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MAGAZINE

Fibro- muscular dysplasia

Trying to get the right
treatment, when nobody
knows what's wrong

*Nurse and
Stroke Survivor
Pam Mace*

- **Meeting Big Goals**
- **Have You Heard the One About...**
- **Actions Speak as Loud as Words**



The String of Beads No One Wants

Fibromuscular dysplasia is a serious blood vessel disease that has no unique symptoms and can only be diagnosed with advanced imaging techniques.

by Jon Caswell

The first clue that Seema Agarwal-Harding had a rare disease called fibromuscular dysplasia came in an exotic land. She had a stroke at the airport in New Delhi, India.

It was October 2004, and her flight to Mumbai (formerly Bombay) had been delayed. A senior education adviser for Asia and the Near East for the U.S. Agency for International Development (USAID), she was visiting her native India as part of a team negotiating development projects with Indian organizations.

“At 4:55 p.m. I felt fine, a little tired so I bought some tea. Waiting in line I felt a strange tingling in my arm, and by 5:05 my head was bursting,” said the 48-year-old mother of two. “The room was spinning, and I was losing my bearings. I started to sweat.” She collapsed into the arms of two co-workers.

She was “rushed” by ambulance through the notorious New Delhi traffic to one of the city’s best hospitals, where an MRI showed a subarachnoid hemorrhage (bleeding from a blood vessel on the surface of the brain into the space between the brain and skull) that precipitated multiple strokes. But a diagnosis is not necessarily an explanation, and no one could explain the burst artery.

For two weeks the doctors puzzled over her case, tentatively deciding on a type of vasculitis called Takayasu’s arteritis. This very rare blood vessel disease occurs in only two to three cases per million people.

She was medivaced from India to the Johns Hopkins neurology ICU in Maryland. There leading experts from the Johns Hopkins Vasculitis Center eventually ruled out the Takayasu’s diagnosis after four months of tests and diagnostic work. Using magnetic resonance angiography (MRA), the doctors finally determined Seema had fibromuscular dysplasia (FMD).

While FMD is more common than Takayasu’s arteritis, it is often misdiagnosed and mistreated. FMD is a blood vessel disease that has no unique symptoms and can only be diagnosed with advanced imaging techniques. The first accurate description of FMD occurred in 1958, according to Dr. Jeffrey Olin. Dr. Olin is a professor of medicine at Mount Sinai School of Medicine and Director of Vascular Medicine and the Vascular Diagnostic Laboratory in the Zena and Michael A. Wiener Cardiovascular Institute of The Mount Sinai Medical Center in New York City.

STRING OF BEADS

Pam Mace of Rocky River, Ohio, was diagnosed with FMD in 2001, many months after having a transient ischemic attack (TIA) at age 37. She joined the Fibromuscular Dysplasia Society of America (FMDSA) soon after to raise awareness of this disease. “FMD causes the arteries to narrow, blocking blood flow,” she said. “It often affects arteries to the kidneys, causing the sudden onset of high blood pressure, or blocking blood flow and causing the destruction of kidney tissue. If FMD affects the carotid

(continued on page 18)



FMD changed the direction of Pam Mace's life. Once an ER nurse, she now works part-time and focuses her efforts on raising awareness of FMD in the medical community.

Photo: Jamie Janos Photography

(continued from page 16)

or vertebral arteries, people may experience dizziness and chronic headaches or even neurological symptoms such as stroke or TIA. My symptoms were caused by bilateral carotid artery dissections (tears or rips).”

“The name ‘fibromuscular dysplasia’ refers to the fact that the fibrous tissue and muscle layers in the middle of the artery wall grow in an abnormal manner and deform the artery,” said Dr. Richard Hughes, an associate professor in the neurology department at the University of Colorado Health Science Center in Denver. “This makes the normally smooth tube a bumpy tube.”

The most common forms of FMD produce this bumpy tube, which in the angiography produces the characteristic “string of beads” appearance. This is due to changes in the architecture of the artery wall that cause the arteries to alternatively become narrow and dilated. A less common but more aggressive form of FMD may cause the vessels to become severely narrowed without the “string of beads” appearance.

“FMD cannot be diagnosed without some type of imaging tests such as duplex ultrasound, magnetic resonance angiography (MRA), CT angiography (CTA) or catheter-based angiography,” Dr. Olin said. “Its general prevalence is not known, but it occurs much more frequently in women. It’s usually diagnosed when something happens that makes you suspect it and a diagnostic image is made. Sometimes it is discovered incidentally during an imaging test performed for an entirely different reason.”

IN FMD, TIA MAY BE A SYMPTOM

For Pam Mace, it was dissected carotid and vertebral arteries that began the medical odyssey that would eventually lead to her FMD diagnosis. A follow-up MRA showed aneurysms in both carotid arteries, a fact confirmed by the opinion of a second neurologist, who urged her to see a vascular doctor. “He ordered an angiogram so he could visualize my arteries,” Pam said. “At that point it had been seven months since my TIA and none of my symptoms was better. I still had terrible headaches and a drooping eyelid.

“Within minutes of starting the angiogram the doctor saw the classic ‘string of beads’ formation in my renal



Pam Mace (center) and daughter Chrissy Gribble (far left) join FMD survivors at an FMD fundraiser



Pam Mace (center) and a group of geneticists at a conference in Europe

artery, which indicated I had FMD. That explained the sudden onset of high blood pressure that I’d experienced when I first went to the ER. Although I was a nurse, I had never heard of this disease, but I finally started to feel like I knew what was causing all of my problems.”

There is no cure for FMD. For Pam, treatment included stents in both carotid arteries because of the damage caused



A leading authority on FMD, Dr. Jeffrey Olin estimates that he has seen fewer than 200 patients with the disease but said that there is no way to know how common it is.

by the dissections. “Stents are not approved by the FDA for this purpose,” said Pam, “but I really had no choice.” It had been more than two years since she had first gone to the hospital with “the worst headache of my life” and unequal pupils.

A leading authority on the disease, Dr. Olin estimates that he has seen fewer than 200 patients with FMD but said that there is no way to know how common it is. “The most common presentation is a young woman with high blood pressure because FMD most commonly affects the renal arteries,” he said. “Those with the disease in the carotids can often hear the swooshing noise in their ears. This is caused by turbulence of blood flow, and if a physician listened with a stethoscope, they would hear this noise called a bruit. FMD is often confused with an inflammatory disease of the blood vessels — vasculitis.”

Mattanajah de Vries was diagnosed with Horner’s syndrome when he first visited his doctor with a severe headache, unequal pupils, sensitivity on one side of his face and a drooping eyelid. “These symptoms can occur when nerves to the face get pinched or when a carotid artery is dissected because the nerves are close to the artery,” said Mattanajah, a professor of physical chemistry at the University of California — Santa Barbara. “Normally doctors look for a tumor in that situation, but my CT scans didn’t show anything. The medicine they gave me wasn’t helping my headache. In June 2006, the doctor ordered an MRA, and that showed a carotid artery dissection as well as FMD.”

He was treated with blood thinners, and a later MRA showed that the dissection was healing nicely. “I am trying not to let this diagnosis change my life too much,” Mattanajah said. “I’m careful about exercises that strain my neck, or getting a massage. This is a new experience of fragility that I’ve never had before.”

CAUSE IS STILL A MYSTERY

The vascular physicians who work with FMD have not found its cause. “There is no evidence of an environmental component, although FMD occurs more commonly in individuals who were smokers,” Dr. Olin said. “I don’t know how valid that is because I have seen many patients with FMD who never smoked. There is no preponderance in any part of the world, and weight doesn’t seem to be a factor.”

“Since women in the 20–50 age group represent the majority of cases, many researchers think there is an important hormonal component to FMD,” Dr. Hughes said. “Maybe hormones accelerate the changes of FMD, or maybe it makes their FMD more likely to be symptomatic,

(continued on page 20)



Pam providing information about FMD at a stroke conference



L to R: Pam, Seema Agarwal-Harding, Dr. Nazli McDonnell and Cheryl Golden participating in an FMD research study

Why is the diagnosis of FMD often missed or delayed?



Unfortunately for patients with FMD, there are no symptoms that definitively indicate the disease.

Many FMD patients have no symptoms at all. Those who do often exhibit nonspecific symptoms such as headache, lightheadedness, dizziness or neck pain. In otherwise healthy people, these symptoms are frequently attributed to more common ailments, such as migraine or middle ear infection.

In young patients who experience a stroke or other serious neurological symptoms, the diagnosis of FMD may not be considered due to its rarity, or the need for specialized testing such as MRI or angiogram of the arteries to the kidneys or brain. Several other diseases have symptoms that overlap with FMD, therefore a high degree of suspicion and knowledge about FMD is required so that the correct diagnosis is reached.

As many physicians may never diagnose or treat a patient who has been diagnosed with FMD, awareness of the disease and its presentation is an important part of the work of organizations such as the Fibromuscular Dysplasia Society of America. In addition, various medical organizations, including the National Institutes of Health, are conducting research into the disease and its associated conditions.

Source: Douglas P. Webster, DO, FACEP; emergency room physician, Lincoln Park Hospital, Chicago

(continued from page 19)

and therefore diagnosed. Still, men get this, too, so the hormonal theory cannot be the only explanation.

“There is another theory that the artery or arteries involved are made susceptible to the FMD changes because of some sort of wear and tear, or a viral irritation. The idea is that the artery tries to heal but overdoes it.”

There is some evidence of a genetic cause. However, relatives may have different arteries involved, different levels of severity or not develop FMD at all. Not all individuals with FMD have a family member who has the disease.

LIFE AFTER DIAGNOSIS

For Pam Mace, FMD has changed everything. She now works as an ER nurse on a per diem basis, which allows her to make her own schedule so she doesn't get overworked. Her nursing background has been a plus in her work with FMDSA.

Unlike Mattanjah, her carotids did not heal, which required the stenting. A year after her first stent was placed, she was still having spasms and noise in her ears, as well as unequal pupils. “I was afraid to fly again or do anything for that matter,” she said. “I had already given up running — I had been a marathoner — golfing and scuba diving. At one point I was told not to have my hair washed at a beauty salon because of the position you are in. I was instructed not to do anything that would raise my heart rate or blood pressure.” A second stent was placed in 2002, and FMD was also diagnosed in her right renal artery at that time.

Seema Agarwal-Harding's life has also changed as a result of her FMD diagnosis. “During the course of my illness, I felt like a burden or even an invalid, less than what I was before in the eyes of others. It forced me to regain myself through rebuilding my own self-esteem. It hurt that I was no longer considered by some to be the beautiful, capable, intelligent person I once was.

“FMD created a sense of doubt, uncertainty and loss. I had to grapple with who I had become, what I am capable of today. I lost a lot of self-confidence. For a time I could not walk, read or write, let alone drive or cook or analyze

professional papers. It was devastating. I still felt the same on the inside, but everybody treated me differently. I was now a sick person.

“To regain myself, I set about trying to do little things. I started writing a memoir, working on a quilt for my son, cooking occasionally, and listening to books and music. By doing these small acts, people around me became convinced that I would be okay after all. Six months after my illness, I returned to work full time, resuming my work in international education and traveling once more to developing countries.

“But two years later I am in a different place,” Seema continued. “I have now reconciled myself to the fact that I do indeed have a life-threatening disease that will not go away. I am more accepting of that fact. I have given up my career as a U.S. diplomat, designing and implementing education projects around the world. I am focusing on cherishing my life with family and friends.

“My life is no longer about ambition or success or glory at work, it is more about the value of my time spent on things that really matter — my precious children, my parents, time writing and reflecting on my life and contributions that I have made and that I might still make for those less fortunate than I, and for my children.”

“It's been six years since I dissected,” said Pam Mace, “and it was only about a year and half ago that I started to move on with my life. Every now and then I worry about having stents in my head. With FMD I will always be at risk of a stroke, but I take every precaution I can: I watch my diet, walk, take my medication, and I never miss a doctor's appointment. And I have lots of doctors — a primary care physician, a neurologist, a vascular specialist, a nephrologist for my kidneys and a cardiologist. At age 42, I have already had five angiograms, but I have gone from weekly doctor visits to yearly checkups.

“There are many aspects of this disease, and no one fully understands it. And few doctors have heard of it, so I have shifted my focus to raising awareness of FMD. It is my hope that one day everyone will be aware of this very special ‘string of beads’.” **SC**



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— Seema Agarwal-Harding



“It is my hope that one day everyone will be aware of this very special ‘string of beads’.”

— Pam Mace

What is Fibromuscular Dysplasia?

COMMON SYMPTOMS

The signs and symptoms of fibromuscular dysplasia depend on the organ the affected artery supplies.

If the affected arteries lead to the kidneys, patients could experience high blood pressure, ischemic renal atrophy (where the kidney shrinks) or, in rare circumstances, kidney failure (when FMD progresses in both kidneys). The renal arteries are the most commonly affected blood vessels in the body.

If the affected arteries are the carotid and vertebral arteries, patients may complain of dizziness, temporary blurring or loss of vision, vertigo, neck pain, ringing or swooshing noises in the ear, TIA or stroke. FMD patients are also at an increased risk for intercranial aneurysms.

If the affected arteries lead to the intestines, liver or spleen, patients may experience abdominal pain after eating, and unintended weight loss. FMD in the arms and legs can cause limb discomfort with use (claudication).

DIAGNOSING FMD

Diagnostic imaging is the only means for diagnosing FMD. CT angiography, MRA (magnetic resonance angiography), duplex ultrasound and catheter-based angiography are all effective ways to diagnose FMD. In the most common form of FMD, called medial fibroplasias, these imaging methods show a distinctive “string of beads” appearance. Because FMD is not commonly encountered, not all healthcare professionals know what to look for.

COMMON MISDIAGNOSES OF FMD

Because FMD is uncommon, it is often misdiagnosed as:

Vasculitis — an inflammatory condition of the blood vessel walls

Atherosclerosis — buildup of plaque on artery walls causing “hardening of the arteries”

Traumatic dissection — rupture of an artery

Buerger’s disease — an inflammation of the arteries, veins and nerves in the legs caused by smoking and leading to restricted blood flow. Left untreated, Buerger’s disease can lead to gangrene and ultimately amputation of the affected areas.



This MRI angiogram of a carotid artery demonstrates the dramatic “beading” effect (highlighted) caused by FMD.

TREATMENT OF FMD

There is no cure for FMD, and there is no set protocol for treating it. Treatment often involves attempts to increase blood flow through the affected vessel. The kind of treatment used depends largely on which arteries are affected as well as the severity of the symptoms. Balloon angioplasty is most frequently used to open the renal (kidney) and carotid arteries. Unless there is a dissection of the artery, stents are usually not required. Most people with FMD take some sort of antiplatelet agent (usually aspirin) every day.

POSSIBLE CAUSES OF FMD

The cause of FMD is not known, but several theories have been suggested. Because it has been identified in multiple members of the same family, including twins, some experts believe it has a genetic cause. However, not all individuals with FMD have relatives with the disease.

Because FMD is more common in women than men, some investigators have suggested that hormones play a role. This theory is supported by the fact that most women are premenopausal when diagnosed.

Other suggested causes include tobacco use, abnormal development of the arteries that supply the vessel walls with blood resulting in inadequate oxygen supply, and the anatomic position of the artery within the body. It is possible that many factors are involved in the development of FMD.

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