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Case Challenges in MS: Tailoring Therapy to Patient-Specific Characteristics

Narrator:

Welcome to CME on ReachMD. This activity, “Case Challenges in MS: Tailoring Therapy to Patient-Specific Characteristics”, is jointly provided by Global Education Group and Spire Learning and is supported by an educational grant from Genentech

This case-based program focuses on individualized treatment of MS in special populations, including African American patients, and patients who are contemplating pregnancy.

Your expert for this activity is Dr. Scott Newsome, Associate Professor of Neurology and Director of Neurology Outpatient Services and Infusion Center at Johns Hopkins Hospital in Baltimore. Dr. Newsome works within the Johns Hopkins Multiple Sclerosis and Transverse Myelitis centers.

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Dr. Newsome:

Hello, my name is Scott Newsome. I’m a neurologist at Johns Hopkins Hospital, currently Associate Professor of Neurology, and Director of our Neurology Outpatient Services, and Director of our Neurology Outpatient Infusion Center.

Thank you for joining this presentation today.

Multiple sclerosis, as many of you know, is an immune-mediated disease of the central nervous system that when we look histopathologically, there are several hallmarks including inflammation, demyelination, axonal loss, and neuro-degeneration. The primary etiology of multiple sclerosis is unknown, and it’s likely multifactorial. There have been a number of risk factors identified for increasing one’s risk to go on to develop multiple sclerosis including having chronically low vitamin D, smoking, and likely a number of other risk factors that have yet been identified, including environmental exposures. Multiple sclerosis is not a one-hit phenomenon. A perfect storm situation needs to ensue in order to develop multiple sclerosis

Multiple sclerosis is the most common cause of non-traumatic disability from the ages of 18 to 60. Similar to other autoimmune conditions, there’s a female predominance, and peak incidence between 20 and 40 years of age. However, I usually will relay to people that multiple sclerosis is non-age or gender biased. We certainly see pediatric onset MS and people well into their 60s and 70s present with their first clinical attack of multiple sclerosis. Now, there are recent studies that allude to a higher incidence of MS within African-American women which will be relevant later, because there are certain clinical and paraclinical factors that we take into consideration with treating patients with MS, in terms of how aggressive the patients present, and some of this is based on their demographic information.

Now, multiple sclerosis hits people in the prime of their life, so many clinicians will treat people when they’re not only working, but interested in getting pregnant. A study showed that approximately 58% of neurologists treat two or more people who get pregnant per year, which will be important as we discuss later.

Multiple sclerosis is a clinical diagnosis supported by paraclinical testing. Patients will present with a neurological attack, or progressive neurological decline that are suggestive of central nervous system involvement, which will help lead us down the path of working the patient up, including doing an MRI of the brain and often spine, along with laboratory testing, to rule out things that can mimic multiple sclerosis.

With respect to making a formal diagnosis of multiple sclerosis, the McDonald criteria can help. Now, with the McDonald criteria from 2010, and soon-to-be 2017 revised criteria, we can make a diagnosis of multiple sclerosis after a single clinical attack. For example, if someone presents with optic neuritis and they have brain lesions that are in characteristic areas that we see get involved with multiple sclerosis, one of which is a gadolinium-enhancing lesion that is not directly causing the person's symptoms, and in this case optic neuritis, as long as you've ruled out mimickers of MS, at that first attack with one MRI, you can say the person has multiple sclerosis Once a patient is diagnosed with MS defining their subtype is critical as it does help guide our treatment choices, and also, just as important, guide communication between the clinician and patient, with respect to what our expectations are for that treatment intervention.

I figured I would go through a case study to give you an idea of who we see in clinic and who you may see in clinic. So, this is Beth, an otherwise healthy 28-year-old African-American female who is currently a schoolteacher, comes in with double vision that's been progressive over about a week, along with some unsteady gait. Upon further questioning, you elicit that approximately a year ago, while training for a marathon, she noticed left lower extremity weakness that persisted in a constant fashion for at least a couple of weeks. Detailed medical, surgical, family, and travel history, all unremarkable. Social history is unremarkable as well, outside of occasional alcohol on the weekends, but not a smoker or drug user. The regular general medical exam for this individual was okay. Her detailed neurological exam demonstrated a left internuclear ophthalmoparesis, ataxia of the left upper extremity with finger-to-nose testing; she did have some spastic weakness of her left lower extremity, and diminished vibratory perception in both feet. This physical exam is quite indicative of central nervous system involvement, especially given the patient's presenting history. And the first things that we'll do, is an MRI. MRI still, to this day, is the most sensitive tool that we have, in terms of helping in aiding the diagnosis of multiple sclerosis, and give you an idea of how aggressive the MS may be.

So, Beth had an MRI of her brain and spine which demonstrated an enhancing, active, demyelinating lesion in the left pons which correlates with that internuclear ophthalmoplegia and double vision, non-enhancing lesion in her right pontine region, and a number of other non-enhancing lesions throughout her brain and spine. She underwent a lumbar puncture that showed five oligoclonal bands restricted to the cerebrospinal fluid. She had several serological studies that did not reveal any other etiologies for her symptoms. So, as I mentioned, we're able to diagnose someone with multiple sclerosis, even if it's at the first time you see them. For Beth, she had two relapses: one the year prior to her presentation with the left lower extremity weakness, and then the double vision with that pontine attack., We can confidently say that she has multiple sclerosis.

Now, the typical MRI features in MS, if we're thinking about what regions like to get involved which are part of the McDonald criteria, to make a formal diagnosis of MS, the periaraventricular region, juxtacortical region, infratentorial region including brainstem and cerebellum, and then the spine. So, with Beth, after she was diagnosed with relapsing-remitting MS in-between her episodes, she was stable neurologically, she was treated with steroids for her acute relapse because of the disability that she had was persisting.

So, as I mentioned, there are a number of clinical and paraclinical factors that have been associated with a more aggressive onset of multiple sclerosis which we will consider upfront in terms of what therapy we may recommend. Some of the clinical factors include: if the individual is male, older age of onset, African-American, initial neurological attack involves the motor fibers, the cerebellum, or sphincter control, and if they have poor recovery from a relapse. Beth recovered after receiving steroids from her double vision; however, her gait ataxia was still present. So, I would consider that a poor recovery from a relapse. Having frequent relapses within a very short period of time, for example, if someone has two or more relapses in a year's time. The average number of relapses per year, in natural history studies with MS, is one per year. Someone who has multifocal involvement at onset of their disease, including having double vision and gait ataxia, for example, or optic neuritis and dragging a leg. The paraclinical factors largely are related to MRI. Features, on MRI, that have been shown in studies to be a predictor of more disease activity down the road and disability; high lesion burden on imaging, or multiple gadolinium-enhancing lesions at the onset, especially if they're in eloquent areas of the nervous system, like the spinal cord.

There was a recent study that looked at 330 patients and tried to ascertain, were there specific factors that predicted having a second MS relapse within the first year of onset? And what was found, in this particular study, was that non-white race was a very strong predictor, and specifically African-Americans seemed to be driving that.

There have been several studies looking at African-Americans compared to Caucasians, and what the level of disease activity is. when we look at clinical markers, African-Americans have a greater chance of going on to develop disability earlier in their disease course.

They often will present with more eloquent areas of the nervous system being involved from the start including spine, cerebellum. There is a higher level of disability at diagnosis. When we look at imaging markers, many African-Americans have a higher lesion burden upfront than Caucasians. And when we look at disease-modifying therapy outcomes, it seems like African-Americans don't tolerate, or have poorer treatment response, to the interferon therapies, but have very good control with higher efficacy therapies, and maybe even more than Caucasian patients.

So, if we go back to Beth, we established that she had relapsing-remitting multiple sclerosis. The conversation in clinic was, "you've had two clinical attacks already. You have lesions on MRI that are suggestive of MS. Let's be proactive and prevent future attacks and new MRI lesions," and hopefully, that will translate into preventing disability long-term.

So, the decision was that we would start her on a disease-modifying therapy. Our current disease-modifying therapies are all approved for relapsing-remitting multiple sclerosis. Beth tolerated the therapy well, and she had strict compliance. Unfortunately, several months later, she experienced another relapse that consisted of progressive right-sided weakness and urinary urgency, which to me sounds like a spinal cord attack. She was compliant and adherent to the medications, so this was not an adherence breakthrough attack; this was truly what I would deem as a suboptimal treatment response to the therapy that was chosen. A suboptimal treatment response from a clinical evidence of disease activity, having two or more relapses within a year, on therapy, or one significant relapse in the past year. Significant relapse meaning those patients that don't recover from a relapse. A suboptimal treatment response from MRI activity, if someone has significant MRI changes at one year, in the absence of clinical symptoms, or ongoing MRI activity on serial MRIs in a short period of time. So, for Beth, she got another round of steroids, had some physical therapy, and then the discussion came up that, she understands that MS disease control is important, but she was young and very interested in pursuing pregnancy

There are studies now that are very enlightening in terms of helping, risk stratify someone upfront who may have a more difficult time, not necessarily during pregnancy, but in the postpartum period. If someone goes into a pregnancy with high disease activity, say they recently had a relapse, or they have multiple new lesions on MRI, and then they get pregnant, versus someone who is stable, hasn't had any relapses or MRI activity in well over a year, that the patients who had disease activity going into the pregnancy have a much higher risk of having postpartum MS disease activity occur. So, for many patients, we will recommend, "Let's see how we can get your MS disease activity under control for a year, and then readdress pregnancy."

The majority of disease-modifying therapies need to be washed out before pursuing pregnancy. The one exception is glatiramer acetate which is widely used in patients who are contemplating pregnancy, because this is a medication that can be taken up until someone finds out they're pregnant. Once they find out they're pregnant, they can stop taking glatiramer acetate. All the other injectables, orals, and infusibles, require a washout. Now, pregnancy is a relative protected time for people with MS, typically in the second and third trimester; the first trimester is not. With respect to breastfeeding there are many studies out there trying to better understand whether breastfeeding is actually protective in the postpartum period, and right now, at least in my mind, the data is conflicted.

In summary, multiple sclerosis is a common, chronic, demyelinating disease of the central nervous system that presents in the prime of individual's lives. The ability to diagnose and treat MS has greatly improved over the last two decades. And upfront, looking at the clinical and paraclinical factors for a given individual may help tailor how we treat that person. identifying optimal therapeutic strategies relevant to patient-specific characteristics is important.

Thank you for joining me today in this review of multiple sclerosis. Thank you.Narrator: This has been CME on ReachMD. The preceding program was jointly provided by Global Education Group and Spire Learning and supported by an educational grant from Genentech. To receive your FREE CME credit or to download this segment, go to ReachMD.com/MSChallenges. Thank you for listening