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Managing Immunotherapy Toxicities in Lung Cancer Patients

Dr. Sands:
The field of lung cancer treatment continues to advance from chemotherapy to targeted therapy and now also including immunotherapy, but patients undergoing immunotherapy sometimes suffer from unexpected toxicities that can even become life-threatening. So what do we need to know about these toxicities? And how can we help manage them?

Welcome to Project Oncology on ReachMD. I'm Dr. Jacob Sands. And joining me today to take a look at immunotherapy toxicities in patients with lung cancers is Dr. Aliyah Pabani, who is a Clinical Assistant Professor in the Department of Medicine at the University of Calgary and Director of the Alberta Immunotherapy Database.

Dr. Pabani, thanks for joining me today.

Dr. Pabani:
Thanks so much for having me.

Dr. Sands:
So let's jump right in. What are some of the most common immunotherapy-related toxicities found in patients with lung cancer?

Dr. Pabani:
That's a great question and I think a very important topic. The interesting thing about these toxicities is they can really cause effects widespread across the body, and so we always have to be really vigilant for these potential inflammatory toxicities that can occur with the use of checkpoint inhibitor therapies. The most common ones that we typically will see will be involving the skin, involving the GI tract, so things like colitis, involving the liver, so hepatitis, and then endocrinopathies. So those are probably the most common toxicities that we see, but again, they can affect potentially any organ.

Dr. Sands:
And are there any underlying diseases or preexisting conditions that could put our patients at higher risk for developing these toxicities during treatment?

Dr. Pabani:
Yeah, that's a fantastic question. I think it was long thought that using these checkpoint inhibitor therapies, particularly in patients who have underlying autoimmune disease, would put them at higher risk of developing these toxicities, and so we're always very careful whenever we see patients who are going to be treated with immunotherapy just to try and make sure we've got a really good sense of what their past medical history may be and if there are any risk factors for those types of underlying autoimmune diseases.

There's now more data that's coming out that suggests that not all of these underlying autoimmune diseases essentially can be seen equally when patients are treated with checkpoint inhibitor therapy. And what I mean by that is patients with, for example, an underlying rheumatoid arthritis where they haven't been on any treatment for many years potentially could still be treated with checkpoint inhibitor therapy. You still just have to be very vigilant in these patients to make sure that you're monitoring for these toxicities. And certainly I have treated certain patients who have underlying rheumatoid arthritis that haven't had a flare despite being on therapy. What I often will do with these patients is make sure I involve their subspecialist early and that they're aware that patients will be treated with immunotherapy so that they can be monitored a little bit more closely.

I think there's still no good guidance about which toxicities are okay and which are not for patients to be treated with checkpoint inhibitor

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therapy, but as a general rule of thumb, if they are on additional immunosuppression, if they have been on high-dose steroids for a while, those are probably the patients that I would be a little bit more concerned about whereas I think other ones where their toxicity has been very well-managed and they have really required little to no treatment for it, potentially these could still be considered. I don't think that that's a blanket statement. And again, I still think that you should work with a subspecialist to manage these patients, but I do think that it's not a complete contraindication for all of the underlying autoimmune diseases.

Dr. Sands:
And to flesh that out a little bit more, let's just dive right into some of the other things that are maybe less obvious or less well-known so that everyone has a better sense of what they're looking for. Can you speak to some of the other areas: adrenal, blood glucose, and diving into some of those deeper possibilities?

Dr. Pabani:
So in that first three months when patients first start on immunotherapy, that is the highest risk period for developing some of these toxicities, and so when I see these patients, I'll try and do a pretty extensive panel to get a baseline for many of these toxicities. So should they develop any sort of weird and wonderful symptoms down the road, at least I have something to compare to. I'll make sure they've got a CBC, they've got lytes done, they have a creatinine, they have a urinalysis, especially to look for things like proteinuria right off the bat. An EKG and a troponin are also really good things to do right off the bat, especially for certain things like myocarditis, which can be very fatal and are not very common; liver enzymes of course, as you mentioned; and sometimes it's even worthwhile to do some other tests for things like TB just in case we need further immunosuppression down the line.

I'll talk about myocarditis a little bit just because I think it's a really important toxicity to know about but again, less common. Patients with myocarditis often get a conduction system disease, so they can present with things like a new bundle branch block or new heart block. There's also some studies looking at some other EKG changes, and they found that patients tend to have a widening of their QRS on the EKG as well. You can also look for things on an echocardiogram like potentially fluid, like a pericardial effusion, and look for any thickening in the wall of the myocardium or changes in patients' ejection fraction. And then things like MRIs are really helpful in that setting.

So for all of those toxicities, the ones that you mentioned, so things like adrenal, heart, or again neurotoxicity, which is another one that can potentially be fatal but isn't very common, it's really good to have those subspecialists' involvement early on because we know that some of these toxicities can potentially be fatal, and so it's very important that they be detected and managed early.

Dr. Sands:
For those just tuning in, you're listening to *Project Oncology* on ReachMD. I'm Dr. Jacob Sands, and I'm speaking with Dr. Aliyah Pabani about immunotherapy-related toxicities in patients with lung cancer.

Now let's dive in a little bit more to that toxicity management that you started with. Dr. Pabani, what are some factors we should consider when assessing our patients for toxicities?

Dr. Pabani:
I think making sure we have a really clear sense of what type of toxicity we're dealing with, what the severity is of the toxicity, so the grading of the toxicity, and then always looking for certain types of overlap syndromes: Could they have another toxicity? Because often times when you see patients with one, there are other things that sometimes go hand-in-hand. So for instance, things like myositis, myocarditis, and myasthenia, things like that we always look for the potential for another toxicity as well, so just to make sure that you've done the full workup to see if there's anything else that you could be missing. So just making sure you have a general sense of their current presentation and then also a knowledge of follow-up for these patients to make sure that either if you're planning on surveillance, and in the case of a grade 1 toxicity, that you're making sure that that toxicity is not becoming more severe, or in the case of a higher grade toxicity where you are treating patients potentially with steroids, that your treatment is being effective and that patients truly are improving and responding to steroid therapy.

Dr. Sands:
One of the challenging jobs as an oncologist is to determine sometimes when symptoms are due to adverse events related to treatment or due to disease progression. Are there any particular challenges related to the immunotherapy toxicities that you think are worth teasing apart?

Dr. Pabani:
Yeah. I think that's a fantastic question. A lot of these symptoms often can be really challenging to diagnose. I'll give an example of fatigue, which is very common in our cancer patients. It can occur with therapies, it can occur with the disease itself, and so it's really important to do a full workup but also always have this on your differential as a potential. And even fatigue within the toxicity world can

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be from a number of different things, so it can be thyroid abnormalities; patients can be hypothyroid on therapy; fatigue can be related to other endocrinopathies, so you want to check their adrenal function. And so although it can be very challenging to tease these apart, I think that that just even further stresses the importance of making sure that patients have full workups when they present with these sorts of vague symptoms.

Dr. Sands:
And finally, Dr. Pabani, do you have any final takeaways that you'd like to highlight for our audience?

Dr. Pabani:
I think these drugs are really exciting. We're seeing more and more patients that are being treated with them. I think the management of these toxicities is going to be crucial not just for the things we discussed. I think we covered a lot of ground in terms of the common toxicities, perhaps the less common but some of these toxicities can become chronic, and so it's really important—especially as now we're starting to use these agents in other settings like the adjuvant and neoadjuvant setting—to make sure that some of these chronic toxicities are well-managed so that patients can have a good quality of life. And the thought behind that is even if we're treating their cancer, if we leave them with a toxicity that's going to impact their quality of life long-term, I think those types of things are really important to consider. And so it's not just what we're dealing with acutely. It's also sort of that long-term management and that survivorship aspect for these patients.

Dr. Sands:
And with those final thoughts in mind, I want to thank my guest, Dr. Aliyah Pabani, for sharing her insights on how we can manage immunotherapy-related toxicities in patients with lung cancer. Dr. Pabani, thanks for speaking with me today.

Dr. Pabani:
Thanks so much for having me.

Dr. Sands:
I'm Dr. Jacob Sands. To access this and other episodes in our series, visit ReachMD.com/ProjectOncology, where you can Be Part of the Knowledge. Thanks for listening.

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