Transcript Details
This is a transcript of an educational program. Details about the program and additional media formats for the program are accessible by visiting: https://reachmd.com/programs/neurofrontiers/gene-therapy-safety-in-dmd-how-to-identify-common-immune-reactions/35681/

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Gene Therapy Safety in DMD: How to Identify Common Immune Reactions

Announcer:
This is *Neurofrontiers* on ReachMD. On this episode, we'll hear from Dr. Kaitlin Batley, who's a pediatric neurologist at UT Southwestern Medical Center. She'll be discussing how we can best monitor and manage immune responses in patients with Duchenne muscular dystrophy, or DMD, receiving gene therapy. Here's Dr. Batley now.

Dr. Batley:
Gene therapy in the treatment of DMD utilizes a micro-dystrophin, which is a shortened dystrophin protein, to provide patients with the instruction manual on how to make this better and improve dystrophin protein compared to what their body is naturally producing. This kind of instruction manual or transgene is packaged inside of a viral vector, and this is administered intravenously and provides the information that the body needs to then go on and produce this improved dystrophin.

So initially after the medication is administered, there can be immune responses to the actual viral capsid itself, and we can see this early on lead to inflammation of the heart or myocarditis. That typically happens within the first four to seven days after the therapy is used. And then later on, we can see inflammation in the liver, leading to hepatic injury and, in very severe cases, acute hepatic failure. And there have even been reports of patients who have passed away from this therapy because of liver inflammation.

We know also that patients can then go on to have an immune reaction to the newly produced micro-dystrophin itself. These can happen in cases of things like immune-mediated myositis, where the patient's own native dystrophin is such that when they see the new transgene, they react to this material as foreign, and that can actually lead to the immune-mediated myositis cases that we've seen in the past.

So one of the most important things when managing immune responses to gene therapy in Duchenne muscular dystrophy is to know that these immune responses can start even before the onset of symptoms. And that is one of the reasons that we have such a regimented and somewhat intense monitoring process. Our goal is to identify the onset of these immune responses even prior to the development of clinical symptoms. So with our weekly and sometimes biweekly lab monitoring, we are analyzing the blood for signs of inflammation in the liver or in the muscles.

So if a patient is in that early time period after administration of gene therapy and they are in the midst of developing myocarditis inflammatory response, we may see that a patient presents with chest pain. But it can also be somewhat confusing because we've seen that several of these myocarditis cases have actually presented with more GI symptoms, and so they've had nausea or vomiting instead, which can be a little bit tricky because we also know that nausea and vomiting are some of the most frequently seen side effects of the administration of the medication. And so it's really important to have a high index of suspicion in those following days. If we are seeing persistent GI symptoms, we should actually be looking towards the heart.

And then there are other symptoms of immune responses to be aware of.

If it is a hepatic inflammation, then we might see our patients present with some nausea and vomiting. If they're more advanced in hepatic disease, they may show signs of poor synthetic function of the liver, so we might see things like bleeding or hematomas as a result of low platelets or signs of jaundice; those kinds of things will tell us that the liver has had injury.

And then immune-mediated myositis is another really important sign of an inflammatory response in the muscles that can be a little bit trickier to pick up with biomarkers. And so this is one where the symptomatology can really lead you to identifying this condition and initiating rapid treatment. With these patients, we have seen a worsening of weakness that begins pretty quickly and progresses rapidly.

This can involve the skeletal muscles—so noticing more difficulties with walking or use of their arms—but it can also affect bulbar muscles, respiratory muscles, so we may see things like trouble swallowing or respiratory impairment. And so if ever a patient has any kind of rapid onset of weakness in that timeframe, medial myositis should definitely be high on the differential.

Announcer:
That was Dr. Kaitlin Batley talking about immune responses in DMD patients receiving gene therapy and strategies for managing them. To access this and other episodes in our series, visit *Neurofrontiers* on ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening!