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Neuro Notes

Zamboni "Venous Insufficiency" Theory of Multiple Sclerosis-Red Flags Warn of Thin Ice

Andrew Wilner, MD, Neurology, 11:28PM Apr 14, 2010

Here in Canada, ice hockey is big sport. But everyone knows you don't go skating on the pond when the ice is thin.

At the request of the National Multiple Sclerosis (MS) Society, the AAN hosted a prime time press conference to create a venue where the controversial theory that "chronic cerebrospinal venous insufficiency" (CCSVI) is the etiology of MS could be discussed by its leading proponent, Paolo Zamboni, MD, Director, Vascular Diseases Center, University of Ferrara, Italy, Robert Zivadinov, MD, PhD, Director of the Buffalo Neuroimaging Analysis Center, Buffalo, NY, Andrew Common, MD, Radiologist in Chief, St. Michaels Hospital, University of Toronto, Ontario, CA, and Aaron Miller, MD, Professor of Neurology and Director of the MS Center at Mount Sinai, NY, NY, and Chief Medical Officer of the National MS Society.

Spurred by Dr. Zamboni's 2009 report of 65 patients who had significant improvement in their MS after percutaneous transluminal angioplasty of their jugular or azygous veins to correct CCSVI, over 4,300 people registered to listen in to the press conference. Over 1,000 questions were submitted in advance.

Before I went to the press conference, I was skeptical. A breakthrough in MS by a vascular surgeon seemed unlikely to me, (particularly since my old chief is a neuroimmunologist and pretty smart guy) but, well, who knows?

After the press conference, I was really skeptical.

Dr. Zamboni defined CCSVI as a "syndrome characterized by stenosis of the internal jugular and/or azygous veins with opening of collaterals and insufficient drainage proved by cerebral MRI perfusional study." Why venous stenosis, if it actually exists, should cause MS is unclear-the first red flag. There were at least 2 neuroimmunologists in the room, and I could see that neither one was buying Dr. Zamboni's theory that venous congestion causes leakage of red cells, deposition of iron, break down of the blood brain barrier, and an immunologic response, and Voila! MS. Reversing the venous congestion would, according to Dr. Zamboni, relieve the symptoms.

Apparently, there are neuroimaging criteria for diagnosing CCSVI. These were not explained during the conference, but are critical to the diagnosis. The criteria were defined by Dr. Zamboni, but it is not clear how they were validated, the second red flag.

The third red flag was the hopelessly detailed and confusing presentation by Dr. Zivadinov of the ongoing Combined Transcranial and Extrancranial Venous Doppler Evaluation in Multiple Sclerosis and Related Diseases (CTEVD) Study. The press room was packed with neurologists and journalists, and the conference was specifically designed for lay listeners. I would be amazed if anyone, including the neurologists in attendance, understood much more than the general gist of the three-Phase study, which was to try and identify the prevalence of venous congestion in patients with MS, normals, and patients with other neurologic diseases by various types of imaging. Frankly, I was really frustrated, because I was eager to understand the current research in order to make some assessment about its validity, and I wanted the flags to stop waving.

The fourth red flag was Dr. Zivadinov's insistence that there had to be "scientifically rigorous research alongside respect for patients' rights and needs." I am not sure why he thought this audience needed a lecture on medical ethics, unless it was to imply that somehow this particular research needed to be rushed through. No one, least of all the attendees at AAN, questions the need for better treatment of MS. Indeed, properly controlled randomized clinical trials have spawned several new powerful MS drugs that are likely to be approved in the very near future (see upcoming Medscape post on MS News from AAN).

The fifth red flag was the disclosure that Dr. Zamboni was working on a "proprietery" doppler machine, which would be the only machine that could really detect the problem of CCSVI.

By now, there were so many red flags waving there was turbulence in the room. I had to hang on to my seat to keep from toppling over.

Dr. Common gave a nice, clear, overview for the journalists and laypeople listening in describing interventional radiology and the treatment of venous diseases, but he admitted to no experiencce treating CCSVI.

To their credit, Drs. Zamboni and Zivadinov emphasized that NO PATIENT should have PTA for CCSVI outside a properly controlled clinical trial.

For me, Dr. Miller said it all, "How, when, and indeed whether CCSVI has any role in the treatment of MS remains to be seen."

I look forward to revisiting this topic when there is more high quality, scientific data, and the ice is thick enough to stand on.

5 Comments

#1, Added By: An_1292247, MD, Neurology, 12:27AM Apr 15, 2010

This is a typical conservative response of a neurologist who is used to thinking in one way

#2, Added By: An_14438006, MD, Neurology, 05:07PM Apr 15, 2010

This is not a typical conservative neurology approach, it is a SANE one. Remember the canine distemper theories, bee sting therapy, etc??

ABOUT THIS BLOG

Andrew Wilner, MD, FAAN, FACP, will provide commentary and analysis on selected topics in Neurology. Stay tuned for blog updates.

Andrew Wilner

Dr. Wilner graduated from Yale University and Brown University School of Medicine. He is board certified in internal medicine and neurology. He was medical director of the Carolinas Epilepsy Center, Charlotte, NC, and then Clinical Associate Professor of Neurology at Brown University School of Medicine, Providence, RI. Currently, he is a medical advisor for the Accordant Health Services Epilepsy Disease Management Program.

Dr. Wilner has a lifelong interest in writing fiction and nonfiction, and writes for many medical and other publications. Dr. Wilner received the American Academy of Neurology's Creative Expression of Human Values Award (2001), the American Academy of Neurology's Journalism Fellowship for Excellence in Medical/Health Reporting (2008), and is the author of two books on epilepsy; Epilepsy: 199 Answers, 3rd Edition, and Epilepsy in Clinical Practice. He is a Section Editor for The Atlas of Epilepsies (in press) and participates in annual medical missions to the Philippines. Dr. Wilner is a neurohospitalist in New London, CT.

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#3, Added By: An_5195135, MD, Family Medicine, 12:04AM Apr 16, 2010

One of my partner's MS patients has already undergone venous angioplasty, on his own initiative, outside any clinical trial--and how? because the neurovascular interventionist he approached happens to be best friends with the guy in California who is starting to do venous angioplasty. Our local guy goes out to California, watches what his friend does and reproduces it back home. For two weeks, the patient seemed like a new man--until the placebo effect wears off. Now, our local interventionist is putting together a clinical trial and has--without the regional IRB yet approving it--received requests from patients all over the world to be part of the study. One of my patients has been enrolled as the first participant, in fact. I tried to talk her out of it, noting that no-one has yet documented the incidence of asymptomatic venous stenosis in the general population; that patient selection would have to be far more rigorous than it seems to be; that separating the effect of angioplasty from that of other treatment in a protean, chronic illness may be impossible; that restenosis after angioplasty is a new and unpredictable kind of problem; and that to be of any real value, the study must include not only a no-intervention arm, but also a sham intervention arm. She's still going to sign up.

Angioplasty for CCSVI is a potential goldmine for interventional neuroradiologists, vascular and neurosurgical specialists. I wouldn't be surprised to see interventional cardiologists get in the act, eventually. I also think a lot of patients will get hurt before the CCSVI hypothesis has had its day and joins the many other inadequate explanations of MS.

Reply

#4, Added By: chagai, MD, Family Medicine, 09:30AM Apr 16, 2010

Question:
What is the stand of the National M.S. Society about Statins and H.D.L.,in diagnosis and treatment of M.S.(Reference please)

Reply

#5, Added By: jhovious, MD, Pediatrics, General, 07:28PM Apr 16, 2010

How does the conventional autoimmune theory of MS account for the fact that blood brain barrier leakage occurs before the myelin is attacked. CCSVI is one attempt to explain why the BBB starts to leak - whether or not this theory holds up remains to be seen. At least it is plausible, unlike the autoimmune theory, which seems to be nothing more than an excuse to prescribe obscenely expensive medications.
I have been on a very low fat diet for MS for 15 years; during that time I have had no further relapses or progression, after having 3 relapses in the 2 years before diagnosis. Even though there have been at least 3 studies showing that a low fat diet is beneficial, the neurology establishment has discouraged this treatment for what appears to be financial reasons.

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