



Multifocal

By Zachary Pugh

Your hands are weak and your legs twitch with involuntary movements. It's not the same weakness that follows you home from the gym after lifting weights. It's a wasting weakness in your hands, in your fingers, in your wrists that depletes your strength like a massive black hole. It's a weakness that never ceases, and the twitching and cramping never let go. This weakness, these involuntary contractions are your reality when you have multifocal motor neuropathy.

According to the Multifocal Motor Neuropathy Center at Johns Hopkins in Baltimore, multifocal motor neuropathy (MMN) is an immune disorder that is typically identified by "focal weakness" in different parts of the body, such as "wrist drop, grip weakness, impaired dexterity or foot drop. ... Only motor fibers are affected in MMN." People with MMN often experience weakness, yet typically do not experience other sensory symptoms such as numbness or tingling.

MMN was first described in 1985 as the result of the examination of four patients experiencing progressive weakness that resembled motor neuron disorders.¹ Often mistaken for amyotrophic lateral sclerosis (ALS), commonly known as Lou Gehrig's disease, MMN affects more men than women. According to an article in the 2006 European Journal of Neurology,² the factors that cause MMN have been narrowed down to motor conduction blockages.

Once associated with chronic inflammatory demyelinating polyneuropathy (CIDP), the medical community now considers MMN an entirely separate entity that is not related to CIDP. Unlike CIDP and other demyelinating neuropathies, studies indicate that patients with MMN show no signs of their condition improving or worsening when treated with steroids or plasmapheresis.³

¹ Parry GJ, Clarke S. Multifocal acquired demyelinating neuropathy masquerading as motor neuron disease. *Muscle Nerve* 1988; 11: 103-107.

² N. Strigl-Pill, A. König, M. Schröder, H. Beranek, B.G.H. Schoser, M. Spaeth, D. Pongratz, W. Müller-Felber. Prediction of response to IVIG treatment in patients with lower motor neurone disorders. *European Journal of Neurology* 2006; 13: 135-140.

³ *Ibid.*

Motor Neuropathy

In a 1993 breakthrough patient study, "High-dose intravenous immunoglobulin therapy in multifocal motor neuropathy,"⁴ MMN patients reported improvement following intravenous immune globulin (IVIG) therapy, establishing the first known case of IVIG being used as an effective therapy for MMN.

In this study, first published in the journal *Neurology*, five patients with MMN were treated with high-dose IVIG "twice with 0.4g/kg IVIG for five consecutive days at a 12-month interval, followed by maintenance infusions up to six to 12 months." The four patients who possessed high levels of "anti-asialo-GM1 had a consistent clinical improvement starting three to 10 days after the first IVIG course." Moreover, although the effects of the treatment only lasted for an average of 20 to 30 days in three patients, one patient displayed complete recovery for 12 months without needing additional treatment.

The National Institute of Neurological Disorders and Stroke (NINDS) states that, although MMN has symptoms similar to ALS, MMN is treatable and "[a]n early and accurate diagnosis allows patients to recover quickly."

Because MMN symptoms vary greatly, treatment is solely dependent on the severity of symptoms the patients experience. According to NINDS, "some individuals experience only mild, modest symptoms and require no treatment." For others, if the symptoms warrant treatment, it "generally consists of intravenous immunoglobulin (IVIG) or immunosuppressive therapy with cyclophosphamide."

Studies have shown that muscle strength begins to improve within three to six weeks after the start of IVIG treatment and, according to NINDS, "Most patients who receive treatment early experience little, if any, disability."

IVIG has continued to be an efficacious treatment for MMN. In a September 2006 interview with *Routers Health*, Dr. Vinay Chaudhry, director of the Johns Hopkins Multifocal Motor Neuropathy Center, agreed with the use of IVIG for patients with MMN. "A trial of IVIG may be

justified in patients with progressive distal asymmetric weakness in a multifocal peripheral nerve distribution even if they don't have conduction block on nerve conduction studies."⁵

Janice's Story

Janice, an active 51-year-old nursing home activities director and recreation therapist, knows all too well the complexity of MMN and the debilitating effect it has on the human body. "Most of my weakness is in my arms and my hands. One side more than the other," Janice says. "It becomes hard to do everyday things."

Despite this, she still works full time and loves every moment of it. "[MMN] makes me tired. I tire easier than maybe other people. I have to work a little harder at finding creative ways to do things that people would take for granted," Janice says. "Especially being in the kitchen, cooking, getting dressed. ... I use some adaptive aids."

In Janice's case, misdiagnosis is no stranger. "I was originally diagnosed in 1983 with Lou Gehrig's disease, or ALS, and many people that have the diagnosis of MMN were originally diagnosed with Lou Gehrig's disease first. Obviously, I was very lucky because that isn't what I have. I walked around, however, with that diagnosis for about nine or 10 years."

Following a decade of thinking that she had Lou Gehrig's disease, Janice's diagnosis suddenly changed to a then virtually unknown condition called multifocal motor neuropathy. "I was sent to a specialist at the University >



⁴ Nobile-Orazio E, Meucci N, Barbieri S, et al. High-dose intravenous immunoglobulin therapy in multifocal motor neuropathy. Abstract. *Neurology* 1993; 43: 537-544.

⁵ Douglas, David. "Immunoglobulin May Be Useful in Multifocal Motor Neuropathy." *Medscape Today* from WebMD 15 Sept. 2006. 14 Aug. 2007 www.medscape.com/viewarticle/544634.

of Cincinnati who had heard that there was this disease that was just kind of classified at that time," she says. "It would have been about 1993 and multifocal motor neuropathy was very rare."

After being seen by the specialist, who conducted many tests, a conclusive finding revealed Janice's condition. "This neurologist that I was going to felt that I kind of fit the picture [of MMN], and did some additional testing. They found it because they found the antibodies in my blood."

Janice's treatment options at the time of her diagnosis ranged from prednisone to Cytoxan to plasmapheresis, but it wasn't until she started IVIG that she was able to live the way she wanted. "I've been doing IVIG for about 10 years. But prior to that, I've done every single thing else that you could possibly do according to whatever the protocol was at the time, so I've had many doses of chemotherapy," she says.

"When I first started [treatment], I was also on high doses of prednisone and they thought, at that time, combined with the Cytoxan, that would be the thing that would really help, and as it was, the steroids were not good," Janice says. "I haven't had to do that, thankfully, for many years and I've just continued on the IVIG."

In Janice's case, the proof that IVIG is an efficacious treatment is apparent to her every day. Initially, she used IVIG for two consecutive days about every five or six weeks and now Janice infuses it one day every four weeks. The only side effect she experiences is an occasional headache, although she did have one startling experience when she switched brands. "I have had a life-threatening reaction when they switched brands, and that was a couple of years ago," she says, adding that since then she's continued to use the same brand and urges others to do the same.

"If I didn't have the IVIG, I wouldn't be doing anything. I'm quite sure of it. I could not live without it," Janice says.

Janice has some advice for those living with MMN. "The thing that helped me is that I've tried to really be my own advocate and stay on top of it," she says. "I think knowledge is power, truly."

Holly's Story

Much like Janice, Holly, 59, shares the same tale of a "mystery disease" and the misdiagnoses that inevitably followed. "I have been extremely frustrated for the past three years," she says. "It took about two and a half years and I finally got diagnosed in November."

For Holly, the symptoms came on strong and unexpected. She says that one day she woke up feeling very disoriented and sick. Thinking that it was not a serious problem, she went out to the local health food store and stocked up on vitamins, hoping to regain her health. "I dealt with it for a couple of weeks, went out and got some more vitamins. It just wasn't going away," she says. "I went to my doctor and they did an MRI of my brain."

With the exception of a small white spot on her brain, which her doctor surmised was the result of a vitamin deficiency, the MRI appeared to be normal—no alarming red flags.

Then, one day, Holly and her husband were hiking, when things took a sudden turn for the worse. "When I came down to the flat ground to go to the car, I noticed that I was limping. I had a very exaggerated limp and my husband asked,

'Did you pull a muscle or something?' I said, 'No, I don't have any pain at all, I don't know what's going on.'"

It was clear Holly needed to take action right away. She went back to her doctor and had another MRI done: still nothing. "Everything was fine. They took it from a different section of my brain. And everything looked OK."

Eventually, Holly was referred to a neurologist, but test after test and, subsequently, neurologist after neurologist, Holly saw no relief. Her condition could not be explained.

It wasn't until Holly was referred to Scripps in San Diego that a seemingly conclusive diagnosis was finally made. "He diagnosed me with Lou Gehrig's disease. Of course, my life just came absolutely crashing down around me."

After this devastating news, she was referred to an ALS specialist in San Francisco who had some interesting news for Holly. "He put me through testing and said, 'You know, I don't think you have ALS. What I think you have, and I can't be sure, is multifocal motor neuropathy. The symptoms are very much like ALS except it doesn't attack your heart or your respiratory [system].'"

Holly then began IVIG treatment on the recommendation



of her physician. “After four days, I noticed that some of the pain that I was having in my leg—almost like a really strong muscle cramp—did feel a little better, but when I went back up to San Francisco, about three months later, my symptoms had not gone away. And at that time, [the ALS specialist] said, ‘I don’t suggest that you go through this again. I just don’t know what else to do for you. There really isn’t a lot more research.’”

Holly continued weekly IVIG treatments for 16 weeks, but had unpleasant side effects. “I was literally in bed and I couldn’t get up. I had a migraine headache. I was shaking. It was pretty bad. Then after that fifth day, I finally started to get my strength back a little bit and the headache started subsiding.”

At that point, Holly decided to take control and she asked her physician about the Mayo Clinic. “I was really needing someone to tell me what I had. I was just tired of being in limbo and not really knowing. Last November I went to the Mayo Clinic in Scottsdale and went through testing again: EMGs, MRIs, all of that.”

After many tests, Holly was finally and conclusively diagnosed with MMN. “It was a professor of neurology there, Dr. Bosch. After four days of being there, he told me, ‘Yes, this is for sure what you have, multifocal motor neuropathy.’”

Holly understands that the rarity of her disease made her diagnosis difficult, and she believes the delay harmed her. “The problem is that it is such a rare disease that a lot of doctors have not seen it. That is why, I believe, I couldn’t get diagnosed. ... If I had been diagnosed [correctly] from the beginning, I wouldn’t be walking with a cane. If I had been treated with the gamma globulin earlier, I really believe that the situation wouldn’t be the same as it is right now.”

Because of her roller-coaster experience, Holly has become wary. “I went to so many doctors over these past three years, I have become very cynical, skeptical, whatever word you want to use,” she explains.

Still, Holly suggests that people actively seek out qualified physicians and medical centers such as the Mayo Clinic. While IVIG was not the answer for her, she does suggest that people should try it, but refrain from limiting their options. Most importantly, don’t lose hope if it doesn’t work, there are always other options out there. “My advice to someone is to definitely go to the Mayo Clinic, try the IVIG because it does work for a lot of people,” she says. ■

How can you learn more about MMN?

The first step is to consult your healthcare provider if you feel that you have this condition. Below are a few resources that provide information and support regarding MMN topics.

American Chronic Pain Association (ACPA)

Established in 1980, the ACPA was founded with the vision to provide resources for people coping with chronic pain. The ACPA is made up of hundreds of support groups throughout the United States—all dedicated to people who want to improve their quality of life.

www.theacpa.org

BrainTalk Communities: Multifocal Motor Neuropathy

BrainTalk is a global online community dedicated to enhancing the lives of neurology patients and their healthcare providers.

brain.hastypastry.net/forums/forumdisplay.php?f=193

Multifocal Motor Neuropathy Center (Johns Hopkins Department of Neurology)

The Multifocal Neuropathy Center, at Johns Hopkins Medicine in Baltimore, Md., provides a comprehensive clinical definition of MMN along with treatment options, FAQs and a detailed listing of current research and references pertaining to MMN.

www.neuro.jhmi.edu/MMN/index.html

National Institute of Neurological Disorders and Stroke (NINDS)

NINDS provides a working definition, current research and treatment options for MMN.

www.ninds.nih.gov/disorders/multifocal_neuropathy/multifocal_neuropathy.htm

The Neuropathy Association

Headquartered in New York City, N.Y., The Neuropathy Association was established in 1995 by people with neuropathy. Today the association is a nonprofit organization dedicated to helping those with conditions affecting peripheral nerves. The Neuropathy Association comprises 50,000 members and supporters, and approximately 120 support groups throughout the world.

www.neuropathy.org