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Neuromyelitis optica

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In their article, “Posterior reversible encephalopathy syndrome in neuromyelitis optica spectrum disorders,” Dr. Magaña and colleagues discuss a rare effect of a relatively uncommon inflammatory illness (*Neurology*® 2009;72:712–717). They carefully reviewed the problems of five women with neuromyelitis optica (NMO) (see About page). All five experienced a syndrome called posterior reversible encephalopathy syndrome (PRES).

In these women, the PRES caused confusion. In three, the confusion progressed to coma. Three patients had visual problems including double vision, blurred vision, and cortical blindness. Although seizures can occur in PRES, none experienced this problem.

The women were on average 48 years old. They had NMO for about 6 years. All had the NMO antibody. Four of the women had a lumbar puncture. This showed evidence of inflammation, consisting of an abnormal white cell count. On average, they had 23 white cells in the CSF. Two had an elevated CSF protein of greater than 80 mg/dL. None had oligoclonal bands: this is a specific protein often found in the CSF of people with multiple sclerosis (see About page).

PRES is an uncommon neurologic problem due to swelling in the brain. Because PRES causes swelling in the brain, it causes headaches. It has been associated with very high blood pressure. PRES also occurs in people who are on immune-suppressing medications. For reasons that are unclear, it affects the back part (posterior) of the brain. The posterior brain is called the occipital region. The occipital lobes are important for vision. This is part of the reason why PRES affects vision. One of the reasons

that this study is important is because this is the first time PRES has been associated with NMO.

In addition, Dr. Magaña found that these women had NMO antibodies. The NMO antibodies attach to a protein on cells called aquaporin (aquaporin 4 also called AQP4). This affects that normal function of aquaporin. Aquaporin is in the cell membrane, and acts as a channel that allows water to go in or out of brain cells. The authors proposed that the PRES caused the swelling because the cells’ ability to manage the flow of water was affected by the antibodies against the aquaporin protein.

However, the authors also admitted that there were other possible explanations of PRES in these women. As mentioned, PRES can also occur when a person has problems with blood pressure. Three of the women had fluctuating blood pressure called orthostatic hypotension. One of the women had high blood pressure. In addition, two of the women were on medications that suppress the immune system. One was on high doses of IV methylprednisolone. Another was on IV immunoglobulins.

WHY ARE THE FINDINGS IMPORTANT? Doctors want to understand why certain medical problems occur. Identifying connections between different problems can sometimes point to a common underlying cause. In the instance of NMO and PRES, the connection may be the aquaporin antibody, as the authors suggest. It is also possible that PRES was due to the treatment of NMO, or due to problems with blood pressure that can occur in NMO. Because the number of patients is small, however, it is not possible to firmly establish a connection. Observational studies like this often suggest questions for future research.

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About neuromyelitis optica

WHAT IS NEUROMYELITIS OPTICA? Neuromyelitis optica (NMO) is also known as Devic disease. NMO is an inflammatory illness that affects the optic nerves and the spinal cord. It is relatively rare, and affects women four times more often than men. Once the disease begins, it follows an unpredictable course. Some people have a mild form of the illness, while others can be seriously affected. Like multiple sclerosis (MS), NMO usually causes clusters of attacks. These attacks often are separated by months or years.

Since the illness attacks the optic nerves, vision is affected. The optic nerves connect the eyes to the brain. When inflammation of the optic nerve occurs, it is called optic neuritis. People with optic neuritis often have pain in the affected eye, especially when trying to move the eye. Their vision gets blurred, or they may have double vision. When severe, loss of vision occurs.

NMO also attacks the spinal cord. The spinal cord is the main connection between the brain and the rest of the body. When inflammation of the spinal cord occurs, it is called transverse myelitis. Inflammation of the spinal cord can affect many body functions. It can cause weakness or numbness in the arms, legs, or both. When severe, it can cause paralysis. Transverse myelitis can interrupt the connection between the brain and the bladder, causing urinary incontinence.

WHAT IS THE TREATMENT OF NMO? When an attack occurs, it is often treated with high doses of IV methylprednisolone, a steroid medication. Steroids are very effective against inflammation. They can shorten the course of the attack, and have been shown to reduce injury to the nerves that the inflammation can cause. However, some people do not respond to steroids. In these instances, the antibodies that cause the illness can be removed through a process called plasmapheresis. Alternatively, the immune system can be “confused” with high doses of IV immunoglobulin. Both treatments have been shown to help.

In between attacks, medicine may be given to suppress the immune system. The result is that the body makes less of the troublesome antibody. Al-

though there are several medicines that can help, many people take azathioprine.

IS THERE A CONNECTION BETWEEN NMO AND MS?

There are many similarities between NMO and MS. Both are inflammatory illnesses. Both illnesses affect myelin. Both are due to problems in the immune system. Both are treated with medicines that reduce inflammation or influence the immune system. Acute attacks are often treated with anti-inflammatory medicines like IV methylprednisolone. In some people, plasmapheresis or IV immunoglobulins can help.

Because of these many similarities, NMO used to be thought of as a variant of MS. However, recent discoveries have changed the way that scientists view NMO. In 2004, scientists at the Mayo Clinic in Rochester, MN, discovered that the people with NMO were making an antibody that people with MS did not make. The antibody attaches to a protein on specific nerve cells called astrocytes. The protein is called aquaporin and acts as a channel to let water into (or out of) nerve cells. The antibody is called the NMO immunoglobulin (NMO IgG) or an antibody to aquaporin (also known as AQP4). About 70% of people with NMO have been found to have the circulating NMO IgG.

The interesting thing is that astrocytes do not make myelin, the “insulation” of our nerve cells. Further, aquaporin is not found in myelin either. So how does an antibody to this water channel cause an MS-like illness? The answer to this question is not yet known.

WHAT IS MULTIPLE SCLEROSIS? MS is an inflammatory disease that affects the CNS (the brain and spinal cord). It affects women about twice as often as men. It usually starts at age 30.

The cause of MS is unknown. However, there are several clues about how MS begins. For instance, MS occurs more often in people who live in northern latitudes. Some have proposed that northerners are exposed to an infection in childhood. The immune system forms antibodies to the infectious agent (it could be a bacteria or virus).

Later in life, for reasons that are unclear, the antibodies attach to a protein in the myelin coating of

the axons. The body becomes confused, and begins destroying the much-needed myelin. Without myelin, nerve cell signals travel much more slowly. This results in weakness, numbness, and other neurologic symptoms.

Something in our genes may be responsible for MS. For instance, MS is more likely to occur in first-degree relatives (mom, dad, brother, or sister) than in distant relatives or unrelated individuals. Twenty-five percent of identical twins, who have identical genetic makeup, develop MS. In comparison, only 2% of fraternal twins, whose genetic makeup is like that of a brother or sister, develop MS.

There are several types of MS. In one, the symptoms come and go. In between the symptoms, the

person may feel fine. This type of MS is called relapsing-remitting MS. The other main type is called progressive MS. This type slowly worsens, resulting in a gradual loss of neurologic function. Some have observed that white matter is more involved in the relapsing-remitting type, while gray matter may be more involved in the gradually progressive form.

FOR MORE INFORMATION

Neuromyelitis optica

National Eye Institute

<http://www.nei.nih.gov/>

Multiple sclerosis

National Multiple Sclerosis Society

<http://www.nationalmssociety.org/index.aspx>

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Neuromyelitis optica

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Neurology 2009;72:e40-e42

DOI 10.1212/01.wnl.0000344808.15883.91

This information is current as of February 23, 2009

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