Medical Xpress

Mayo Clinic unravels a mystery disease for Minnesota lawyer

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Greg Widseth didn't know what hit him. The lawyer felt fine as he coached his son's ninth-grade basketball workout last March. He remembers smiling at a young woman as he left the building.

Now Widseth, who once had a photographic memory, is struggling to reconstruct the events that put him in the hospital and led his wife, a former emergency room nurse, to seek help from the Mayo Clinic.

Specialists at Mayo determined that Widseth, 47, was hit by a rare disease that prompted his immune system to attack his brain cells, resulting in as many as 60 seizures a day.

Mayo is one the world's leaders in the diagnosis and treatment of autoimmune neurological diseases, an emerging specialty that drives about 2,500 patients a year to seek help at its Rochester campus. Widseth said neurologists near his home had no idea what to do for him after standard anti-seizure drugs failed to stop the lightning jolting his brain.

"They were like, 'Well, it just happens,'" said Widseth's wife, Nan. "No, it doesn't just happen," she said, recalling that her husband didn't even recognize her after the first seizures struck.

When it became clear that her husband wasn't getting better, she called her sister in Rochester, whose neighbor happened to be Dr. Jeffrey Britton, a Mayo neurologist specializing in autoimmune encephalitis.

Britton and his colleague, Dr. Andrew McKeon, a neuroimmunologist, agreed to see Widseth within a few days.

Special blood and spinal fluid tests developed by Mayo Medical Laboratories confirmed that Widseth had antibodies known to target certain brain cells. That prompted a round of immunosuppressant drugs that had him feeling nearly normal in just four days.

"It was like a light switch was turned off," Widseth said.

Patients who don't get prompt immunosuppressant therapy can suffer serious memory problems or permanent seizures, Britton said. "Getting here quickly made a huge difference."

In the 1960s, scientists discovered that patients with some types of cancer can develop autoimmune disorders that attack the central nervous system. The immune system sends antibodies to attack the cancer, but sometimes they "cross-react" with normal brain cells, leading to neurological diseases, Britton said.

"It's kind of an innocent-bystander effect," he said.

Then Mayo researchers started seeing patients who had nerve diseases without the underlying cancers, and it occurred to them that the patient's antibodies might be to blame.

Widseth had one of the more common ones, known to attack the brain's limbic system, which is involved in the emotions, memory and learning. But he had no cancer.

Some patients have a fever shortly before the onset of their illness, so it's thought that perhaps they had an infection that set off the immune system, Britton said.

Not Widseth. The mystery deepened.

"I would say at least half the people I've seen don't have an obvious trigger that we can pinpoint," Britton said. "So we don't know right now what sets it off."

Dr. Sean Pittock set up the nation's first autoimmune neurology clinic at Mayo in 2006, and he now directs the Neuroimmunology Laboratory and the Center for MS and Autoimmune Neurology. He said technological advances in the past decade have led to "an explosion" in the identification of antibodies that trigger neurological disorders.

Autoimmune responses have been identified as the cause behind a variety of diseases, including dementia, epilepsy, encephalopathy and some eye diseases and movement disorders, Pittock said.

Some forms can even mimic psychiatric disorders, such as a potentially lethal one with the unwieldy name anti-NMDA receptor encephalitis. Susannah Cahalan, a reporter with the New York Post, brought attention to the disease in her bestselling memoir, "Brain on Fire: My Month of Madness," which is being made into a movie.

More recently, Dallas Cowboys tackle Amobi Okoye spent three months in a medically induced coma as he fought the disease.

Recent research suggests the disease may be triggered in encephalitis patients by the same herpes simplex virus responsible for cold sores.

Last April, Mayo published the results of a trial evaluating patients with presumed autoimmune epilepsy in the journal *Neurology*. Now the idea is spreading to other neurological diseases.

Autoimmune spinal cord disease and autoimmune vision problems "have

also been revolutionized by Mayo labs," Pittock said.

Now, Pittock said, researchers are exploring autoimmune disorders that cause serious, painful gastrointestinal disease. "Remember, the gut has 100 million neurons," he said.

Since getting the right diagnosis, Widseth has been able to stay on the job and said he's grateful he got treatment before much damage was done.

"I've tried eight felony cases to verdicts," he said.

Widseth admits to struggling with some memory lapses, some of which may be permanent. But he's found techniques to keep him on task, such as keeping good lists and asking people to put important things in writing. Only time will tell if he's out of danger.

"Relapse happens in about 25 percent of the cases - but that's usually in the first year," Widseth said. "I'm almost beyond that."

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