Transcript Details
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The Importance and Utility of GEP Testing

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Hi, my name is Dr. Hadas Skupsky. I'm. A board certified dermatologist and dermatopathologist. I do a little bit of clinical dermatology, but most of my work is at the microscope. I am the Founder and Medical Director of Focus Dermatopathology and also Clinical Assistant Professor of Dermatology at University of California, Irvine.

GEP testing is important in the prognostication of melanomas as well as the diagnosis of melanomas. So there's a GEP testing that can be used when the diagnosis is ambiguous, and you want to know if it is truly a melanoma or not and also GEP testing that can be used when you have an established diagnosis and you want to know more about the particular behavior of this particular tumor.

Our existing staging systems, so our AJCC staging system, is based on clinical pathologic features, things like the Breslow depth of the tumor, the presence of ulceration, the presence of nodal involvement. But this traditional staging system classifies tumors as high or low risk in a very broad sense and guides our treatment management.

But when we look at how individual tumors behave, you can have tumors with the exact same clinical pathologic features, so the exact same Breslow depth, the exact same body location, the exact same age, and one patient survives the melanoma and one patient dies. So the idea here is we want to know a little bit more about the exact tumor biology of this particular neoplasm, so personalized medicine is really the basic idea.

Just to underscore this point, when we look at melanomas diagnosed across our nation, the vast majority of them are diagnosed at a very early stage. Those are the patients that we as dermatologists tend to manage on our own. We don't refer these necessarily to oncology, especially the stage 1 thin melanomas and I, as a dermatologist, when I encounter an early thin stage 1 melanoma, and I call my patient to let them know, "Look, you have a stage 1 melanoma," I often reassure them. I'm not good at delivering bad news. I say, "Look, you have a melanoma, but the great news is we caught it early. You're gonna do fine. We have a 98% survival rate when you just cut this out alone." I give them a whole lot of reassurance.

But when you look statistically at melanoma deaths in the country, more than a quarter of melanoma deaths occur in patients initially diagnosed at stage 1. So what that tells me is I'm kind of giving false assurance a lot of times based on the AJCC staging. I'm a misclassifying some patients' tumors as low risk when in fact their individual tumor biology has something different about it that's gonna cause them to go on and die. Another way to think about that and to kind of wrap your head around those numbers is 98% cure rate is great, but another way to think of that is one in 50 are going to die, and I want to find out which of these patients are that needle in the haystack. Who's that one in 50 that won't make it so that I don't give them false assurance and that I refer them appropriately for management, treat them more aggressively, monitor them more closely so that they can truly survive their cancer, or that is to say to risk stratify appropriately so that the patient is getting the care based on their individual tumor biology.

As a dermatologist and dermatopathologist, I can fully attest to the great degree of diagnostic ambiguity and subjectivity that exists when we look at melanocytic neoplasms. I think anybody practicing dermatology kind of has this idea, and they understand that melanocytic pathology is not straightforward. Just the language that we use. If you send to five different dermatopathologists for the same exact neoplasm and even for the same exact endpoint, which is to say it's benign or it's malignant, we might have five different terminologies that we use to describe this lesion. So it's kind of a Wild West in terms of diagnosis.

The reason that this happens is that the diagnosis of melanoma, it's not as simple as a plug and chug, a blood test that you can say it's positive or negative. Or even if we look at PAS staining of a nail and say, is it positive or is it negative? Is there fungus or is there not?

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It's just not that simple and objective. The way we diagnose pigmented lesions is a combination of visual inputs. You have the actual cytomorphology of the melanocytes. How cytomorphologically atypical are the cells themselves? Then you have the growth pattern. So how do the cells grow together? How are they organized? There's different components depending on where you're looking. In the epidermis, is there a pagetoid spread? At the junction, is there confluence? In the dermis, is there appropriate maturation? There are so many features that go into deciding if something is benign or malignant.

You can imagine when there are so many inputs, you can have contradicting features. You can have some features that favor a benign process and others that favor a malignant process. When we have these confusing inputs, we get these kind of gray area lesions. What you end up with is many times we'll look at a lesion and say, 100%, this is clearly benign, or 100% this is malignant. But then there's every shade of gray in between. There's every possibility to have mixed inputs or gray area lesions. When we have these gray area lesions, that's really where that ambiguity comes in, and that's when we often will need to do ancillary tests.

To make things even more complicated, not only are we integrating all of these inputs to arrive at a diagnosis, there are also certain diagnoses that are mimics. So something like a Spitz nevus can really mimic a lot of the architectural and cytomorphologic features of a melanoma. Conversely, you can have a nevoid melanoma that architecturally looks like a nevus and can even mimic maturation and other things that we would expect as benign.

So in addition to balancing all of these inputs, we have these kind of fears of can I be missing something that is truly malignant even though it looks benign or vice versa? So a lot of complexity to the diagnosis, and that's why ancillary tests are often performed, including GEP, which can help us have an objective input as far as is this benign or malignant.

Most of the ancillary tests that we employ, including IHC, are still visual, and so there's still a degree of subjectivity and interpretation. The nice thing about a GEP test is that it is a really objective input. It is a gene expression profile score that is determined based on the expression of genes in this particular tumor and its microenvironment at a particular point in time. The way I think of it is it's a snapshot of the tumor's behavior at any given moment when you did the biopsy.

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