Cavernous Malformations: A Literature Review and Case Study

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Abstract

Cavernous Malformations occur in the central nervous system and can present with neurological and physical symptoms. These malformations can also be asymptomatic, which is why detection using imaging modalities including Magnetic Resonance Imaging, Computed Tomography, and Angiography should be utilized at the earliest onset of clinical symptoms. After identification and diagnosis, treatment options may be decided upon and can include surgery or conservative management of the malformation.
Cavernous Malformations

**Introduction**

Cavernous malformations (CMs) are classified as vascular malformations occurring in the cerebrum, brainstem, and cerebellum. These malformations are described as abnormally formed blood vessels in the brain or spinal cord. The brain is located in the cranium, which is hard and unforgiving of changes in intracranial pressure. When intracranial pressure increases, the space in the cranium remains the same. Any additional mass or fluid, such as blood during a hemorrhage, can compress the nerves in the brain that control voluntary and involuntary functions resulting in potentially life threatening neurological or physical symptoms. CMs can be found incidentally on radiographic images of the brain as well. CMs can be discovered and diagnosed using radiographic procedures including Magnetic Resonance Imaging (MRI), Computed Tomography (CT), and Angiography. Treatment options include surgery or conservative management of the malformation.

Numerous articles and reports have been written on CMs. Discovering and diagnosing these malformations leads to making the decision of treatment. A thorough understanding of these articles allows one to differentiate between CMs and other intracranial lesions. This will determine which, if any, treatment option to choose. Deciding which treatment option to proceed with is a life changing decision.

**Literature Review**

“Cavernous malformations (CM) has long been recognized as one of the major pathologic categories of vascular malformations of the nervous system” (McCormick, 1966, as cited in Aguiar et al., 2012, p.67). They affect “0.4 to 0.9% of the population…or 1,200,000 to 2,700,000 people…and account for 8 to 15% of all vascular malformations” (Bertalanffy et al., 1985, as cited in Aguiar et al., 2012, p. 68). CMs affect a large amount of people and they need
to be armed with the appropriate knowledge of how to recognize and manage these malformations.

Cerebral, brainstem, and cerebellar CMs are classified as either supratentorial or infratentorial, or above or below the tentorium cerebelli which separates the cerebrum and cerebellum. According to a review of CM location in 1055 patients, Gross, Lin, Du, and Day (2011) found that 76% of the lesions were supratentorial, 23% were infratentorial, and 1% were both. Supratentorial and infratentorial were subdivided even more so and out of 747 lesions, 66% were found in the cerebral hemispheres, 18% in the brainstem, 8% in the basal ganglia or thalamus, 6% in the cerebellum, and 2.5% in other locations.

Cerebral CMs (CCMs) are considered to be supratentorial and are a common vascular malformation. These malformations can present asymptptomatically, or without symptoms, and may be found incidentally on radiographic images of the brain. According to Salman (2012) “Cerebral cavernous malformations (CCMs) are common: their asymptomatic prevalence on brain magnetic resonance imaging (MRI) is 1 in 625” (p. 34). Symptoms of CCMs include seizures. Many researchers have linked this to a ring of hemosiderin, an irritant, deposited after a hemorrhage. Seizure(s) commonly afflict those diagnosed with a CCM but do not necessarily occur because of a CCM. Salman found that “for adults without prior intercerebral hemorrhage, CCMs were more frequently multiple in adults with epileptic seizure(s) (9/21, 43%) compared to those without epileptic seizure(s) (3/53, 6%)” (p.37). Seizure(s) have been thought to occur in the same location as the CCM. However, Salman found that there may not be an association between the location of the CCM and the occurrence of the seizure. Seizures are one of the presenting symptoms of a CCM and can affect all aspects of a person’s life. Seizures may be asymptomatic, so there is no way to tell when a seizure is going to happen. Salmon states that
“The risk of epileptic seizure(s) for people with CCMs affects their domestic, social, and professional lives, and may influence their decisions about treatment” (p. 34).

One of the most dangerous CMs is found in the brainstem. These CMs are considered infratentorial. The brainstem is the location of the brain that connects the cerebrum with the spinal cord. It includes the midbrain, medulla oblongata, and pons. These structures control many of the involuntary functions of the body, including but not limited to, heart rate, breathing, and temperature control. Hemorrhage from a CM in this part of the brain can lead to failure of vital functions and, if untreated, death.

Cerebellar CMs affect the cerebellum and are considered infratentorial. The cerebellum is considered the conduit of motion. Therefore, when experiencing a cerebellar CM, neurological symptoms may be present such as loss of coordination and fine motor control. Physical symptoms include serious physical inhibition and debilitation, such as paralysis. Recent research has shown that the cerebellum might play a role in other activities of the brain. Oderdick and Sillitoe (2011) state that the cerebellum is not only in control of movement, but it may play a role in cognition and emotion as well. Bellebaum and Daum (2007) agree and argue this point even further by stating that the cerebellum plays a critical role in executive processing and is strongly connected to the lateral prefrontal cortex (PFC), the area of the brain associated with executive control. Executive processes include, but are not limited to, “(i) Attention and inhibition,(ii) task management, (iii) planning, (iv) monitoring the contents of, and (v) coding representations in working memory (19)” (Smith and Jonides,1999, as cited in Bellebaum & Daum, 2007, pg.185). These studies have linked the cerebellum to processes other than motor control and this possibility must be considered before making the decision to operate.
**Imaging Modalities**

Imaging modalities used to identify and diagnose CMs include MRI, CT, and Angiography. These imaging modalities of the brain should be utilized as soon as possible after the presentation of symptoms suspicious of a hemorrhage. With the advent and improvement of MRI, knowledge of CMs has improved. This is a significant technological breakthrough as before the era of MRI, CMs were found during autopsy or surgery (Aguiar et al., 2012). CMs on a T2-weighted MRI have a popcorn ball-like appearance. When a CM hemorrhages it leaves a ring of hemosiderin. These depositions of degraded blood products appear as a halo around the lesion and show as a signal of hyperintensity on a T1-weighted MRI (Ginat & Meyers, 2012).

Salman, Berg, Morrison, and Awad (2008) argue that the appearance of a hemosiderin ring without a previous MRI or other evidence suggesting hemorrhage does not indicate hemorrhage of the CM. A follow up MRI would indicate if the CM has hemorrhaged since the previous MRI. Also, hemorrhaging of the CM may obscure the CM itself, which is another reason for the importance of a follow up MRI. MRIs are done with and without contrast. The contrast enhances blood flow to and from the lesion. If no enhancement is seen, the possibility of a tumor can be ruled out. A hemosiderin ring, previous MRIs, and pre and post contrast are all things the radiologist looks at when diagnosing or differentiating between a CM and other intracranial lesions.

CT is a technological advance that has aided in the identification and diagnosis of CMs. Salman et al., (2008) found that:

Evidence of acute blood can be easily and accurately identified on CT, which should be performed ideally within 1 week of the onset of a clinical event to reliably demonstrate high density consistent with recent hemorrhage although it may still be apparent for
several weeks. To be considered a recent hemorrhage, the high density on CT should be new, when compared to any previous CT imaging of the CM, and should have a Hounsfield value consistent with acute blood, or should resolve on CT imaging performed at least 2 weeks later (p. 3224).

CT is an important imaging modality for CMs and is best right after a hemorrhage has occurred. However, CMs can be asymptomatic or can be found incidentally on brain imaging studies. The CM may not be found in time for diagnostic CT information to be useful.

“Cerebral cavernous malformations are angiographically occult vascular malformations” (Lunsford et al., 2010, p. 23). Digital Subtraction Angiography (DSA) is used to aid in surgery but is not used for the actual diagnosis of a CM. According to Aguiar et al. (2012), “Digital subtraction angiography is unnecessary to establish a diagnosis of CM, but it is very important to show the venous drainage pattern when choosing an approach – subtemporal, interhemispheric or subtemporal” (p. 70). However, DSA is used to diagnose other vascular processes. According to Li et al., (2012) “DSA is still the most common method or “golden criterion” for diagnosing and treating vascular disease because it is a direct, dynamic, and low interference method for obtaining vessel imagery” (p. 116). Angiography is used in the process of diagnosing more menacing vascular malformations, such as aneurysms and arteriovenous malformations (AVMs). These malformations must be ruled out before making the diagnosis of a CM. An aneurysm is the bulging out of an artery that supplies blood to the brain. An AVM consists of an artery connected to a vein by a fistula. Aneurysms and AVMs are considered first priorities as these malformations can hemorrhage without symptoms and can result in brain damage or immediate death. AVMs can present with seizures (Salman, 2012), therefore it is important to differentiate between an AVM and a CCM, which also present with seizure(s). Once an aneurysm or AVM is
diagnosed they are clipped and removed surgically or if they are ruled out, a diagnosis of a CM may be made and follow up treatment can be decided.

**Treatment Options**

Treatment options include surgery or conservative management of the CM. There are many approaches to surgery and which approach to choose is up to the physician and the patient. Conservative management is available for those patients not wanting surgery. It entails numerous radiographs of the brain in order to watch the lesion and make sure it isn’t growing, hemorrhaging, or changing in any way. The age at onset of the hemorrhage, gender, location and accessibility of lesion, and repeat hemorrhage rate are a few of the factors one must consider before deciding on a treatment option.

Age at the onset of the first hemorrhage is a deciding factor in a lot of surgical cases. A 20-year-old may take the risk of having surgery performed on a CM instead of conservative management to avoid a repeat hemorrhage where as an initial hemorrhage occurring in the brain of an 80-year-old may warrant conservative management to avoid the risks associated with surgery. It is important to differentiate between an initial hemorrhage and the treatment option of surgery. According to a literature review by Gross, et al., (2011), age was considered in only one out of 31 studies as a risk factor for hemorrhage. Therefore, age is not a considering factor for the risk of hemorrhage but it is a major factor to consider when making the choice to have surgery.

Gender is a risk factor for hemorrhage and repeat hemorrhage and must be considered when making a treatment decision. According to Gross et al., (2011), “Three of 5 reviewed natural history studies reported female sex as a risk factor for hemorrhage” (p. 3). In agreement, a study by Aguiar et. al., (2012) states that females have a higher risk for hemorrhage than men.
Surgery of a CM needs to be considered by both genders, but females are shown to be at more of a risk for hemorrhage than men.

The location of the CM may indicate whether or not surgery is an option. For example CMs in the brainstem are of surgical importance as they can affect the voluntary and involuntary functions of the brain. This is supported by Gross, Dunn, Du, and Al-Mefty, (2012) who state that “brainstem CMs clearly follow a more aggressive clinical course, as subtle morphological changes of this brainstem lesion can have dramatic neurological consequences” (p. 1). If the CM is located in an accessible part of the brain, surgery is an option. However, the more difficult location decreases the option for surgery. According to Aguiar et al., (2012) “Brainstem cavernomas represent a formidable treatment challenge because of their location within a parenchyma that has critical neurological functions, rendering them much more difficult to remove than those in other locations” (p. 68). The location of the CM can determine the type of surgery to be done.

Repeat hemorrhage rate is also a factor in considering a treatment option. Brainstem CMs have an annual event rate of 10.6% (Porter et al., 1997, as cited in Gross et al., 2012, p. 1) and CCM annual hemorrhage rate is estimated at 0.1–2.5% per lesion-year and 0.25–16.5% per patient-year. Re-hemorrhage risk of a CCM increases with the number of previous hemorrhages. “Hemorrhage rate can exceed a 34% annual risk of bleeding once 2 bleed events have been confirmed through the detection of new neurological deficits and MR imaging evidence of new blood products” (Lunsford et al., 2010, p. 23). Possible repeat hemorrhage of the CM should be considered when deciding on a treatment option.

Case Report

The patient was a 26-year-old Caucasian female who presented with a loss of
coordination and weakness in the right hand. She also experienced slurred speech and disarticulation of words. These symptoms were present for an estimated 1 month before medical attention was sought.

A preliminary MRI was done with and without contrast. The pre-contrast MRI showed a lesion in the right cerebellar hemisphere. (See Figure 1) The post-contrast MRI showed that there was no enhancement of the lesion after administration of contrast. (See figure 2) Both MRIs showed that the lesion demonstrated changes consistent with blood of various ages. The appearance suggested a clot with surrounding edema. In the radiology report it stated the lesion could possibly be from trauma, rupture of a vascular malformation, drug abuse, hypertension, and a tumor (Radiologist, personal communication, November 2012). The patient ruled out trauma, drug abuse, and hypertension as possibilities of the lesion. A brain MR angiogram was performed and was normal. This was done to rule out the possibility of an aneurysm. (See Figure 3) Conservative management of the lesion was the chosen treatment of the patient at this time.

A follow up MRI was performed 30 days after the initial MRI. A pre-contrast MRI indicated that the lesion was smaller than the previous MRI. The lesion measured 1.6 x 1.9-cm. (See Figure 4) The edema had decreased as well and was of unappreciable importance. The patient consulted with the physician and made the decision to intervene surgically and remove the lesion.

Before surgery a stereotactic MRI was done with contrast. (See Figure 5) The radiologist stated that the lesion had a T1 and T2 hypo-intense rim consistent with a CM. All other anatomy appeared normal. The surgical outcome was successful and the lesion was removed. The patient reported improvement of neurological and physical symptoms and did not report any new symptoms.
Discussion

CMs can be potentially life threatening vascular malformations of the central nervous system. A large number of people are afflicted with these malformations and they must be armed with appropriate information to make an informed decision on treatment options. An important fact about CMs is that they can present with neurological and physical symptoms or they can be asymptomatic. CMs can be found in the cerebrum, brainstem, or cerebellum. CCMs are supratentorial and can, but not always, present with seizures. CMs found in the brainstem are infratentorial and can be potentially life threatening, as many of the body’s involuntary functions are controlled there. Cerebellar CMs are thought to present with more physical symptoms, such as loss of coordination and balance. These malformations can be identified and diagnosed through the use of MRI, CT, and Angiography. Once a CM is identified and diagnosed, treatment options of surgery or conservative management must be considered. Age at onset of hemorrhage, the location and accessibility of lesion, and the repeat hemorrhage rate are valuable factors to consider when deciding which treatment option to choose.
Figures

Figure 1. T2 pre-contrast axial MRI showing a lesion in the anterior medial aspect of the right cerebellar hemisphere. The lesion measures 2.1 x 2.0-cm. (Images used by permission of patient and facility)

Figure 2. T2 post-contrast axial MRI with no enhancement of the lesion. (Images used by permission of patient and facility)
Figure 3. Normal brain MR angiogram. (Images used by permission of patient and facility)

Figure 4. Flair axial MRI indicating a decrease in lesion size. (Images used by permission of patient and facility)
Figure 5. Stereotactic MRI with contrast. (Images used by permission of patient and facility)
References


