Transcript Details
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When and How to Use Ancillary Testing

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So the use of ancillary testing is quite common in dermatopathology. As I discussed, it's really complex to diagnose pigmented lesions. And when there's any degree of ambiguity, that will often jump to our first ancillary test being immunohistochemistry. Immunohistochemistry, it's cheap, it's quick, it's readily available, and it's been around forever. When I think about ancillary testing, I think about where it falls on the spectrum of our paradigm of DNA is transcribed into RNA and translated into protein. When we think about IHC, we're really looking at the proteins. We're basically just decorating proteins in the tissue with antibodies and making them turn a different color. So we see is this neoplasm expressing this protein? How and where is it expressed? So that's a very simple basic test that's been around forever. And so that's usually where we'll start. We'll usually use melanocytic markers to get a better view of the melanocytes.

And then there's even things like PRAME, preferential antigen expressed in melanoma, which is a nice IHC test that approximately, and this is a simplification. Approximately 90% of melanomas are PRAME-positive, and approximately 90% of benign nevi are PRAME-negative. So again, really nice additional input, but it is not by any means a magic bullet. There's still that somewhat limited sensitivity and specificity, and it is also a somewhat subjective interpretation. The interpretation of the IHC is not necessarily as clear-cut as plus or minus. There's gradations, so it's plus one, plus two, plus three. Which cells are expressing it? Are they all expressing it? Is it expressed strongly, et cetera. So IHC is one method that is really widely used.

Beyond that when we still have ambiguity despite using IHC, we still have questions that's when we'll often consider molecular testing. And so from the DNA side, we have things like next-gen sequencing. We have comparative genomic hybridization, and we have FISH, fluorescent in situ hybridization. These are all methods that are looking at the DNA.

GEP is unique in that it is looking at the RNA. So this is looking at the RNA that's actually transcribed in the tissue at the time you do the biopsy. So it's looking at the RNA that is produced by the tumor and it's environment, measuring the expression of specific genes of interest, and looking at... A proprietary algorithm will look at the amount of the genes that are being expressed, compare that to a widely studied and validated group of lesions that had a known outcome, meaning they're non-melanoma or they're non-benign, and able to categorize, give a score and say, "This is more likely to be benign. Or this is suggestive of malignancy." So it is giving an objective input to weigh in along with all your other inputs.

It's really important to realize that GEP is not meant to be a be-all end-all answer. It's not meant to replace the pathologist, or all the other ancillary tests that you may have done, or the clinical information that you have. It's meant to be one additional input that you then integrate with all the other information that you have. So the reason that I might order IHC on any given specific lesion might be different from case to case. But it's always to answer specific question that I want. Whether it's, "Do I label this melanoma, or not label it melanoma? Or do I excise it, or excise it?" I have a different question when I'm ordering the GEP and I have that GEP result help guide my final diagnostic line in combination with all the other information that I have.

So GEP can help guide treatment decisions, and that depends on which GEP test you are using. So for a diagnostic GEP for example, the 23-GEP that helps to distinguish benign nevi versus melanoma, that clearly helps guide our treatment because before we can treat something, we need to know what exactly we're treating. So if there's any ambiguity in the diagnosis, it is helpful to resolve that ambiguity to say, "Okay. No, we're going to treat this as for melanoma, or we're going to not treat this as for melanoma. We're going to treat this as for benign." And I order the test for a variety of different reasons. As a dermatopathologist, it's not always, "Is it melanoma or not?" Sometimes it can be as simple as, "Do I label this melanoma, or do I label this severe?"

But it can also be, "I know I want this cut out, but do I want it cut out, or do I want it cut out?" And I'll order it for that purpose. Even if I can't call it a melanoma, histologically based on our gold standard diagnosis, if it is expressing genes that are more in line with malignant behavior, I will be much more likely to recommend a wider excision because my providers are relying on me for how to treat lesions that I'm diagnosing.

As far as the other GEP which is more for prognostication, so for example the DecisionDx-Melanoma from Castle, that is going to be helping guide treatment decisions for things with a known diagnosis, whether it's very clear cut, you have a diagnosis of melanoma, or you have a diagnosis of squamous cell carcinoma, but you need to know how to manage the patient best. What's the next step for this patient? And if I have a patient, especially on my patients with a thin melanoma, I'd like to know which are the ones that I can keep in my dermatology practice and just say, "Cut it out and we're done. We don't need imaging. We don't need follow-up with oncology. We don't need a sentinel node," versus those that I want to monitor more closely.

I could do that based on NCCN Guidelines, which are in turn based on AJCC staging. But as we discussed earlier, that leaves a lot of tumors mistratified. So a lesion that is truly high-risk might be called low-risk or vice versa. And so in this day and age of personalized medicine, I really want to know as much as I can about this individual tumor biology and treat my patient appropriately. One example that I can think of in terms of recent management, I had a patient that was in her 40s and had a 0.7, T1a thin melanoma on her thigh that was diagnosed. No aggressive features, no mitosis. And she was my own patient clinically.

And so when I called her to let her know her results, I reassured her and I told her, "We're just going to cut this out." I scheduled her for an excision. But about a week later, I received her Castle score. And I initially did not mention the possibility of a sentinel node biopsy. Why? Because as a T1a melanoma by traditional NCCN Guidelines, she does not qualify for a sentinel node discussion. As a thin T1a tumor less than 0.8 millimeters, you have a less than 5% chance of sentinel node positivity, so you do not discuss a sentinel node.

However, her Castle score came back as a 2A, so an elevated risk for recurrence and metastasis. And moreover, she had an individualized sentinel node risk predicted by the Castle testing of 11%. So now she went from less than 5% risk, which is you don't discuss a sentinel node. She skipped over five to 10%, which is when you can consider a sentinel node, and went to over 10%, which is when you recommend a node. So she ended up canceling her excision in the dermatology practice, being referred to UCI for an excision with a sentinel node biopsy. And she qualifies for ongoing imaging over the next few years so that if she does have a recurrence, it could be detected earlier and smaller.