receive intensive surveillance, while sparing the time and expense for low risk patients. For class 2 patients, I recommend liver imaging every 6 months, alternating with blood test to check for liver enzymes. By doing this, we catch metastatic disease earlier and are able to intervene with more effective targeted therapies such as hepatic chemoembolization. Soon, we will offer class 2 patients enrollment into clinical trials to receive medications that may potentially delay or prevent their metastatic disease from developing. This is a recurring theme in my practice; to provide individualized, customized patient care so that high-risk patients get the special attention they need while sparing unnecessary testing and treatments for low-risk patients.

RT: How do you treat for a patient with uveal melanoma?

Dr. Harbour: It depends on a number of factors, such as the size and location of the tumor. About 90% of patients receive plaque radiotherapy, in which a device called a plaque, which looks like a bottle cap made of gold with little radioactive seeds inside, is sewn onto the surface of the eye, left in place for a few days, and then removed.

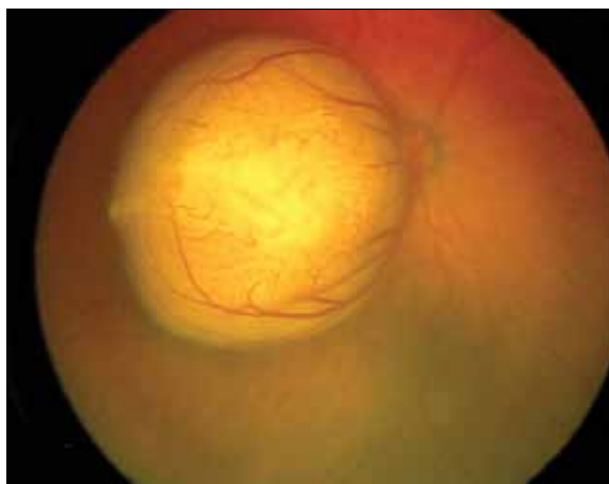


Figure 3. Retinoblastoma.

This treatment is very effective at killing the melanoma, and we are able to boost the success rate even further by using ultrasonography in the operating room to accurately localize the plaque over the tumor. A further technique that I pioneered a few years ago is to check the plaque with ultrasound again at the time of plaque removal. By doing this, we can determine if the plaque may have become tilted away from the eye during the days the plaque was in place. As we reported, a significant proportion of plaques become tilted sufficiently to compromise the radiation dose delivered to the tumor. By identifying these at-risk patients, we can offer them adjuvant diode laser hyperthermia, also called transpupillary thermotherapy (TTT). Some centers perform TTT on every patient, but we found that it is only needed in a minority of patients, and our results speak for themselves: Our local treatment success rate is as good as or better than any reported for plaque radiotherapy or proton beam therapy. This is another example of individualized, customized patient care, where selected patients get adjuvant laser therapy, rather than a 1-size-fits all approach where many patients receive a treatment they may not need.

RT: What kind of complications can arise after plaque radiotherapy?

Dr. Harbour: Some patients have very few complications, but others will develop radiation-induced damage to the retina and optic nerve, transient serous subretinal exudation, sub- and vitreous hemorrhage from intratumoral bleeding, and neovascular glaucoma. The risk of complications depends on a number of factors, including the size and location of the tumor, and the patient's intrinsic sensitivity to radiation. In the past, we had no effective treatments for most of these complications, but today we are making significant progress. For the occasional tumor that bleeds after radiation therapy, causing a vitreous hemorrhage, research that my team and others have done has shown that it is safe to remove the hemorrhage by vitrectomy, as long as the tumor received the full radiation dose. In the past, neovascular glaucoma often led to enucleation for a blind painful eye, but the rate of secondary enucleation has plummeted dramatically in recent years due to the availability of intravitreal anti-VEGF therapy. Usually 1 injection is sufficient to dramatically reverse this process. Anti-VEGF therapy can also improve anatomic outcomes associated with radiation maculopathy and optic neuropathy, but there is still controversy as to whether it results in better visual outcomes. There is also controversy as to whether anti-VEGF therapy should be instituted in an adjuvant (pre-emptive) setting or only after maculopathy and/or neu-

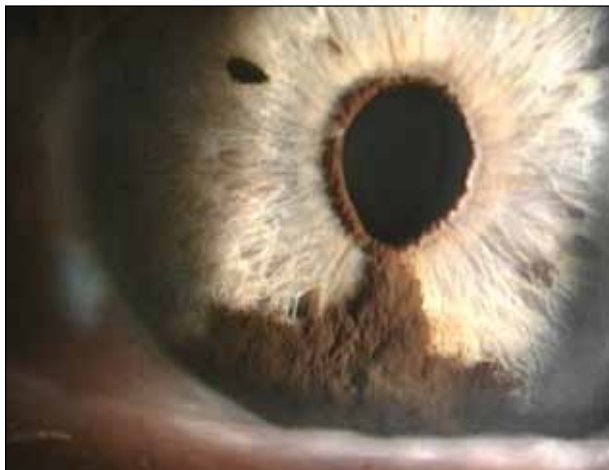


Figure 4. Iris melanoma.

ropathy become clinically evident, and how long injections should be continued. This is an area in which I am working to establish individualized, customized patient care by measuring intraocular VEGF levels to guide therapy, rather than using a 1-size-fits all approach.

RT: What about treating retinoblastoma in children?

Dr. Harbour: Treatment for retinoblastoma depends on the size and extent of disease. Laser therapy and cryotherapy can successfully eradicate most small tumors. Plaque radiotherapy, similar to that for uveal melanoma but with a much lower radiation dose, can be used to treat selected medium-sized tumors that are not amenable to laser or cryotherapy. Chemotherapy is often required when there are large, multifocal tumors and when there is seeding of tumor cells into the vitreous or subretinal space. Chemotherapy can be delivered in several ways, the most common being systemic intravenous infusion and ophthalmic arterial infusion using an interventional radiology approach. Intravenous chemotherapy has been the mainstay for the past 15 years or so, but ophthalmic arterial chemotherapy has taken on a more prominent role in recent years. These 2 chemotherapy techniques have not been compared scientifically, and the appropriate indications for each have not yet been elucidated. Enucleation is occasionally required when there is massive intraocular tumor involvement or invasion of the optic nerve and choroid.

Treatment preferences for retinoblastoma always seem to be in a state of flux and controversy, so I find it critical to keep my own clinical judgment grounded in solid scientific evidence and clinical rationale, rather than the latest popular trend. Obviously, I want to preserve every eye for which it is safe to do so, but I

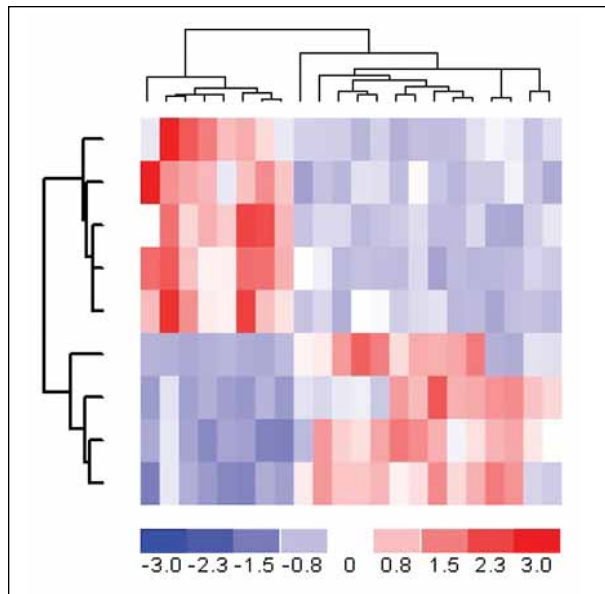


Figure 5. Gene expression profiling for molecular prognostic testing in uveal melanoma.

always have to put the life of the child first. So I employ an individualized, customized management strategy for my retinoblastoma patients, in which all of the available treatment options are employed in the most appropriate settings, rather than a 1-size-fits all approach.

RT: How do you follow your pediatric patients with retinoblastoma?

Dr. Harbour: It depends on many factors, such as whether the patient is receiving chemotherapy, how long it has been since they last had a new or active tumor, whether they had unilateral or bilateral involvement, and how old they are. In general, retinoblastoma patients start out being seen very frequently, often every 3 to 4 weeks. As time goes by and their disease is under control, the follow-up visits become less frequent. Usually by 5 or 6 years old they can be seen just once or twice a year. I obtain genetic testing whenever possible to guide my follow-up regimen. In patients with unilateral involvement who are not found to have a mutation in the retinoblastoma gene from a blood sample, I can usually see them much less frequently and spare them many exams under anesthesia. This is another example, such as the gene expression profile test for uveal melanoma, where molecular testing can allow individualized management that greatly reduces unnecessary examinations and health care costs for low-risk patients while focusing the enhanced surveillance on high-risk patients who need it.

RT: How is it different when your eye cancer patient is a child?

Dr. Harbour: When a child has eye cancer, usually retinoblastoma, it is emotionally and psychologically challenging for everyone. The parents are often dealing with feelings of guilt, thinking that they did something wrong or that they should have detected it earlier. Parents often feel compelled to seek the latest trends in treatment, even when those trends may not be appropriate for their child. It goes back to building a trusting relationship with the parents so that they know you are an expert in what you are talking about and that you are doing what you would for your own child. Having those conversations became much easier after having my own children. Every time I see a child patient, it reminds me of my own daughter, and that provides great clarity about what is best for the child.

RT: Do your patients require longer follow-up than typical retina patients?

Dr. Harbour: With eye cancer patients you never really get to a point where you can tell the patient they don't need to be followed anymore. You have to be concerned about tumor growth, response to therapy, complications of therapy and systemic issues. However, I am very sensitive to the inconveniences that patients endure to travel long distances to see me, so I partner with referring physicians to allow as many follow-up visits as possible to take place closer to home.

RT: It's obviously important to you to spend adequate time with your patients, but are you compensated for that time from a financial standpoint?

Dr. Harbour: The short answer is no. To really do this job well you have to get comfortable with the idea that you're going to do a lot of things that are very important that you are not going to be reimbursed for, at least in the current broken health care system. I have a great ancillary staff, but there is no substitute for my sitting down with the patient and taking an adequate history, performing a thorough examination, reviewing their lab work, fully informing them and answering their questions. That is the basis for the relationship that I try to build with each patient. ■

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