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Top 10 Things to Look for on the MRI when Diagnosing CIS
Anthony Traboulsee, MD

Operator: The conference is now being recorded.

Ms. Dottie Pfohl: Welcome to the CMSE website, mscare.org, and this, our inaugural podcast.

I'm Dottie Pfohl, Director of the website project. And I'm pleased to have as my guest tonight, Dr. Anthony Traboulsee. You'll find links to his slides and superb lecture, "The Top Ten Things to Look for on MRI When Diagnosing Clinically Isolated Syndrome" on our websites highlights from our annual meeting 2008.

Dr. Traboulsee is a practicing neurologist at the University of British Columbia in Vancouver where he serves as Director of the Clinical Trials Research Group, Assistant Professor and Associate Staff Neurologist. He's also a consultant for the Northeastern Health Authority for the British--for British Columbia, Canada and lists of his disclosures for his lecture, having received honoraria from several of the disease modifying therapy companies, having a research grant from the Canadian MS Society. He's a member at large for the Consortium of MS Care Board of Governors and Vice President for the Canadian Network of MS Clinics.

Dr. Traboulsee's interests in the brain and MS include expertise in neurodegeneration, neuroimmunology, MRI, image analysis, functional MRI, MR spectroscopy, and magnetic transfer. He's completed fellowships with Dr. Donald Pate



[sp] in Vancouver, and Dr. David Miller at the Institute of Neurology in the United Kingdom.

He has published numerous referee papers, given teleconferences, webcasts, and educational videos. He serves as a population guest lecturer, conference organizer, and chair. His committee memberships are too numerous to list, but he is a popular international speaker for the Consortium of MS Center's annual meeting.

Dr. Traboulsee generously offers his time on editorial boards such as Rendezvous and Neura and other peer review journals and he's recognized for his work in neuroimaging in MS, new lesion activity as an outcome for assessing therapeutic response, translating MRI research into practical guidelines for clinicians and patients, and looking at long-term benefit of treatments for MS, going far beyond the readily visible--that which is readily visible with conventional MRI toward new frontiers in MS research.

It's with great pleasure and pride that when I introduce Dr. Traboulsee, and the dog, which we'll start again with that. Okay.

But, it's with great pleasure that we introduce Dr. Traboulsee.

Welcome, Tony.

Dr. Anthony Traboulsee: Oh, thanks Dottie. It's a pleasure to do this.

Ms. Dottie Pfohl: This is the first of a planned series. Having listened to your lecture on the top ten things to look for, you are able to distill, amazingly, such complex information into a 20-minute, extremely practical guide to making the most of MRI and diagnosing CIS, and ultimately, having earlier diagnosis of MS in patients who may not fulfill clinical criteria.



Could you walk us through the diagnostic criteria for clinically isolated syndrome?

Dr. Anthony Traboulsee: Well, the criteria for clinically isolated syndrome is quite important, because it's based on a clinical determination that someone has had symptoms, neurologic symptoms, that are consistent with inflammation of the brain, spinal cord, or optic nerve. A lot of people have neurologic symptoms. You sit with your legs crossed too long and your foot goes to sleep or you wake up and your arm's tingling. Those aren't necessarily enough to be suspicious for inflammation.

And so, the key feature, before you even start doing MRIs on people, is to ensure that these symptoms have been going on for at least 24 hours. And it's a story that's believable for inflammation of the nervous system before we start doing all the tests and trying to interpret those tests.

So, the first approach is to make sure the symptoms are consistent with inflammation of the nervous system. And this is quite critical because once an MRI is done and a few little white spots are seen, it creates a whole level of anxiety of whether or not I have MS. And so, the most important test to begin with is the story of the patient and the neurologic examination to determine if that is consistent with inflammation.

Ms. Dottie Pfohl: I see.

And the criteria we hear of so often, Poser and then McDonald, do you feel that these changes have made it easier or more straightforward to reach a diagnosis of MS?

Dr. Anthony Traboulsee: You know, they have made it easier to make an earlier diagnosis. The traditional criteria for multiple sclerosis, which is recurrent episodes or multiple episodes of inflammation required at least two clinical attacks. And



in the past, that could take up to five years from the time a person has their first attack until they have their second attack.

With the newer criteria, the McDonald criteria and the revisions to those criteria, we can now make a confident diagnosis soon after patients had only a single attack. And so, we can give them that information. We can counsel them about multiple sclerosis and perhaps even get them started on some early treatments that might impact on their health in the long run.

Ms. Dottie Pfohl: Sure. Well, that's enormously helpful. And I was very impressed, too, by the use of contract imaging numbers as you selected your top ten. And the first of your things to look for when diagnosing CIS is to use a standardized protocol.

Now, your--being your number one recommendation, you mentioned the consensus guidelines from 2006, and I know those are available on the website. But, I'd also like to ask, is this the most recent recommendation, or are there other locations that you'd like us to check as well for standardized protocol?

Dr. Anthony Traboulsee: The standardized protocol, MRI protocol for diagnosing multiple sclerosis was put together through the Consortium of MS Centers with a group of international experts and day-to-day clinicians coming up with a practical set of guidelines. That was a work in--that's taken years to put together. And MRI is based on technology and knowledge, and both of these have evolved in the past five to seven years.

Therefore, we were planning a revision to these guidelines in the fall of 2008. And again, we'll bring together a group of experts as well as people in practice and



review what we've done, what we know now, and how we can make it better so that we can again, accurately diagnose MS and follow patients consistently with this very straightforward MRI protocol.

Ms. Dottie Pfohl: Super. It sounds like with many things in MS it's a work in progress.

Do you consider CIS early MS?

Dr. Anthony Traboulsee: Well, CIS is very interesting in two main ways. One way is that it's the earliest time we can diagnose multiple sclerosis and get people started on an education program and a treatment program. But, the other important thing is to realize that at least half the people with a clinically isolated syndrome that's very suspicious for multiple sclerosis do not go on to having multiple sclerosis.

And these people have very high anxiety. They're worried about MS. They're worried about the impact MS will have on their life and their relationships and their work. And if we can undiagnose them--in other words, tell them they don't have MS early--that can have a significant, important impact on their life.

Ms. Dottie Pfohl: Sure. Sure.

We all hear about MRI, but could you take a few moments in basic terms to describe just what MRI is and how these T1, T2, and flare images that you so nicely illustrate in your lecture, and gadolinium enhanced images identify, date and track lesions?

Dr. Anthony Traboulsee: Oh, MRI is relatively new technology. It's been around for about 25 years. And it's a way of taking pictures of the brain and other



structures within the body. Most of us are familiar with using x-rays to do that. And, of course, everyone's concerned about being exposed to too many x-rays.

Well, the nice thing about MRI is it does not use x-rays. It takes advantage of the natural energy within water molecules in our body, and uses those properties to take pictures of the brain. And it's absolutely beautiful technology and the resolution or the quality of the picture is even better than one could get with a--with x-rays, which would be called CT scanning.

Basically, what we're looking for are white spots in the brain. And there's a variety of ways the radiologist can design the protocol to find these white spots. And the classic sequence, or set of pictures, is called T2 weighted imaging, which means anything abnormal will show up as white spots, much like fluid would show up.

And sometimes we want to know, when we're looking at white spots, if they're new or old. And to do that, we use a very safe chemical called gadolinium that's put into the veins and normally doesn't go into the brain unless there's a new area of damage or inflammation. And that chemical, gadolinium, will go into that new lesion and give us a sense of all the lesions we see, which are the most active or the newest. And it gives us even more diagnostic information as well as information for monitoring people's response to treatments.

That information can also help us sort out different types of lesions. For example, tumors and brain infections or abscesses will have a different look with that contrast gadolinium agent compared to multiple sclerosis lesions and other diseases such as strokes.

Ms. Dottie Pfohl: Are these the red flags you speak of?



Dr. Anthony Traboulsee: That's right. These are some of the red flags, because what we see with the MRI, it's so sensitive for finding anything that's potentially abnormal that sometimes it can't distinguish a stroke or a tumor from multiple sclerosis. And by collecting more information, such as we can get with gadolinium, we can determine what's a red flag - in other words, an abnormal enhancement pattern for multiple sclerosis versus a typical enhancement pattern for a brain tumor.

Ms. Dottie Pfohl: Okay.

I know the importance of accurate and timely diagnosis allows for identifying patients with aggressive disease and also earlier intervention and treatment that would support treatment choices and options. But, why do you consider CIS to be an especially hot topic?

Dr. Anthony Traboulsee: It--one of the reason's it's so hot is our concepts of treating multiple sclerosis is to treat this disease as early as possible to prevent irreversible damage. And quite often, at the earliest stages of MS when people are clinically isolated syndrome, they feel well. They don't have any physical signs of damage. They've recovered well from their attack.

But on the MRIs, we already see signs of damage, such as the scars or the plaques and other diffuse elements of damage that we can see with newer MRI techniques. And that concerns us because once you lose brain tissue, you can't replace that very well. And we're not just talking about the myelin, we're talking about the wires within the myelin called the axons.

And our treatments for multiple sclerosis are geared to preventing damage. They're not necessarily geared to repairing damage. We believe the body has a limited



capacity to do that. Therefore, if we can prevent future damage, then patients will continue to feel well. And our strategy is to treat the disease as early as possible. And that's why CIS gives us that perfect opportunity to catch people at the very beginning of their disease and to maintain that good quality of life they're enjoying now.

Ms. Dottie Pfohl: How did you develop this interest in neuroimaging? Where do you see it taking us in the future?

Dr. Anthony Traboulsee: I've always been fascinated by technology and I remember when computers first came out when I was in high school and how interesting it was. And I'm a very visual person and enjoy looking at pictures. And I understand things better when I can see a picture.

I--interestingly, I initially wanted to be a radiologist, but I enjoy patient contact so much I chose neurology, and now I have the best of both worlds.

Ms. Dottie Pfohl: Ah, now I understand your unique view on communicating with a radiologist as well as the patient.

Dr. Anthony Traboulsee: Well, that's the interesting thing about multiple sclerosis - it's such a team effort. Radiologist, neurologists, physicists, nurses, physiotherapists, occupational therapists, we all work together to help our patients have the best quality of life. And the nice thing about MRI, it is technology based and it's going to constantly get better.

If you just look at the evolution of a simple computer from a bunch of key cards we would put through a machine to these fancy telephone, smart phones we carry around nowadays. They have more computing power than some of the earliest MRIs. It's--it means that we can look more closely at the fine structure of the brain. And--.



Ms. Dottie Pfohl: --Yeah--.

Dr. Anthony Traboulsee: --That's the key to discovering new therapies for stopping this disease. And I really think that's our window of opportunity.

Ms. Dottie Pfohl: Do you think spinal cord imaging should be part of an initial study, or really just as a zooming in, so to speak, on suspected pathology or bolstering diagnostic confidence?

Dr. Anthony Traboulsee: I quite like spinal cord imaging. One of the main reasons I like it is quite often, I see patients just because of an abnormal MRI. And the problem we have with MRIs is the older we get, meaning once we're over the age of 40--

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Ms. Dottie Pfohl: --Oh, yes--.

Dr. Anthony Traboulsee: --You know, that's getting pretty old--we can start getting little white spots in our brain that have absolutely no meaning. It's just part of the natural aging process. And so, of course, people worry. You know, is that signs of MS, or is that signs of something else?

Well, the nice thing with spinal cord imaging is it doesn't develop white spots or lesions with normal aging. And so, seeing lesions in the spinal cord imaging and patients where I'm really struggling with the diagnosis can be very helpful in sorting them out. And it's quite useful in that setting.

Ms. Dottie Pfohl: Now, when we say spinal cord, are we just talking about cervical spines or an entire study?



Dr. Anthony Traboulsee: Sometimes, I do the entire study, so the cervical, thoracic, and lumbar spine. But, most of the information can be gathered from the cervical spine.

What we find in most patients with multiple sclerosis, if they've had the disease for over five years, the majority will have lesions in their spinal cord. And most of those are in the cervical cord. Often these--they're not even aware of symptoms related to those lesions.

So again, that sensitivity for detecting a clinically silent disease can be quite helpful in terms of a differential diagnosis for MS.

Ms. Dottie Pfohl: Well, the lecture that we're presenting in your slides that are available on the site by going to the highlights from the annual meeting, really focus on clinically isolated syndrome. And yet, these basis of understanding of, as you mentioned, the white and the dark spots and the time and space, but how do you interpret all these parameters, especially when you're talking about non-classic MS? How does it all fit in? How does it fit together?

Dr. Anthony Traboulsee: I don't understand the question, Dottie.

Ms. Dottie Pfohl: Well, the clinically isolated syndrome--.

Dr. Anthony Traboulsee: --Okay--.

Ms. Dottie Pfohl: --And you have someone who's just presenting and we have to balance off what you're seeing on the MRI--.

Dr. Anthony Traboulsee: --Okay. Right, right--.

Ms. Dottie Pfohl: --But also, the aspects of time and space. And then, you--.

Dr. Anthony Traboulsee: --Right--.



Ms. Dottie Pfohl: --Had raised the question of non-classic MS. It just seems like a lot to consider in someone who's maybe having their first presentation of symptoms.

Dr. Anthony Traboulsee: It does. It's a lot of information to consider, and so I take a very step-wised approach.

So, the first approach was the clinical determination. Are those symptoms suspicious or consistent work with demyelization? And then, I look at the MRI of the brain and is it normal or abnormal? And that's a perfectly normal brain MRI. I can immediately counsel the person that they're low risk for having MS.

If it's an abnormal MRI, then I'd look to see if it looks MS-ish. In other words, are the lesions somewhat classic for MS, ovoid and affecting the corpus callosum or other white matter structures that just look typical for MS, or are they rather non-specific looking?

And then, the other great advantage with the MRIs, in those patients with that abnormal brain MRI, meaning they have at least two or three white spots, if I wait for three to six months and repeat the brain MRI and I find new white spots which have occurred in the absence of any symptoms, then that gives me that evidence for a disease of the central nervous system separated in time affecting different places of the nervous system, which is the official or classic diagnosis of multiple sclerosis, a disease of inflammation separated by time and by space meaning multiple attacks, either clinically evident or clinically silent and affecting different parts of the nervous system, such as a spinal cord or optic nerve or throughout the brain.

So, that follow up MRI can be quite helpful. And that's where we really stress that a standardized MRI protocol is used to make that determination. We've seen a lot of



cases where people have had two or three MRIs done on even the same scan at the same institute where the protocols have been so different. And we see new white spots, but we're not sure if those new white spots are real or simply seen now but missed on the earlier studies. And if we're going to counsel our patients that they now officially have MS because you have new white spots, we want to be sure that that data's accurate.

And again, going back to our standardized MRI protocol, particularly the one we've put together with a consortium of MS centers, I think that'll be very helpful for clinicians and patients throughout North America and the world.

Ms. Dottie Pfohl: It sure sounds it.

You know, the big ten in your lecture suggests that MRI can be a predictor for new relapses. Could you elaborate on the value of imaging as a prognostic tool?

Dr. Anthony Traboulsee: Well, a lot of people had hoped that MRI would be a crystal ball into the future of multiple sclerosis in terms of how bad will my MS be and it hasn't completely played out that way. I think it's been a good predictor of whether or not a person has MS and to get them on a pathway of treatment.

We have seen some relationships though that the worse the MRI looks at the first attack, the more likely they're going to have their second attack within the next two years. And they're at higher risk for disability 10 to 15 years later.

Again, that argues towards this concept of early treatment of patients with MS. But in general, we're only getting a bit of information, or a piece of the puzzle--.

Ms. Dottie Pfohl: --Uh-huh--.

Dr. Anthony Traboulsee: --From that first MRI. And there's probably more information we can gather from that MRI using newer techniques or perhaps from some



blood tests or spinal fluid analysis that can give us a better prediction of how well they're going to do and perhaps even what treatment they should go on so that we can individualize for patients much better.

Ms. Dottie Pfohl: You know, in your lecture you mentioned zebra and horse. What was that all about?

Dr. Anthony Traboulsee: Oh, the zebra and horse. There's this old saying in diagnostic medicine - if you hear hoofs, you should be thinking horses, not zebras.

Ms. Dottie Pfohl: Oh, got you.

Dr. Anthony Traboulsee: That means when you--if you see some white spots on an MRI in someone with the symptoms classic for MS, you should be thinking of--you know, MS should be the first thing that comes to your mind as opposed to some exotic infection from deepest, darkest somewhere.

Ms. Dottie Pfohl: Oh, wow.

Well, the other thing I was thinking of was, with all the interest in the Olympics and Beijing, I understand you've also looked at prevalence and prognosis in Chinese Canadians with MS or the prevalence of MS. Is that true?

Dr. Anthony Traboulsee: Well, MS is a worldwide disease and we mostly think of it as being in North America and Europe. But, anyone from anywhere in the world, unfortunately, can get MS.

Ms. Dottie Pfohl: Yeah.

Dr. Anthony Traboulsee: But, in some countries it seems to be less common. And there's very few reports of MS in Asia.



Well, in Vancouver have a very large Asian population. We're kind of the gateway to Asia Pacific, much like San Francisco and Seattle. And our center sees all the MS patients for the whole state or province. And so, we've been looking at the prevalence of MS in our Chinese Canadian community and, in fact, we do find it's less common than in the general population, but much more common than we were expecting based on reports out of China.

Ms. Dottie Pfohl: Wow.

Dr. Anthony Traboulsee: And so, we wonder if that's a combination of genetics and environment interacting. In other words, being in North America puts people at slightly higher risk, but being of Chinese descent puts people at perhaps slightly lower risk.

Ms. Dottie Pfohl: Very, very interesting.

I really want to thank you for providing us with this adjunct information to supplement the excellent lecture. I really hope people will go to the site--it is available on audio as well--and take advantage of what you outlined for us. I know it's enormously well received and we want to thank you very much for taking time to discuss it with us.

We also welcome comments and feedback.

Are there any things, Dr. Traboulsee, you would like to add at this point, or questions that we haven't raised, or thoughts on having given this lecture that if you'd had to do it over again you would add?

Dr. Anthony Traboulsee: Well, I guess I go back to my basic thoughts of MS and, you know, I'm really excited to be involved in the field of MS and being associated



with the Consortium of MS Centers. I truly believe this is an era of hope for people with MS. And MRI's going to be an important tool in, not only diagnosing, but monitoring patients. And there's a lot of exciting treatments in the pipeline for folks. So, it's a--it's always bad to have MS, but it's a good time to have it.

Ms. Dottie Pfohl: Thank you so much for your contributions across the board and for spending time with us now.

I'd also like to give a special thanks to June Halper and the staff of the Consortium of MS Care, David Ketterhenrick [sp], who serves as our consultant, and particularly our web manager, Rochelle Ramirez.

So, with that, Dr. Traboulsee, thank you.

Dr. Anthony Traboulsee: Thanks Dottie.

Ms. Dottie Pfohl: And we'll say goodnight.

Dr. Anthony Traboulsee: Bye.