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Case Applications in Multidisciplinary Care for Endometrial Cancer

Episode 10

Dr. Slomovitz:
Hi. I'm Dr. Brian Slomovitz. This is CE on ReachMD, and still joining me today is Michelle Flint and Casey Cosgrove.

Now we're going to talk about a case of endometrial cancer. I know, Michelle, you've been preparing a case that you and I have seen in clinic over the last couple of weeks.

NP Michelle Flint:
Thank you. Yes. So this case is a review of endometrial cancer. We had a 65-year-old post-menopausal female present to the ER complaining of 2 days of intermittent vaginal bleeding. She had a past medical history of hypertension, hyperlipidemia, had coronary artery disease, and two MIs. Past surgical history is a cardiac ablation. Family history was a mother with colon cancer. On physical exam, there was a mass filling the upper vagina and bilateral side wall involvement.

Dr. Slomovitz:
Wow, oh, so I was going to say you had me at one MI, let alone two MIs. Now, that doesn't sound like a great surgical candidate here. And really a tumor filling the pelvis. A biopsy was taken, sent over to the lab. Casey, what kind of work are we going to do on this biopsy to figure out the best way to treat this patient?

Dr. Cosgrove:
Yeah, for this patient, obviously it sounds like they're a pretty high-risk disease, they also might not be an optimal surgical candidate. So we're going to be looking at opportunities to provide them the best therapies possible.

For this patient, we're going to probably do a mismatch repair immunohistochemistry profile with reflex MLH1 methylation, if that's needed, checking for ER and PR status, as well as looking for HER2 through immunohistochemistry.

For these patients that are at higher risk, I oftentimes will strongly consider also sending it off for next-generation sequencing, which will provide us some opportunities for targetable mutations. It may also provide us tumor mutational burden, which can be independent for response for immunotherapy, should they be mismatch repair intact, and then also can give us an idea about HER2 amplification even beyond immunohistochemistry.

Dr. Slomovitz:
Michelle, will you tell us some of the pathologic features she had?

NP Michelle Flint:
So on imaging, the pelvic ultrasound showed a 9.7-cm solid, hypervascular mass in the region of the cervix, lower uterine segment, highly concerning for malignancy.

We did get a CT scan of her chest, abdomen, pelvis, which again showed that mass and enlarged right external iliac and aortocaval lymph nodes, concerning for nodal spread of disease.

So on the office endometrial biopsy, it showed dedifferentiated endometrial carcinoma composed of undifferentiated carcinoma and endometrioid FIGO grade 3 carcinoma. For MLH1, intact nuclear expression, MSH2 was a loss of nuclear expression, MSH6 loss of nuclear expression, and PMS2 intact expression.

Dr. Slomovitz:
Casey, back to you. What do you think about this when you hear this signature?

Dr. Cosgrove:
Yeah, so when we have loss of MSH2 and MSH6, it tells us that this individual has a mismatch repair deficiency. This is a non-methylation event that has caused this. And there's two primary ways that this can occur. Either the individual has a Lynch syndrome or they have a double somatic – so both DNA alleles actually get a mutation, kind of a lightning strikes twice situation.

So this individual would need to get genetic testing for germline testing to rule out Lynch syndrome. And for these double somatic and Lynch syndrome, it's about 50/50. We know that this is a great indicator, though, also for immunotherapy response. And so for this individual, I would have a little bit of silver lining with their high-risk histology and are more locally advanced disease from what this exam sounded like to say, hey, we got a really targeted, great approach that we can kind of take care of you with.

Dr. Slomovitz:
That's a predictive biomarker in real time. So we put it on to KEYNOTE-868: carboplatin, paclitaxel, pembrolizumab. Michelle, tell us how well she did.

NP Michelle Flint:
So yes, following KEYNOTE-868, she was started on pembrolizumab in combination with the carboplatin paclitaxel. She did very, very well. So when she underwent her interval debulking, there was no evidence of residual tumor whatsoever. She also, symptomatically, had vastly improved after only one cycle. So it was really great to be able to see her in clinic and note that her symptoms had already vanished after one cycle with the addition of the pembrolizumab.

She completed a total of six cycles of the triplet therapy and then started the maintenance pembrolizumab, 400 mg every 6 weeks, and she tolerated it well.

Dr. Slomovitz:
How long are we going to keep her on the pembro? Just to remind everyone.

NP Michelle Flint:
So the pembrolizumab, she's going to be staying on for 2 years.

Dr. Slomovitz:
Really exciting. We're almost done here, but this patient would not have done so well a couple of years ago, before immunotherapy, dedifferentiated, not a surgical candidate. These are the ones we'd walk down the hall scratch our head and say the biology of disease gets us, it gets us. Immunotherapies really change that. So, so exciting to see outcomes like this.

That's the time we have today for our endometrial case. Michelle, Casey, thank you, as always, for your time, and we look forward to the next session.