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Case: Treatment Selection for *ROS1*-Rearranged NSCLC Patient with Brain Metastases

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Dr. Aggarwal:
Hello and welcome. Today, we're going to talk about a case involving treatment selection for ROS1-rearranged non-small cell lung cancer in a patient with brain metastases. I'm Dr. Charu Aggarwal. I'm an Associate Professor at University of Pennsylvania, and I'm joined together by my colleague, Dr. Alex Drilon.

So, Alex, I saw a second opinion in my clinic. This is a patient, 60-year-old, never-smoker presented with headaches actually to her primary care physician. No significant past medical history. Well-controlled hypertension. Physical exam was fine. A CAT scan was performed because of ongoing headaches and revealed a solitary brain lesion measuring about 2 cm that was confirmed with an MRI. A CAT scan of the chest, abdomen, and pelvis was subsequently performed that showed a left lower lobe lung mass, mediastinal and hilar lymphadenopathy, bronchial biopsy was performed and demonstrated non-small cell lung cancer consistent with an adenocarcinoma. And initial IHC features supported a diagnosis of adenocarcinoma, and PD-L1 testing revealed a score of 90%. The patient was seen by a local oncologist and was initiated on immunotherapy with pembrolizumab, based on the PD-L1 status, as well as referred to radiation oncology for management of this somewhat symptomatic brain met. And then the patient came in to see me.

You know, it's not unusual that we see this. So, when I saw the patient, I ordered genomic sequencing. And lo and behold, given that this patient had a never-smoking history, we found that the patient had a ROS1 fusion. Two cycles into immunotherapy, how would you manage this patient at this point in time?

Dr. Drilon:
Yeah, there are lots of layers to this case, Charu. And the first thing to call out is the approach to the never-smoker with metastatic lung cancer. And many other people have shared my strategy, which is, you know, you assume that there's a very good likelihood that you'll find a driver in the cancer, in which case you might start targeted therapy. And we also know that the second piece is that these cancers with oncogenes, most of them don't really respond well to immunotherapy. So certainly, even in the setting of PD-L1 high, a PD-L1 high result, I would not have chosen, for this never-smoking patient, single-agent immune therapy. And what I would have done would be to give platinum-based systemic therapy without immunotherapy, and wait for the sequencing to see if, true enough, there is a driver that's present.

Is that your approach as well for a never-smoking patient, Charu?

Dr. Aggarwal:
Yeah, absolutely. And I think it's so incredibly important to potentially wait for the next generation sequencing results if we can. If patients don't have a lot of symptoms, I tend to wait. But I agree with your approach that if we have to begin with something, begin with chemotherapy, and never immunotherapy for these folks.

Dr. Drilon:
Yes, and going to what we would do now. So, someone's been on single-agent checkpoint inhibition for two cycles, there's also a brain met that sitting there, I think that as long as there are no concerns on the side effect front, going to tyrosine kinase inhibition here would be the preferred strategy. And we know that because the likelihood of response, both intracranially or extracranially is high, and the likelihood of longer durability compared to chemotherapy is also good.

Charu, there is one question though, which is fairly common, is radiation something that you would consider for this brain metastases?

Dr. Aggarwal:
Yeah, so I think this is a tough one. And the reason why I say this is because this patient is moderately symptomatic, you know, the lesion is sizable. There is some edema, but there are headaches. So, I think this is a patient that we could have a very candid conversation with, not just with the patient, but also with the radiation oncologist. There's one of two approaches we could do; we could go ahead and treat with a stereotactic approach or Gamma Knife approach, or secondly, we could say let's start with an intracranial-penetrant TKI and really observe within a very short window, maybe get a scan in 4 to 6 weeks to see where we land and then make a decision about radiation. But really, I think, in this case is going to be driven by symptoms.

And then finally, Alex, just wanted to ask you what your thoughts are about the holding immunotherapy and changing the chemotherapy or going on to TKI in cases such as this?

Dr. Drilon:
So, this is another nuanced conversation, because we know that there are several cases of increased side effects with TKI therapy in the wake of having received immune therapy. And in my practice, it really boils down to how pressing the need is for debulking the cancer. If someone is highly symptomatic and you can't really afford to wait, then I think coming in with your best therapy, which is in this case, a TKI, and watching that patient very closely, watching their LFTs and other potential irAEs, is a strategy to take. If somebody who has relatively indolent disease is not symptomatic, feels well, then it's not unreasonable to wait to start the next therapy, especially in this case, where you've given two cycles, you can perhaps do follow-up imaging to see if there was any effect before switching to another systemic therapy.

Dr. Aggarwal:
This has been terrific insights. Thank you for joining me in this case discussion and we'll see you later.

Announcer:
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