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/advanced-treatments-innovations-mayo-clinic/paraneoplastic-encephalitis-how-new-discovery-relates-testicular-cancer/11130/

ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Paraneoplastic Encephalitis: How This New Discovery Relates to Testicular Cancer

Announcer:
Welcome to ReachMD. This special program titled Autoimmune Disease Associated with Testicular Cancer is brought to you by Mayo Clinic. Here's your host, Dr. Jennifer Caudle.

Dr. Caudle:
Why might severe neurological symptoms be associated with testicular cancer? That's the question Mayo Clinic and other researchers asked and answered with the discovery of an autoimmune disease that appears to affect men with testicular cancer. Not only does this discovery have the potential to be just the tip of the iceberg for identifying other paraneoplastic autoimmune diseases waiting to be discovered, but it's also the topic of today's discussion. This is ReachMD, and I'm your host, Dr. Jennifer Caudle. And joining me to discuss these new discoveries is Dr. Div Dubey from Mayo Clinic. Dr. Dubey, thanks so much for being here.

Dr. Dubey:
Thank you, Dr. Caudle, I'm happy to be here.

Dr. Caudle:
Absolutely. Well, we're delighted. So, Dr. Dubey, let's just dive right in here and have you start by telling us more about this discovery. What exactly is it? And how did you come to find it?

Dr. Dubey:
This is a new paraneoplastic syndrome which affects mainly men in various age groups, and affects the part of the brain to the back that is the brainstem and the cerebellum. Most of these cases usually have associated testicular cancer, which triggers this autoimmune response. And while evaluating patients and their serum or spinal fluids, we were able to find a biomarker that is kelch-11 or KLHL11, which we are actively working on validating as a biomarker for discovering more and more of these cases. This has been a biomarker that we discovered in collaboration with UCSF and is going to probably help people diagnose these conditions early. Here at Mayo Clinic for the last 20 years, we have been testing patient samples that is blood and spinal fluid by placing them on thin slices of mouse brain. And when we tested these patient samples from this particular disease, it gave a very unique pattern, which looks like stars or constellations in certain regions of mouse brain. Every time we saw these patients or contacted their managing physician, the story was always similar; these patients had neurological presentations and most of them had underlying testicular cancer. At the same time, colleagues at UCSF, Dr. Michael Wilson, and Dr. Caleigh Brehm were working on another patient which Michael saw in his clinic. He had the same disease. Using a very new and exciting technology called a phage display, they were able to find the underlying protein against which the antibodies were being made. And as we interacted in the process, we found that the pattern that was sparkles and this new antibody were one in the same. This led to the discovery of kelch-11 antibody in this new paraneoplastic disease.

Dr. Caudle:
Before we explore this new KLHL11, Dr. Dubey, let's first talk about this new form of paraneoplastic encephalitis that's associated with testicular cancer. You know, what are its symptoms? And what challenges are often encountered in a diagnostic stage?

Dr. Dubey:
The way I think about paraneoplastic syndromes are these are conditions where there is an aberrant or a misguided immune response, which is triggered by an underlying cancer against a protein. These proteins are expressed not only in the tumor, but also into the central nervous system or peripheral nervous system. So the patients with KLHL paraneoplastic encephalitis nearly all of them have a

testicular cancer. And the immune response against the testicular cancer leads to development of specific form of encephalitis. It seems to affect the region to the back of the brain, specifically the brainstem and the cerebellum. And most of these cases, the way they present to us are having difficulty walking, difficulty with their eye movements, or hearing loss. Interestingly, hearing loss in about one-third of cases comes first, and then many months later, other aspects of the syndrome: trouble walking, trouble moving their eyes, seeing double, illusions of things moving around, as they stare at stationary objects, these symptoms come in months and months later. It's a very debilitating syndrome, especially if it's not diagnosed early. If we are able to catch these patients and diagnose them early, we can potentially suppress the immune system and limit the amount of damage done by the inflammation inside the brain.

Dr. Caudle:
Excellent. And I think that's a really important point about catching it early. So you know, maybe you can stress just a little bit more for us why it's important that these patients – you know, you mentioned the importance of catching it early, but that these patients receive a timely diagnosis. And are there any resources available that can help us achieve that?

Dr. Dubey:
This is an autoimmune or paraneoplastic syndrome where these patients have significant amount of inflammation in their brain. It is important to catch these patients early as the inflammation on going, it can cause irreversible damage to the neurons or to the brain. If we catch them early, we can do appropriate therapies in the form of immunosuppression and that can limit the amount of damage. Because we have come across many cases in whom the diagnosis was not made in time, and most of them went on to have irreversible damage to the brain, and with time, requiring a wheelchair or a walker, which they have been using for many years now.

Dr. Caudle:
Excellent. For those of you who are just tuning in, you're listening to ReachMD. I'm your host, Dr. Jennifer Caudle, and today I'm speaking with Dr. Div Dubey about the KLHL11 and
the newly discovered autoimmune disease associated with testicular cancer. So Dr. Dubey, before you were talking about the importance of an early diagnosis. So with that in mind, what are you and the team at Mayo Clinic currently working on to help diagnose these patients with paraneoplastic encephalitis?

Dr. Dubey:
After discovery of these biomarkers here in our neuroimmunology lab, we tried to develop assays which we can offer to managing neurologists and oncologists throughout the country. And we are actively developing and validating assays so that we can offer kelch-11 antibodies to the managing physicians, as well. We're trying to develop a high proof of assay which can test for hundreds and hundreds of samples we receive in our lab. In addition to developing diagnostic assays, we are also trying to understand more about this disease. Is antibody truly pathogenic, or is there a role or strong role of T-cells, which the patients have in causing this disease. Since kelch-11 protein is hidden inside the cell, we think it's not the antibodies which cause the damage to the brain, but the immune cells in the patients blood which transfer over to the spinal fluid are the ones which attack the brain. So we are trying to study these cells and see which aspect of these cells are actually pathogenic. What other things we are trying to do is analyze genetic associations in the form of HLA, which predisposed patients with testicular cancer to develop this paraneoplastic syndrome. Analyzing these things and understanding more about the mechanism of the disease would help provide answers in terms of therapies we can provide these patients, which can safely and effectively stop the progression of this disease.

Dr. Caudle:
Absolutely. From your vantage point, what's the value of developing and adding this test to the protocol? You know, what kind of impact are you hoping this will have?

Dr. Dubey:
Based on an epidemiology study we did in Rochester, Olmsted County, Minnesota, we found that the incidence and prevalence of this particular antibody in this particular disease seems relatively high compared to other paraneoplastic syndromes. And if we extrapolate the data from here, we estimate there are about 4,000 to 5,000 cases across the U.S. However, right now, we know of only a few patients, of whom we have published 13 of them in the first paper. In a follow-up study, we already collected around 40 cases with this particular antibody. By offering this test as a part of the Mayo neuroimmunology lab paraneoplastic encephalitis panels I think we will be able to capture and know about more and more cases, and potentially be able to help them by providing the right treatment required to stop this disease from getting worse. It will also help find some of the hidden cancers, as not all of these testicular cancers are found in the scrotum. Some of the patients we have found, they had testicular cancer either in the mediastinum, that of the chest, or sitting at the back in the abdomen, as well. So this antibody not only helps diagnose the neurological dysfunction, it will also help in finding occult malignancies.

Dr. Caudle:
Excellent. And lastly, Dr. Dubey, what's the greatest takeaway you'd like to leave with our audience today?

Dr. Dubey:
I would like to emphasize that this discovery was made using a collaborative team-based approach between two academic institutions. And even since this discovery, patients with kelch-11 encephalitis we have been seeing here at Mayo Clinic, are being managed by a team of doctors, nurses, and pharmacists. It is not only neurology which is involved in this management, but also oncology and urology play an important role. Therefore referral of these patients – evaluation of these patients at Centers of Excellence or centers with a lot of experience in managing this rare, debilitating condition, such as Mayo Clinic, is extremely important. Having a team of physicians who have experience with managing this condition would not only help in early diagnosis of these cases but would also help selecting the right therapies these patients require. If you think if a patient who has symptoms which are similar to the disease such as kelch-11 paraneoplastic encephalitis, I would recommend these patients to be referred to a Center of Excellence. Here at Mayo Clinic, we work with our referring providers, as well as our colleagues in various departments, and come up with ways to help with these patients in the best possible way.

Dr. Caudle:
Well, this has certainly been a fascinating look into some of the latest research being conducted. And I'd like to thank my guest, Dr. Div Dubey, for helping us better understand the biomarker, kelch-like protein 11 autoantibody, and the newly discovered autoimmune disease associated with testicular cancer. Dr. Dubey, it was wonderful speaking with you today.

Dr. Dubey:
Thank you, Dr. Caudle. It was a pleasure discussing this biomarker and kelch-11 paraneoplastic disease with you.

Announcer:
This was a special program titled Autoimmune Disease Associated with Testicular Cancer, brought to you by Mayo Clinic. To access other episodes in this series, visit reachmd.com/MayoClinicInnovations. Thank you for listening to ReachMD, where you can be part of the knowledge.