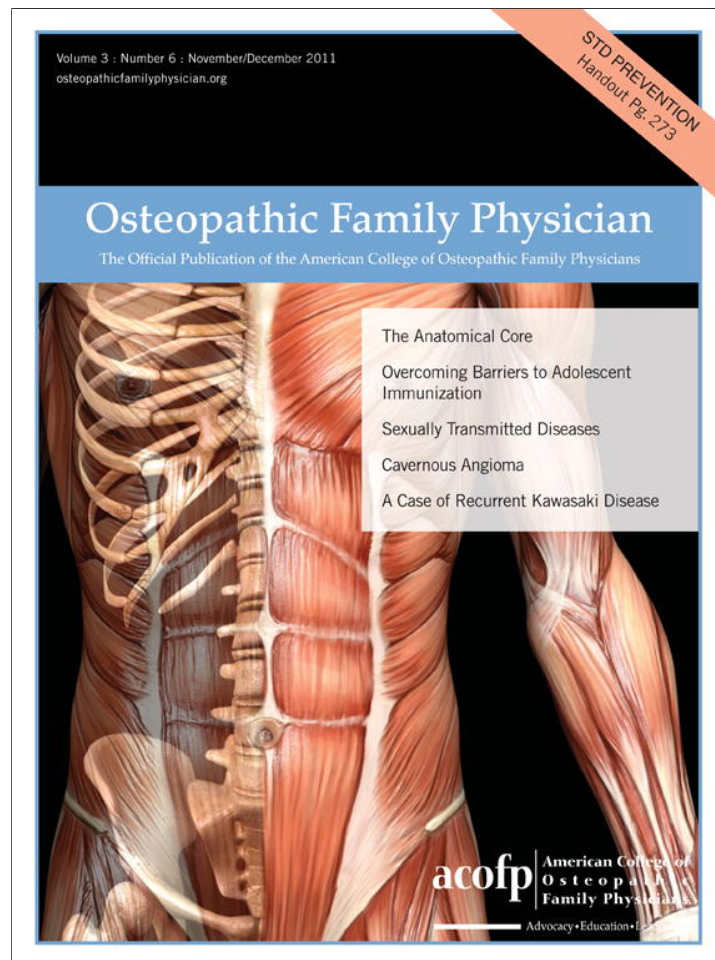


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Cavernous angioma: a literature review and case report

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Cavernous angioma is one of several vascular malformations whose presentation is usually seizures, headaches, or neurological deficits. The frequency of such malformations is controversial and appears to be more common than once thought because of the availability of magnetic resonance imaging (MRI). A 16-year-old presented to an emergency department with the complaint of headaches and oral numbness. She was found to have mild dysarthria and right-sided hemiparesis. Computed tomography (CT) scan of the head revealed a large hemorrhage present in the left posterior frontal region with two smaller lesions in the vertebral hemispheres. MRI later confirmed the lesions to be compatible with cavernous angioma. The mother also complained of having a long history of headaches with numbness in her hands but had a negative CT scan. This raises the question of familial pattern, which has been well documented in the literature. A review of the literature looking at etiology, differential diagnosis, and management options is included.

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Headache is a very common presentation to the family practitioner, nearly on a daily basis; most headaches that present are of a benign nature. This complaint in a 16-year-old with associated oral numbness and difficulty eating cereal should raise a red flag and prompt further work-up. Cavernous angiomas (CAs) are congenital vascular malformations composed of thin-walled neural or glial tissue and calcifications are commonly present. They are composed of a mass of sinusoidal-type vessels in opposition to one another. In general, there is no recognizable intervening neural parenchyma.¹ Cavernous malformations usually hemorrhage in episodes separated by months or years. It is vital for the primary care physician to be able to recognize, as well as diagnose, this disease and be well informed of its treatment plan. CAs are very rare, with reported incidence of only 1% of all intracranial lesions and 15% of all cerebral vascular malformations.² The actual incidence of cavernous malformations is often difficult to estimate because the lesions may be mixed with other varying forms of vascular malformations.

CA is frequently extra-cerebral, involving the retina, skin, liver, and pancreas.³ The most common presentation in affected patients includes seizures (38-51%), hemorrhage (11-32%), and focal neurological deficits (12-45%).⁴ CAs are congenital vascular malformations composed of thin-walled neural or glial tissue⁵ and calcifications are commonly present. The lesions are well circumscribed, often encapsulated, and may be associated with additional cutaneous and visceral malformation.¹⁻³ The risk of bleeding varies but is probably between 1 and 3%, with a possible increase in risk after the first hemorrhage and with deep or brainstem hemorrhages.⁶ Some cavernous malformations, although in small numbers, may present with significant hematoma and severe neurologic deficit. In this case report, a patient with hemiparesis and dysarthria was found to have a large hemorrhage of a CA.

Case report

A 16-year-old female presented to a family care provider complaining of numbness inside the right side of her mouth that had started the day before. She also complained of

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having a headache the night before that never went away. Recent history included an incident of passing out two days previously as she was on her way to the bathroom. At the time of her syncopal episode, she denied numbness or headache. At presentation, the headache was mainly over the left side of her head, and she denied having photophobia or blurred vision. However, she admitted to having numbness of her face on five other occasions. She also complained of the first three fingers on her right hand becoming numb, but otherwise denied numbness of her upper or lower extremities. The patient was scheduled for a magnetic resonance imaging (MRI) of the head and an electrocardiogram because of the presentation of stroke symptoms and palpitations by her primary care provider. Within 24 hours, the patient presented to the emergency department with similar symptoms. Her mother also stated that her daughter had problems eating that morning and her speech was slurred at times. Past medical history included headaches for one year but was otherwise negative. The patient did admit to occasional tobacco usage but otherwise denied alcohol or drug usage.

Family history included strokes and migraines. Examination revealed very mild right facial palsy and speech with a slurred quality to it. Facial sensation was intact externally, but the buccal mucosa sensation was decreased on the right side. Physical examination was otherwise negative. A computed tomography (CT) scan without contrast revealed a hemorrhage in the left posterior frontal region, with only minimal effect on the ventricle. There also appeared to be an additional lesion in the deep white matter of the left frontal region. Neurosurgery was consulted and the patient was admitted to intensive care for observation. Dexamethasone and phenytoin were prescribed for seizure prophylaxis. Cranial magnetic resonance imaging confirmed the diagnosis of CA with a total of 10 separate lesions. The large lesion had an area of previous hemorrhage within it, suggested by the hemosiderin ring. The patient remained stable and was later discharged home receiving phenytoin and dexamethasone.

Discussion

Cavernous malformations, which are vascular in nature, are located primarily in the central nervous system and can occur anywhere in the intracranial parenchyma.⁴ The malformations may also be found in the spinal cord or on the cranial or spinal nerve roots. Historically, the most CAs have been discovered only incidentally on post-mortem examination between the second and fifth decades of life when symptoms of seizures, headache, or neurological deficits are investigated.² Rarely are CAs documented in the first few years of life. CAs can be seen as an incidental finding on MRI studies. The MRI scans show the typical “popcorn-like” lesion, with a well-delineated complex reticulate core of mixed signal intensity representing hemorrhage in different stages of evolution.² Products of blood in

varying ages may be present throughout the lesion. MRI seems to offer the most sensitive means of diagnosing CA at this time, especially when they have an infratentorial localization.^{1-3,5} CT scans give 10% false-negative results.² Before MRI and CT scans, this disorder was most often misdiagnosed as a demyelinating process.

Recent literature suggests that CAs in the population are more benign than initially thought.² The estimated risk of hemorrhage has been calculated to be 0.25% per person-year of exposure by Del Curling et al. and 0.7% per lesion-year by Robinson et al.³ Occurrence of problematic symptoms results from the localization of the malformation in critical areas on a more frequent basis than from the malformation growth or intracerebral bleeding. It is quite common to find lesions consisting of both cavernous and venous malformations.⁷ Patients may present initially with symptoms including seizures, headaches, and neurological deficits. In a large series of patients who presented with CA, about one-third of the patients presented with seizures, one-third with hemorrhage, and one-third with some form of focal neurological symptoms,⁵ although few patients report having movement disorders associated with CA. All groups were found to have lesions that produced some symptoms. In one study there was a strong correlation between age and the number of lesions in patients with symptoms and in symptom-free relatives.⁴ The peak incidence of symptoms is generally in the third decade of life.³ Mexican-American patients account for an estimated 50% of reported cases.⁴ CA does not seem to be more common in males or females, although it has been found to be somewhat familial in nature. CA tends to appear in two forms—sporadic and familial. CA can be inherited as an autosomal dominant disorder known as familial cerebral cavernoma (FCC).^{4,8} It was found that in individuals with lesions who also developed symptoms (54% by age 50), the incidence is higher among FCC families than among patients with sporadic CA. Rigamonti et al. suggest that the familial form is much more prevalent than expected and is transmitted in an autosomal dominant fashion.⁸

It is important to study families with familial CA because they can provide insight that may eventually lead to the location of the abnormal gene responsible for this disease. In an ongoing study of the natural history of familial cavernous malformations, it was found that those with symptomatic cavernomas had a family history.⁶ At least one of the family members had seizures. In this study, it was evident that patients with familial cavernomas were more likely to develop new ones. Around 75% of patients who have multiple cavernous lesions and who present as sporadic cases in fact have a hereditary form of the disorder.⁴ It is difficult to determine whether surgery is warranted in patients with multiple lesions. It is felt that surgery should be reserved for the more significant hemorrhages, intractable seizures, or progressive deficits.

Only a few large families with CA have been reported. In the findings of Gil-Nagel et al., 47 members of four-generation non-Hispanic kindred were studied.³ Thirteen mem-

bers were affected. Of those 13 members, 85% had epilepsy, 38% had hearing loss, 23% had significant cerebral hemorrhages, one had dementia and progressive pseudobulbar palsy, one had compressive myelopathy, one had asymptomatic CA identified by MRI, and one had an adrenal angioma, found at autopsy.

The exact incidence of bleeding in CA remains uncertain. Two recent studies that monitored a large number of patients for a relatively short interval of time suggested that the annual risk of hemorrhage was 0.7% in one study and 0.25% per lesion per year in another study.¹ It was suggested in another study that the actual rehemorrhage rate is higher, about 2% per year.¹ The risk of bleeding is probably lower in small lesions without evidence of hemorrhage than in angiomas of large size or with previous hemorrhage.³

CA may affect crucial areas such as the speech cortex, the motor cortex, or the brainstem. It is important to make the final decision very carefully about whether to treat. It is important to weigh two determining factors—the patient's age and the number of years the patient has been at risk. The second factor is the exact location of the lesion in terms of potential risk for neurologic deficit with treatment. The intimate association between cavernous and venous malformations is important in predicting the outcome of a surgical excision.⁷

Management and follow-up

Therapy seems to remain controversial because of our incomplete understanding of the history of the disease. It is suggested that the use of valproic acid and other drugs interfering with coagulation be avoided in patients with this condition, because of the possibility of aggravating spontaneous bleeding of angiomas.³ Surgery is often considered when patients present with recurrent hemorrhage and progressive neurologic deterioration.¹ It seems that for adults with epilepsy, the best management is probably a trial of anticonvulsants, with surgery only reserved for those with intractable seizures.⁶ The exact location of the lesion is of the utmost consideration, in addition to its surgical accessibility. A woman with accessible lesions and one who is contemplating pregnancy may also consider surgery as a current acceptable therapy.³ Surgery offers an option in terms of complete excision of the lesion with stabilization of symptoms. Prophylactic surgery is generally not performed on patients with multiple lesions. The best management of these lesions is a periodic MRI that is usually performed once a year.⁶

Stereotactic radiosurgery has been used commonly on patients with CA that otherwise were thought to be inoperable. These patients who have undergone radiosurgery present with progressive worsening of neurologic symptoms. It was difficult to determine whether these patients actually benefited from stereotactic radiosurgery until they had been followed for longer intervals of time. The results from a

large study involving a highly selected group of patients receiving stereotactic radiosurgery for cavernous malformations were quite impressive. The patients were highly susceptible to hemorrhage. The proportion of patients with recurrent hemorrhage is (44/47) before treatment and (6/47) after treatment.⁶ Not all studies depict these encouraging results. The authors openly stated that the patients chosen were highly selected.

All patients that may have lesions in more critical areas in the brain and brainstem are more likely to have complications with treatment. The rate of these complications must always be carefully considered because of balanced-age and comorbidities, etc. In general, hemorrhage from cavernomas is much less devastating than from aneurysms or arterial venous malformations. A fatal outcome is very uncommon, but severe deficits can certainly follow a hemorrhage, especially one from a deep lesion.

The patient described in the case report was diagnosed very early in her disease process and did very well with supportive treatment. Headache is a common presentation to both the emergency department and the family physician's office. This case is an example of why there should be an extensive workup when neurological symptoms are also present. This patient's symptoms were very mild and atypical for the presentation of CA. There were no articles that the author reviewed that described patients with "numbness inside their mouth". Another interesting finding in this case was that the mother had a long history of severe headaches and numbness in the arms. This presents a question of whether there is familial pattern. The mother had a CT scan of her head, which was done through the emergency department, which precluded the use of MRI because of time factors within the department. The CT scan was found to be normal, but there is a very low sensitivity for CA with CT scan. An MRI is the preferential diagnostic test.

There remain many uncertainties about CA, with its true etiology lacking. Diagnosis is now made possible through the use of MRI. Because management of CA is still questionable, surgery is only indicated in a select group of circumstances. At this time, prophylactic removal of the lesion is generally not recommended. Brainstem cavernomas require surgery after one significant hemorrhage, if it is accessible.⁶ On the horizon, there will possibly be new techniques that could remove this potentially lethal lesion. Conservative management continues to be the most acceptable way to manage these lesions.

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