JOHNS HOPKINS MEDICINE

PhysicianUpdate

NEWS FOR PHYSICIANS FROM JOHNS HOPKINS MEDICINE

FALL 2013

Per week, Sally Mitchell and Clifford Weiss see 10 to 15 patients with vascular malformations, such as the one shown in the illustration below.

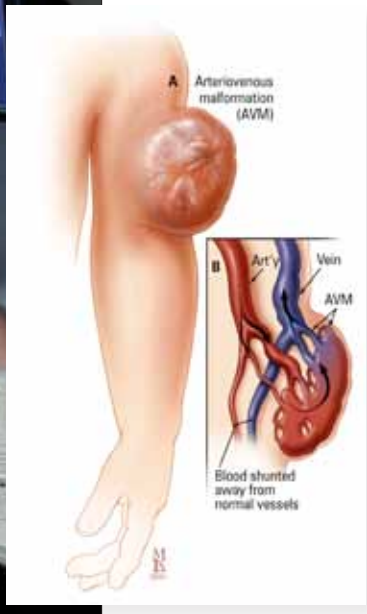

Illustration by Michael Linkinhoker, Department of Art as Applied to Medicine

Vascular Malformation: A Rare but Treatable Condition

The trouble with vascular malformations is that they're masters of disguise. Indeed, says **Sally Mitchell**, director of vascular anomalies at The Johns Hopkins Hospital and associate director of the Interventional Radiology Center, these congenital vascular anomalies of arteries, veins, and/or lymph vessels "are extremely rare, can occur almost anywhere in the body, and are easy to mistake for tumors or cysts." As a result, patients may be referred to oncologists, orthopedic surgeons, dermatologists, vascular surgeons, ENT surgeons or other specialists.

The good news, says Mitchell, is that when these benign aberrations—which can emerge at any age—are correctly diagnosed, they are very responsive to nonsurgical treatment. Because the disease is so easily misdiagnosed, estimates of incidence can range from 1 in 100 to 1 in 5,000. Mitchell and interventional radiologist **Clifford Weiss** see about 10 to 15 patients a week with these disorders from all over the world.

A large percentage of patients with vein or lymphatic malformations, says Mitchell, can be treated with ultrasound- and X-ray-guided injections that are delivered directly into the growth. Some require only one percutaneous dose of alcohol, sotradecol, doxycycline, bleomycin or other powerful sclerosing agents. This burns the inside of the lesion and causes it to shrink away. The treatments that Mitchell uses are based on algorithms that she developed for the various types of lesions that can occur.

But it's not always a one-shot deal, because the condition can recur with hormonal cycles, pregnancy or adolescence. "It's not just a matter of looking at an MR image," says Mitchell. "You also need to see the patient, figure out what it is and what the treatment is now and for the long term."

Although some cases are straightforward, such as those that are small or on an extremity, others are more complex. "We've seen

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An Elusive Diagnosis, Then Reprieve

Three years ago, Leonard Piotrowski developed neck pain that became progressively worse. He went to see his primary care doctor, who, knowing that Piotrowski had a history of arthritis in his cervical spine, referred him to an orthopedic surgeon. The surgeon sent Piotrowski to a pain specialist, who performed radiofrequency catheter ablation to kill nerve receptors. Piotrowski felt relief for a brief period, but says the pain then returned "with a vengeance." Another ablation followed, but again the relief was short-lived.

By then, Piotrowski, could barely function. Every turn of his head became excruciating. He sought help from a neurologist, who diagnosed him with a tumor on the branch nerve at the base of his neck. Two other neurologists confirmed the diagnosis, and Piotrowski was referred to Johns Hopkins for specialized imaging.

Alan Belzberg, the neurosurgeon reading the image, suspected that the lesion wasn't a tumor but a vascular malformation. So he referred Piotrowski, 61, to interventional radiologists Sally Mitchell and Clifford Weiss.

Mitchell and Weiss confirmed that Piotrowski had a venous malformation. Weiss targeted the lesion percutaneously, with an MRI-guided Sotradecol treatment. The procedure took more than three hours because the lesion was tiny and deep in his trapezius muscle. "It was hard to distinguish on standard imaging what was muscle and what was lesion," says Weiss. "Using our specialized interventional MRI sequences, the lesion was more easily seen and targeted, something which would have not been possible using ultrasound and fluoroscopy." As soon as he came out of anesthesia, Piotrowski says, "I was pain free." Before the treatment, he says, he hadn't been able to sleep more than two hours a night. "Now I get a good night's sleep, take out the garbage and travel to see my grandchildren. I'm a happy person."

For more info, contact 410-502-6611 or http://www.hopkinsmedicine.org/vascular/conditions/malformations/

Complex **Late-Stage Cardiomyopathy**

When Mark Olkon, 61, entered The Johns Hopkins Hospital in preparation for a complex ablation last January, he had been coping with hypertrophic cardiomyopathy for more than 25 years. In spite of medical therapy, a pacemaker/defibrillator implantation and an ablation for atrial flutter four years earlier, his condition continued to deteriorate to the point that, in 2011, he was in late-stage cardiomyopathy with atrial fibrillation and congestive heart failure.

"I was retaining a lot of fluid," says Olkon. "I was short of breath and very weak."

Olkon's cardiac electrophysiologist, **Alan Schneider**, who practices at Suburban Hospital in the Washington, D.C. suburbs of Maryland, referred Olkon to Johns Hopkins heart rhythm specialist **Joseph Marine** for consideration of a complex catheter ablation for atrial fibrillation.

"Mark is one of the most complex patients out there," says Schneider. "His heart was badly out of rhythm. We thought that if we could get his heart back into a normal rhythm with the ablation, he would feel much better."

However, during testing at Johns Hopkins prior to the ablation, Olkon was found to be anemic and edematous, and his kidneys were not functioning properly. He was admitted to the hospital for more tests and treatment to improve his hemoglobin and heart failure symptoms. While his condition improved, his doctors began to reconsider whether the ablation was the right course of action.

Joseph Marine and Alan Schneider collaborate to provide Mark Olkon with the best treatment option. Here, Schneider interrogates Olkon's defibrillator as Marine watches.

"We thought that there was less than a 50 percent chance that the ablation would be successful and since Mark's heart was so weak, we knew that the procedure would present greater risk. So after thorough discussion, we made a shared decision that the ablation was not the best course of treatment," says Marine.

Schneider and Marine then considered another option—to upgrade his device to a biventricular pacemaker/defibrillator to pace his left ventricle, as well. Schneider performed that procedure for Olkon at Suburban Hospital, and it proved to be a good decision.

"With cardiac resynchronization therapy, we were able to improve his forward flow and cardiac output," says Schneider. "His atrial fibrillation is here to stay, but at least now his bottom chamber is pumping stronger and he is feeling better."

"While I'm still limited in my activities," Olkon says, "I no longer feel any chest discomfort or shortness of breath, and so it worked out well."

Olkon says he is pleased with the coordinated care he received. "My care at Johns Hopkins was very good and the doctors there were in constant touch with Dr. Schneider."

☎ 443-997-0270 for information

The Case for **Live Donor** Liver Transplants

With the right team and protocols in place, live donor liver transplants are safe, says Ahmet Gurakar.

Thousands of children and adults who were once in liver failure are alive today because of live donor liver transplantation (LDLT). Yet in recent years, interest in LDLT as a viable alternative to cadaveric donation has waned. In part, that's likely because of the emergence, in 2002, of a priority-based national model scoring system for wait-listed liver recipients. Those patients with higher MELD (model for end-stage liver disease) scores based on the urgency of their condition—bilirubin and creatinine levels and prothrombin time—can receive cadaveric livers sooner. Even so, the average wait time for a cadaveric liver donation in the US is 149 days for adults and 86 days for children.

But for those whose MELD scores aren't high enough, a healthy, appropriately matched live donor can shorten the recipient's wait time significantly, says **Ahmet Gurakar**, The Johns Hopkins Hospital's medical director of liver transplantation.

Though LDLT surgery is more complex, he says, "our experienced team does a rigorous workup, and only after the donor has been deemed a good match surgically and psychologically will we consider doing the operation." Still, ever since a highly publicized donor death in New York in 2002, perceived high mortality risk for living liver donors persists.

So, is it really safe to donate part of a liver?

Under skilled hands and with standardized protocols, the answer, says Gurakar, is yes. According to a widely cited 2012 study published in *Gastroenterology* by transplant experts at The Johns Hopkins Hospital, including Live Liver Donor Surgical Director **Nabil Dagher**, the risk of early death among live donors in the United States is 1.7 per 1,000. Furthermore, mortality of live liver donors does not differ from that of healthy, matched controls during a mean of 7.6 years.

"From the moment a potential donor is identified," says Dagher, "our program is exceptionally attuned to that person's safety." Each case is discussed among a team that includes a hepatologist, surgeon, transplant coordinators, living donor advocate, social worker, psychologist and nutritionist. The process takes between three to four weeks. The age cutoff for adult donors is 60.

> "ONCE A PORTION OF THE LIVER HAS BEEN RESECTED, IT IMMEDIATELY STARTS TO REGENERATE AND STAYS IN TUNE WITH METABOLIC NEEDS."

After the surgery, it takes about three months for the donor's liver to regenerate. Roughly 30 percent of the liver is taken from an adult for a child recipient; about 60 percent is resected in adult-to-adult donation. "The liver is a wonderful organ," says Dagher. "Once a portion of it has been resected, it immediately starts to regenerate and stays in tune with metabolic needs."

Johns Hopkins has been performing LDLTs since 1992. Recently the program was reinvigorated with the addition of Gurakar, Dagher and **Ayman Koteish,** live liver donor medical director. Since January 2012, the team has performed four successful LDLTs—three adult to child, and one adult to adult (in 2012, 246 LDLTs took place nationally). Most recently here, a firefighter donated part of his liver to his infant daughter. He was back to work in two months, says Gurakar, and he and his daughter are doing well.

"LDLT provides the best chance to help our patient population," he adds. "A live donor can save another life as well by freeing a cadaver liver for a patient who can only go that route." ■

☎ 410-614-2989 for information

Ziya Gokaslan and his colleagues have unique expertise in removing chordomas, tumors that are often exceptionally difficult to treat.

Curing **Chordomas**

The chances of being diagnosed with a chordoma are literally one in a million. These rare cancers are thought to arise from remnants of the notochord, cartilage that serves as a scaffold for the backbone during development. When genes for proliferation turn on by mistake later in life, these residual cells can form slow-growing tumors that can be fatal if they aren't removed.

While these tumors can occur anywhere in the skull or spine, having a chordoma in the sacrum comes with its own special set of challenges, says neurosurgeon **Ziya Gokaslan**. "There, the tumor can affect nerves for bowel, bladder and sexual function," he explains. "If the tumor isn't removed properly, these functions can be permanently harmed."

Because chordomas usually present as a soft tumor contained in a bag of fluid, it's critical to remove the tumor in one piece without breaking the bag. If its contents are spilled, Gokaslan says, malignant cells can take up residence in the surrounding tissue and metastasize throughout the body, making a cure impossible.

Gokaslan and his colleagues have amassed significant experience in treating chordomas, including very large tumors that necessitate removal of the entire sacrum. The team has developed techniques that can spare critical nerves if the tumor location is amenable, keeping bowel, bladder and sexual function intact.

When Gokaslan and his team need to remove a patient's entire sacrum, the lumbar spine becomes dissociated from the hips and pelvis, he explains, requiring total reconstruction with multiple screws, rods and bone grafts.

These operations can take up to 16 hours and may need to be completed over two days.

For such large surgeries, wound closure is a critical element, he adds. Gokaslan and his team regularly work with plastic surgeons skilled in techniques to repair these wounds. These complicated procedures often require pulling an island of vascularized tissue from the abdomen through to the other side, replacing tissue removed during surgery.

To develop better treatments, Gokaslan and his colleagues are conducting basic research to understand why these tumors arise. Recent findings suggest that small RNAs might be able to block the expression of tumor-specific genes in chordoma cells, offering a way to control disease in patients whose tumors couldn't be removed completely.

"We're hoping to take some of these discoveries from the lab," he says, "and move them to the bedside to increase our cure rate even further." ■

☎ 410-955-4424 for information

New Hope for Those with **Klinefelter Syndrome**

Boys and men with the chromosomal disorder Klinefelter syndrome, or XXY male, have a new resource for treatment and medical management.

The Johns Hopkins Klinefelter Syndrome Center is the only multidisciplinary program of its kind in the country serving adult males, says endocrinologist **Adrian Dobs**, the center's director. (A comprehensive clinic in Colorado is dedicated solely to children with the syndrome.)

One in every 750 males is born with an extra X chromosome. This can lead to a range of health issues seen in Klinefelter syndrome, including infertility, underdeveloped genitals and learning disabilities. The condition has been linked to increased risk for depression and autoimmune disorders, like lupus and rheumatoid arthritis. Affected males are also at higher risk for breast and blood cancers.

"There's a real gap in the care of men with Klinefelter syndrome," says Dobs. "These men are complicated, and many are not diagnosed until puberty or adulthood, she says. Up to two-thirds of men with the syndrome are never diagnosed.

At the center, all patients see Dobs initially for a complete medical history, exam and discussion about hormone treatment. Then the clinic can coordinate appointments with Hopkins experts in pediatrics, primary care, genetic counseling, urology, neuropsychology (for problems with learning, thinking or mood), and psychology (for gender identity issues).

Testosterone replacement therapy, when started in adolescence, can help ensure proper development of muscles, bones and male sex characteristics, Dobs says. For men interested in fertility preservation, other approaches to hormone therapy should be considered. Infertile men can often father children via assisted reproduction.

Klinefelter Syndrome Center Director Adrian Dobs meets with psychiatrist Cynthia Munro to discuss a patient.

The center, which opened a few months ago, so far has seen five patients. "We're filling a need for a rare disease in which we have expertise," Dobs says. ■

☎ 855-695-4872 for information

(Vascular Malformations continued from page 1)

massive malformations in the face, neck, hands or deep in the belly," says Weiss. These can pose dangers when critical organs are involved and may trigger severe pain and bleeding.

Because the lesions can develop anywhere in the body, Weiss and Mitchell work in tandem with other specialists, including dermatologists, orthopedic surgeons, hematologists, ENT surgeons, MRI specialists, geneticists and plastic surgeons. This multidisciplinary group meets in a monthly conference in which they present complex cases to help educate clinicians about the malformations' many guises and to sort out appropriate treatments for patients.

The future, says Mitchell, will likely bring drugs to treat various types of vascular anomalies. Meanwhile, she says, "It's incredibly gratifying to help patients with these rare conditions." ■

☎ 410-502-6611 for information

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Johns Hopkins Medicine offers the following resources for you and your patients.

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☎ 1-800-765-5447
(Continental United States)

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