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Familial Mediterranean fever can occur without Middle Eastern roots

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Bill DeVore and his sister Heather Zelonis are both affected by familial Mediterranean fever.

Their paternal grandmother used to call it “the pain.” Their father had no name for it.

Siblings Heather Zelonis and Bill DeVore know it as familial Mediterranean fever, an inflammatory disorder that causes recurrent, sometimes high, fevers and painful inflammation of the abdomen, lungs and joints.

Muscle aches, a red rash on the legs and constipation followed by diarrhea are other symptoms.

Familial Mediterranean fever is caused by a defect in a gene that produces pyrin, a protein that regulates inflammation in the body. The defect causes inflammation to “run up and get out of control,” said Dr. Larissa Sachs, a rheumatologist with Rheumatology Associates, PinnacleHealth Internal Medical Associates.

“Attacks commonly last from one to three days, and the person may then be symptom free for days, weeks, months, even years,” she said.

As a child and young adult, DeVore, now 62, had intense cramps in the chest that took his breath away as well as a rigid abdomen. In college, he would sometimes have to lie in bed for two or three days until the pain went away and he could resume studying.

“Nothing helped,” he said. “It was disabling.”

Zelonis, who is 53, started having symptoms in her early teens, pain that could come on “like a snap of a finger,” and lay you flat. It could hit anywhere, even her Achilles tendon.

It was only when an older sibling was diagnosed by a Philadelphia medical center as having familial Mediterranean fever that the explanation for the entire family fell into place.

The diagnosis took them, their two equally afflicted siblings and the doctors who diagnosed and treat them by surprise. FMF is found primarily among people of Middle Eastern descent — Sephardic Jews, Arabs, Turks, Armenians — and sometimes Greeks and Italians. The background of Zelonis and DeVore is Northern and Western European.

“But familial Mediterranean fever can occur in any ethnic group,” Sachs said.

FMF is genetic, or, to be more precise, an autosomal recessive disorder. That means you have to get a defective gene from both parents, who may be carriers even if they don’t show symptoms. That was apparently the case with the four siblings’ asymptomatic mother.

It became clear that the family tree of Zelonis and DeVore — both Silver Spring Twp. residents and co-owners of Integra Print & Imaging — is riddled with FMF. That includes their father and two of his siblings; two of DeVore’s children; and Zelonis’ one child and two grandchildren.

Difficult to diagnose

Upon the first appearance of symptoms, the physician might not suspect FMF. The picture becomes clearer if symptoms persist, and blood work shows no other disease.

“You want to rule out surgical emergencies, or other inflammatory diseases, such as lupus or vasculitis,” Sachs said.

DeVore had his abdominal pain misdiagnosed at age 5 when he underwent an unnecessary appendectomy.

Zelonis said her first doctor diagnosed her on family history.

There is a genetic test to determine FMF, but there are so many possible gene mutations that the test doesn't cover them all, and the physician might still miss the diagnosis.

Diagnosis is more direct if the person is in the middle of an attack, when all inflammatory markers in the blood, such as the white blood cell count, will go up.

The symptoms of familial Mediterranean fever usually begin during childhood. Ninety percent of all people initially diagnosed with the disorder are younger than 20, according to the Mayo Clinic.

Complications of FMF can be profound. The disease can lead to adhesions of fibrous tissues building up in the abdomen or, even more seriously, to amyloidosis. These are difficult-to-treat extra protein deposits that accumulate in the kidney and other organs.

"Patients have to be monitored to make sure amyloidosis isn't developing, at least once a year," Sachs said.

According to the Mayo Clinic, complications might also include chronic arthritis, infertility and nephrotic syndrome, or damage to the kidney's filtering system usually related to amyloidosis.

There are no definite triggers for familial Mediterranean fever. There is also no known cure. But there is effective treatment.

A successful treatment

The most successful treatment is a drug called colchicine, a medication also used to treat gout.

Colchicine, which works by reducing inflammation in the body, is most effective when it's taken to prevent symptoms from occurring, rather than for treating symptoms after they appear, Sachs said.

The usual daily dose for adults is 1.2 to 2.4 milligrams, and is administered in one or two divided doses. Pediatric doses are lower; children as young as 4 to 6 years old can take colchicine.

“The dose should be increased as needed to control the disease and as tolerated in increments of 0.3 mg/day to a maximum recommended daily dose,” Sachs said. “It should be decreased by the same increment if intolerable side effects develop.”

Side effects of taking colchicine are mostly gastrointestinal, with diarrhea being the most common. Nerve and muscle damage can be seen, but these are mostly in the elderly and individuals with renal impairment.

Patients with FMF now have to pay for a brand-name version of the drug.

While some manufacturers had been making a generic version of colchicine for decades, it lacked approval from the U.S. Food and Drug Administration. In 2010, the FDA ordered the manufacturers to stop production on those drugs. Only Colcrys, a trademark single-ingredient oral colchicine product that received FDA approval in 2009, was left on the market.

That has driven the cost up considerably, Zelonis and DeVore said.

Eventually, FDA approval is expected to be granted for generic versions of the drug, which should help to make it more affordable.