

Antisynthetase syndrome: Some stories

By Theresa Reynolds Curry



Julie Lewington

Julie Lewington thought she had the flu. Mike Peck thought he had asthma. Wayne Parnell thought he had a lung infection. All three got worse very quickly. Mike's fingers were turning purple, Julie got stuck in a bathtub, and Wayne could barely leave his bed. All three spent some time with

prescribed antibiotics, pain killers, or asthma medications, trying to tough it out until the sheer gravity of their illnesses finally landed them in a hospital, where they were correctly diagnosed with antisynthetase syndrome, a collection of severe symptoms that includes dermatomyositis or polymyositis.

All were very aware their lives were threatened. Wayne heard the doctors saying that if the massive dose of prednisone didn't kill him, the disease surely would. Julie was asked to make a decision about intubation, and Mike was asked about his next of kin.

"This disease should be called 'total devastation,' instead of antisynthetase syndrome." Norma Mondragon wrote in an email. Norma emailed TMA in mid-May, after losing her husband. He was hospitalized for five weeks, without a diagnosis, before he died. The timing of Norma's email made TMA members' efforts to educate the public and the medical profession during Myositis Awareness Month seem even more urgent. Any sign of this syndrome should be taken very seriously.

What is antisynthetase syndrome?

Former TMA medical advisors Drs. Fred Miller of the NIH and Lisa Christopher-Stine of Johns Hopkins University recently fielded questions from patients in a podcast produced by the Rare Genomics Institute.

"It's called a syndrome because it generally groups a bunch of clinical features together," said Dr. Christopher-Stine. "So, when you ask how many different kinds of antisynthetase patients or different kinds of syndromes, we can answer it a few ways. You could look at the antibodies or the immune system proteins that are targeted in this syndrome. You may have heard of anti-Jo-1, for example. Others are PL-7, PL-12, EJ, and OJ. Those five are clinically testable in specialty laboratories.

"Other antibodies are more rare and generally not as often tested in a clinical laboratory. These would be anti-KS, anti-ZO, and anti-HA. Fewer people seem to express those.

"In general, the syndrome itself can be comprised of many things, which can include interstitial lung disease and myositis and then various other clinical features," she said. "Some patients have all of the features."

Mike, Wayne, and Julie all experienced the profound muscle weakness of PM or DM, but also experienced attacks on other major organs. Some common targets include:

- ✚ **Joint as well as muscle inflammation.** Arthritis is a common part of the syndrome.
- ✚ **Thickening of the lung lining, making it hard to breathe.** For the three patients we interviewed, this was the most dangerous symptom. Although not every patient with antisynthetase syndrome has lung disease, many will develop it.
- ✚ **Thickening and cracking of the hands, known as "mechanic's hands."** This distinctive skin sign looks just like you've skinned your knuckles badly over and over again.

✚ **Raynaud's syndrome** is a very common complication that involves extremely reduced blood flow to the hands in response to cold or emotional stress. This explained Mike's purple hands. Julie and Wayne later developed Raynaud's as well.



Mike Peck

About a third of patients develop myositis before some of the other symptoms, about a third develop them all at the same time, and about a third develop the lung disease first before any other symptoms of myositis.

"It appears that the different antibodies have slightly different frequencies," Dr. Miller said. "So the Jo-1 patients, for example, which is the most common form of antisynthetase syndrome, tend to have more muscle disease, mechanic's hands, joint pains, and arthritis. The non-Jo-1 patients tend to have more fevers and the interstitial lung disease."

What causes antisynthetase syndrome?

Dr. Miller said that some hints as to what causes these diseases come from other researchers, with some evidence that cigarette smoking is a risk factor in people with certain genetic backgrounds.

One genetic factor is the HLA-8.1 haplotype gene. The human leukocyte antigen (HLA) genes are important in immune responses to different environmental agents. These genes are present in a number of different Caucasian populations.

"They are frequent and not really abnormal genes that people have," he said, "but there are different spellings of this gene and the spelling that seems to be a risk factor for the antisynthetase syndrome is the HLA-DR3, part of the 8.1 haploid type."

Another possible risk factor is having an occupation that provides exposure to dust and certain gasses or fumes.

"In fact, it's probably a combination of these genetic risk factors and certain environmental risk factors that together result in these diseases," Dr. Miller said.

Dr. Christopher-Stine and other researchers are involved in a study through the NIH that compares patients with antisynthetase syndrome with other myositis patients and with healthy controls. Patients who are interested can call the NIH recruitment office 1-800-411-1222 and ask to be referred to the MYORISK study.

How is antisynthetase syndrome treated?



Wayne Parnell

Between Mike, Wayne, and Julie, they've received almost every possible treatment. The traditional approach is to start with steroids. Current thinking calls for more aggressive steroid treatment early on. Additional medications may be prescribed, even

from the very beginning of the disease: methotrexate, mycophenolate cyclosporine, tacrolimus, and intravenous Cytoxan, especially when there's lung involvement. A recent study of rituximab in myositis showed that those with the antisynthetase syndrome were especially responsive, and many people respond well to intravenous immunoglobulin (IVIG).

Drs. Miller and Christopher-Stine expressed excitement about growing interest from pharmaceutical companies in these previously neglected rare diseases and the developing knowledge of gene therapy as future sources of more effective, less risky treatment.

Wayne acknowledges that, although risky, the extremely high doses of prednisone saved his life: "I was up and walking within days," he said. "It was my own personal miracle."

Julie felt better after a few hours of her first steroid infusion; she also received Cytoxan. Mike was able to remain stable after the addition of methotrexate to his regimen. But all experienced some unwelcome effects from the massive steroids that saved their lives, including facial swelling and hip necrosis.

Dr. Christopher-Stine says that antisynthetase syndrome is absolutely treatable, and she and Dr. Miller offer this advice for the newly-diagnosed:

- ↙ **Do whatever you can to get to a tertiary care center** (a large teaching center) with experience in myositis. To find one, email TMA at tma@myositis.org.
- ↙ **Find out about myositis on TMA's website, www.myositis.org.**
- ↙ **Join a study**—the “MYORISK” study mentioned above or find another one at www.clinicaltrials.gov.
- ↙ **Find support.** Julie, Mike, and Wayne have benefitted from the antisynthetase syndrome closed Facebook group. Drs. Miller and Christopher-Stine recommend attending a TMA Annual Patient Conference; Mike attends every year.

Julie, Mike, and Wayne are much better than they were at the start of their diagnosis, and in all three cases, lung symptoms have been reversed. They also mentioned coming to a sense of peace about their disease: doing what they can to be upbeat and find a balance.

Dr. Miller agrees with this approach. “Exercise, maintaining weight, controlling blood pressure, avoiding stress, trying to maintain and enhance those close personal relationships that you already have or developing some if you don’t, are important because being part of community is a very important step for all humans overall.”

Synovitis

Many people with the syndrome experience this, including Matt Steven, who contributed to this story. Synovitis is a swelling of the joints caused by an inflammation of the joint lining. It can be very painful—much more painful, our members tell us, than it would appear from the outside.

Dr. Christopher-Stine will speak on antisynthetase syndrome at TMA's Annual Patient Conference, September 1-4 in New Orleans. Dr. Dana Ascherman will speak on myositis and lung disease. Other sessions will include medications, exercise, skin symptoms, finding mind-body strength, caregiving, and coping. To register, go to www.myositis.org.

To read the whole transcript of Drs. Christopher-Stine's and Miller's podcast on antisynthetase syndrome, go to www.niehs.nih.gov/research/clinical/assets/docs/antisynthetase_transcript_508.pdf.