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An Elusive Diagnosis, and One That Comes With a Risk of Cancer

It took Renée Parcover, right, 64, of Glenwood, Md., more than two years to get a diagnosis of myositis.
Stephanie Kuykendal for The New York Times

By Roni Caryn Rabin
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When Renée Parcover found out there was a name for the disease that left her so weak she needed a wheelchair to get to doctors' appointments, she was so relieved she started sobbing.

She was only in her late 50s, but she could barely hold a glass of water. She coughed constantly, ran fevers and, in one two-month period, lost 60 pounds. When her grown children treated her and her husband to a four-day trip to Las Vegas, she spent the entire time sleeping.

She consulted a rheumatologist, a dermatologist, a pulmonologist, an immunologist and a cardiologist. One doctor wanted to take out her gallbladder. Another prescribed antidepressants. They all assumed she had rheumatoid arthritis, even though she was never in pain, so for more than a year she received monthly cortisone shots.

"I just wanted to know what I had," said Mrs. Parcover, now 64, who lives in Glenwood, Md. "At one point I realized I didn't even care if it was fatal. I didn't care about anything — I just wanted to know what it was, and know there was a reason."

After two years of dead ends, an infectious disease specialist finally diagnosed the problem: a rare muscle disorder called myositis.

Myositis (my-uh-SIGH-tis) is an autoimmune disease, in which the immune system attacks normal healthy tissue. It causes persistent muscle swelling, inflammation and weakness, as well as other complications like lung disease. One form, dermatomyositis, is often accompanied by a skin rash.

The disease is diagnosed in just 1 in 100,000 people a year, though some experts suspect that many cases may go unidentified because it is so often mistaken for the symptoms of aging or, in women, depression. One survey found that the average patient sees seven doctors before getting the right diagnosis.

This month, in an effort both to improve diagnosis and treatment and to advance research, the Johns Hopkins Bayview Medical Center in Baltimore opened a new multispecialty myositis center. Researchers there are especially intrigued by the high rate of cancer associated with dermatomyositis. (Mrs. Parcover had a treatable form called polymyositis, also sometimes linked to cancer; she is cancer-free, she said.)

This close association is seen as a tantalizing clue by many scientists, who say myositis could hold important insights not just about autoimmune disease but about the role the immune system plays in tumor development, and possibly the development of cancer itself.

Doctors have known since 1916 that patients with myositis were at high risk of cancer. Recent studies have quantified the risk, finding that dermatomyositis patients face a threefold risk of cancer, while patients with polymyositis face a 40 percent increase in risk, said Dr. Stuart M. Levine, co-director of the Hopkins vasculitis center and an author of a recent paper on the subject.

What is intriguing is that cancer and myositis often appear around the same time. The cancer is usually diagnosed within a year of the muscle disease; while both may go into remission after treatment, the recurrence of one often augurs the recurrence of the other.

“Sometimes I tell my patients the myositis saved their life, because it’s an outward sign of an internal tumor,” said Dr. Lisa Christopher-Stine, co-director of the new center at Hopkins, who rigorously screens her patients for cancer, especially adenocarcinomas of the lung, breast, ovary and colon.

“The big question we have is: why are autoimmunity and cancer linked, as occurs in myositis?” she said. “We think it’s telling us something.”

The immune system’s role is to recognize and attack foreign infectious agents like bacteria and viruses, and it is also believed to take part in tumor surveillance. But what if the immune system becomes overzealous or misfires — or if a tumor starts producing proteins that the system recognizes as threatening and foreign, but that are also found in other normal cells?

Dr. Antony Rosen, director of the division of rheumatology at Hopkins, says myositis patients in their 40s, 50s and 60s — the time of life when cancer rates increase — may actually be cancer survivors.

Melissa Leonard, 25, of Easton, Md., suffered her first symptoms of dermatomyositis at 19.
Bill Crandall for The New York Times

"I believe the autoimmune rheumatic diseases that occur in people over age 40 may reflect an anticancer immune response in a large number of people," he said. "These people may be effective cancer survivors."

Dr. Levine, of the vasculitis center, said the muscle cells might be like "innocent bystanders," accidentally harmed during the immune system's assault on the tumor.

In a study published two years ago in The Journal of Experimental Medicine, Dr. Livia Casciola-Rosen, together with Dr. Rosen, Dr. Levine and others, reported that the antigens that produce the immune response are present in normal muscle tissue, but at low levels. They are much more prevalent in myositis patients' cells and in muscle cells that are regenerating, as after an injury.

Dr. Rosen believes a vicious cycle occurs when damaged muscle cells start to repair themselves. These cells express higher amounts of the antigens, causing the immune system to respond; the immune response causes further damage to the muscle, which in turn repairs itself, its regenerating cells expressing even more antigens, and continuing the cycle.

Even more intriguing, Dr. Rosen said, was the study's finding that the antigens associated with myositis are expressed at increased levels in tumors of the breast and lung. The signature of the antigens expressed by tumors is the same as the signature of antigens expressed by regenerating muscle cells.

“The immune response that’s potentially directed against the cancer may also be directed against regenerating tissue in some circumstances,” he added.

In fact, Dr. Rosen said, anticancer immunity and autoimmunity may be closely related and may simply be “two sides of the same coin.” Dr. Rosen’s laboratory now hopes to develop a mouse model in which to test this hypothesis.

So far, however, the hypothesis is just that, said Dr. Paul H. Plotz, one of the authors and chief of the arthritis and rheumatism branch at the National Institute of Arthritis and Musculoskeletal and Skin Diseases. “It is a speculation. It’s a very good idea, but it isn’t really proven in the world yet.”

There is no question about the association with cancer, however, and experts say patients must be closely monitored. Melissa Leonard, 25, of Easton, Md., suffered her first symptoms of dermatomyositis at 19. (When she passed out and suffered a head injury, doctors told her the cause was depression.)

She has responded to medication and is able to work and take care of her child, but she is closely monitored for signs of cervical cancer: she has had a series of abnormal Pap tests and must go in for the screening test every three months instead of the usual once a year.

Other studies of myositis are pursuing other avenues of research. A study of twins and siblings at the National Institutes of Health is exploring why one child develops an autoimmune disease while another does not, said Dr. Fred Miller, chief of the environmental and autoimmunity group at the National Institute of Environmental Health Sciences; the study is examining environmental exposures, including toxins and certain medications, as well as genetic factors.

A study sponsored by Scripps Health is trying to determine whether muscle diseases, including myositis, are linked to the cholesterol-lowering drugs called statins. (This trial is called Imposter-16, which stands for “Is Myopathy Part of Statin Therapy?”)

Other clinical trials are testing new drugs to add to the arsenal of corticosteroids, immunosuppressants and intravenous immunoglobulin, a plasma product. Scientists are conducting trials of rituximab, an artificial antibody used to treat certain types of cancer; infliximab, which blocks the effect of a protein called tumor necrosis factor that is associated with inflammation; and etanercept, which blocks tumor necrosis factor-alpha, also involved in inflammation.

For patients with polymyositis and dermatomyositis, existing medications often do wonders, though many of the drugs have serious side effects and may cease being effective over time.

Once Mrs. Parcover received the correct diagnosis, she was treated with a combination of prednisone, a corticosteroid, and Imuran, a medication that suppresses the immune system. When she started the drug regimen, “I was so bad I could not walk,” she recalled.

“Within a week, I woke up one morning and my eyes popped open and I said, ‘I feel wonderful.’ My legs were walking. It was bizarre. The years in between disappeared, as if none of that had happened.”