Cavernous hemangiomas

Steven Karceski, MD

In their article, "The prospective hemorrhage risk of intracerebral cavernous malformations," Dr. Flemming and colleagues[1] carefully evaluated a large number of people with this condition at Mayo Clinic. Their reason for this study was simple. Although the medical literature contains several case series, many of these series have a few patients with intracerebral cavernous malformations (ICMs). As a result, there is some confusion or "vagueness" in this information. Dr. Flemming and colleagues wanted to make this much clearer.

In the medical literature, the risk of bleeding from an ICM is unclear. Some series quote a low risk of 0.7% per year. Others have identified a higher risk, as much as 4.2% per year. In addition, many studies have assumed that the risk of bleeding from an ICM is linear. In other words, the risk is always the same, as long as a person has the ICM. Dr. Flemming and colleagues evaluated this in a large group of people with ICM, and tried to discover if there were risk factors for bleeding.

THE STUDY At Mayo Clinic, between 1989 and 1999, Dr. Flemming and colleagues found 292 people who had ICM. Since the diagnosis of ICM depends on adequate imaging, all of these patients had confirmed diagnosis of ICM based on MRI. Dr. Flemming and colleagues performed a retrospective review, meaning that she and her colleagues looked back to charts and information that had already been collected. After finding people with ICM, they carefully monitored how they did over time. The average time for follow-up was about 7 years for these patients.

In order to best determine how often the ICM caused bleeding, Dr. Flemming and colleagues needed to set specific criteria. A definite bleed was a new event for which the MRI showed a new change. A probable bleed was one in which the patient experienced a problem, and had testing; however, the testing was done at an outside hospital, and the study doctors had only the reports (and not the actual studies) to review. An undocumented bleed was one in which the person with the ICM had a new neurologic problem, but never had an MRI to look again at the ICM. In this group 81% had several MRIs, over time, making it possible for Dr. Flemming and colleagues to see what kinds of changes occurred in the ICM.

THE PATIENTS Dr. Flemming and colleagues found 292 people who were diagnosed with ICM on MRI between 1989 and 1999 at the Mayo Clinic. A little fewer than half were men (47.3%). Their average age was 45.8 years (ranging from 3.5 to 88.9 years). A total of 182 of the 292 (62%) were symptomatic, meaning that they had a neurologic complaint like headache. It was the neurologic complaint that led up to the MRI and discovery of the ICM. For 95 of the 292 (33%), the diagnosis of the ICM was incidental, meaning that the ICM was not related to the person's complaints. In the last 5% (15 patients), a relationship between the ICM and their complaints was not clear.

In the overall group (both symptomatic and asymptomatic), 32 (16%) had bleeding due to the ICM. A total of 20 were documented, 8 were probable, and 4 were undocumented. Of the patients who were symptomatic, 74 were found (on MRI) to have a recent bleed. Forty of these also had neurologic problems due to the ICM and the bleeding. Fifteen of these had seizures. Thirteen had headache only (without neurologic problems like weakness).

WHAT DOES THIS MEAN? First, we need to go back to what we used to think was the risk of bleeding from ICM: 0.7% to 4.2% per year. Dr. Flemming and colleagues found an overall rate of bleeding that was 16%. This number seems higher than what has been previously reported; however, it occurred over the course of the study. As Dr. Flemming and colleagues reviewed the results, she and her colleagues found that if the ICM was incidental, the risk of bleeding was very low. If the person had already had a hemorrhage, the risk of a second bleed was high. On average, the second bleed occurred about 8 months after the first one. Further, Dr. Flemming and colleagues showed that the risk decreases over time. This finding is different from many other studies, where the risk is described as linear. In other words, in the other studies, the risk is the same, and persists year after year, whereas Dr. Flemming and colleagues showed that the risk goes down year after year.

Dr. Flemming and colleagues also looked at risk factors for bleeding from an ICM. She found that previous bleeding, young age, being male, and having more than one ICM all increased the risk of bleeding. In people who had 2 or more ICMs, the risk of bleeding was 2 times higher. The number of ICMs did not determine the risk, just whether or not there were 2 or more.

Unfortunately, they did not identify a modifiable risk factor. If one was present, people with ICMs could take steps to prevent or at least minimize the risk factor. For instance, if smoking were a risk factor for bleeding, it might be possible to quit, and therefore reduce the risk of hemorrhage. However, this was not the case in this study.

Studies like this are very important to doctors and patients. Often, understanding the risk is important in making decisions about treatment. For instance, a person with a high risk may opt to have surgery. If there is a low risk, "watching" the ICM over time may be the best option. It is only with studies like this that doctors and patients can make the best informed decisions.

Section Editors
David C. Spencer, MD
Steven Karceski, MD

About cavernous hemangiomas

WHAT IS AN INTRACEREBRAL CAVERNOUS MALFORMATION? There are several terms that are applied to this kind of brain problem: intracerebral cavernous malformation, cavernous hemangioma, cavernous angioma, and cavernoma. The term applies to an abnormality of the capillaries. Capillaries are very small (microscopic) blood vessels. They have very thin walls, making it easy for oxygen to go from the bloodstream to the body's organs. Oxygen-rich blood flows to the capillary from the arteries. Blood, now oxygen-poor, is taken away from the capillaries by the veins.

Just like capillaries, cavernous hemangiomas have very thin walls. Just like capillaries, they lack the muscles and support structures that help to give arteries and veins their strength. It is their "weakness" that makes cavernous hemangiomas prone to bleeding. In the older medical literature, it was estimated that bleeding from a cavernous hemangioma occurred anywhere from 0.7% to as high as 2% per year. If an average of 1% is used as an example, if a person had a cavernous hemangioma for 10 years, the risk of bleeding would be 10 × 1% or 10%. In other words, each year a person lives with a cavernous hemangioma, the overall risk of bleeding goes up.

HOW ARE CAVERNOUS HEMANGIOMAS FOUND? In a sense, there are 2 kinds of cavernous hemangiomas: ones that cause problems or symptoms (called symptomatic) and ones that are silent (called asymptomatic). When a cavernous hemangioma causes problems, a person most often has headache, seizures, or may show signs of a stroke (like weakness or numbness on one side of the body). If symptoms occur, they are most likely to first show up in a person's 20s or 30s. In these instances, an MRI is the best test. It shows the cavernous hemangioma very clearly.

The second kind of cavernous hemangioma is asymptomatic. The hemangioma is not causing a neurologic problem. This kind is often discovered by accident. For instance, an MRI might be done to look at the sinuses in someone who has chronic sinus problems. The sinuses are in the bones of the skull. When an MRI of the skull is done, it will show the surrounding organs, including the brain. In short, even though the MRI was requested to look at the bones, it might show something nearby. In this case, the abnormality is unexpected, and is often called incidental.

WHAT CAUSES CAVERNOUS HEMANGIOMAS? For many years, cavernous hemangiomas were thought to be congenital. In other words, cavernous hemangiomas were considered as an error in the way that some of the capillaries formed, as the baby was developing and growing in the womb. Recent research has shown that many cavernous hemangiomas are genetic. Several genes are known to cause cavernous hemangiomas. The gene is transmitted in an autosomal dominant pattern, meaning that a person needs to inherit only one copy of the gene (from either parent) to be at risk for developing the problem. Other cavernous hemangiomas occur sporadically or without a clear genetic cause. In addition to this, research has shown that not all hemangiomas start at birth: some develop later in life.

WHAT KINDS OF TREATMENTS ARE AVAILABLE? The answer to this is in some ways simple: surgery. Surgery can be done to remove the cavernous hemangioma. By removing the abnormality, the risk of bleeding is also eliminated. Two types of surgery are possible. The first is "traditional" surgery, using scalpels and sutures. This kind of surgery is more common, and can address most kinds of cavernous hemangiomas. However, some hemangiomas cannot be operated on without risking more problems. In these instances, stereotactic radiosurgery may be considered.

Stereotactic radiosurgery is a minimally invasive type of surgery. It uses high-speed computers to target specific areas of the body or brain. Using the computers, many beams of high-energy radiation (gamma frequency is most often used) are focused on a single spot in the body. Each beam is too weak to have any effect. However, a large amount of energy is concentrated at the point where the beams "cross." In this way, without using scalpels or sutures, certain kinds of problems can be treated "surgically." The surgeon will use many factors to decide which type of surgery is best. A full evaluation by a person

trained in these techniques is needed to make these decisions.

FOR MORE INFORMATION

AAN Patients and Caregivers site: American Academy of Neurology
http://patients.aan.com
Angioma Alliance
http://www.angiomaalliance.org
National Organization for Rare Disorders
http://www.rarediseases.org

REFERENCE

1. Flemming KD, Link MJ, Christianson TJH, Brown RD Jr. Prospective hemorrhage risk of intracerebral cavernous malformations. Neurology 2012;78:632–636.