

Cavernous Malformations: A Review and Current Controversies

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Abstract: Cavernous malformations, also known as cavernous angiomas, are a specific type of cerebrovascular anomaly. Cavernous malformations have characteristic pathologic, radiographic, and genetic characteristics. Conservative management, radiation therapy, and surgical resection have been employed in the management of these lesions. In this review, we will discuss various aspects of cavernous malformations. We will present the pathology of the lesion and the differences between normal microvascular architecture and that found in cavernous malformations. We will present the epidemiology, clinical presentation, and natural history of intracranial and spinal cavernous malformations. Radiologic characteristics and the genetic and molecular causes of these lesions will be reviewed. Current treatment strategies will be discussed and controversies will be addressed.

Key Words: cavernous, malformation, vascular, angioma

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CAVERNOUS MALFORMATIONS

Numerous anomalies are known to affect the vasculature of the central nervous system (CNS). These cerebrovascular anomalies include arteriovenous malformations (AVMs), venous malformations or developmental venous anomalies (DVAs), capillary telangiectasias, and cavernous malformations.¹ Although these vascular malformations are all thought to be developmental anomalies, each is unique and possesses distinct clinical, radiographic, pathologic, and genetic characteristics.

Cavernous malformations, also known as cavernous angiomas or cavernomas, are a specific type of cerebrovascular anomaly. Clinically, their natural history is complex.^{2–6} These lesions may be clinically silent or present with specific neurologic signs and symptoms. Cavernous malformations can present throughout the entire neuraxis and their clinical evolution is not entirely predictable. Radiographically, they display complex but distinct magnetic resonance imaging (MRI) characteris-

tics.^{7,8} Pathologic studies have shown that cavernous malformations are composed of an aberrant ultrastructure.⁹ Genetic and molecular analyses have identified mutations in 3 genes (CCM1, CCM2, and CCM3) that give rise to cavernous malformations in some affected families.^{10–14}

Over the past 20 years cavernous malformations have been the subject of numerous research studies that have sought to determine the natural history of the lesions. These studies have permitted a more accurate description of the imaging properties of cavernous malformations, pathology of the lesions, and molecular causes of this cerebrovascular malformation.

PATHOLOGY

Cavernous malformations that are located in the CNS have a stereotypical lobulated, “mulberry” appearance when examined macroscopically.¹⁵ These lesions have characteristic pathologic, histologic, and ultrastructural features that create this mulberry appearance. They consist of sinusoidal vascular channels that are dilated and contiguous.^{16–18} The walls of these vascular channels are fragile, lined only by vascular endothelium. Neither smooth muscle nor elastic fibers are present in these thin vessel walls. Brain parenchyma is not located between the vessel walls within a lesion. Generally, normal brain tissue is only localized at the periphery of the lesion.

Certain histologic features are associated with cavernous malformations.¹⁹ These features include evidence of recent and recurrent hemorrhage and intraluminal thrombosis of the vascular channels. Signs of thrombus recanalization can be observed. Calcifications are frequent histologic findings. Signs of ossification or inflammatory change are less common. Hemosiderin-stained white matter adjacent to cavernous malformations is uniformly observed around these lesions, although in varying degrees.

Electron microscopy and immunohistochemistry studies of cavernous malformations have identified specific differences between the architecture of normal cerebral blood vessels and those in cavernous malformations.^{9,20} In contrast to normal cerebral blood vessels, astrocytic processes or pericytes do not surround the vascular channels of these lesions.⁹ Instead, the sinusoidal vascular channels are composed entirely of endothelium and a basal lamina embedded in a dense collagenous matrix. Additionally, the tight junctions between the

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endothelial cells are perturbed, leaving significant gaps between the endothelial cells.²⁰

Normal cerebral blood vessels have a highly regulated blood-brain barrier that prevents undesirable contact between intraluminal blood components and extraluminal parenchymal substrate.^{21,22} It has been postulated that the absence of adequate support parenchyma for endothelial cells and the absence of tight junctions between the endothelial cells create a dysfunctional blood-brain barrier in cavernous malformations.⁹ This dysfunctional blood-brain barrier gives rise to several histologic features of cavernous malformations. This inadequate barrier likely permits chronic extravasation of red blood cells through penetrable gaps between endothelial cells and results in microscopic hemosiderin deposition in brain parenchyma around the lesion. In addition, this incompetent blood-brain barrier may allow extraluminal parenchymal factors that enhance blood coagulation to contact intraluminal blood components and promote intraluminal thrombosis.

CLINICAL PRESENTATION

Cerebrovascular malformations including arteriovenous malformations, cavernous malformations, venous angiomas, and capillary telangiectasias have been observed in autopsy studies in up to 4% of the population.²³ Most of these lesions are indolent. The majority are generally asymptomatic, discovered only at autopsy or incidentally during radiologic evaluation. Only a fraction of cerebrovascular malformations comes to clinical attention.

Cavernous malformations are present in approximately 0.4% to 0.8% of the general population according to autopsy or MRI studies.^{2,24-26} These lesions comprise approximately 10% to 15% of all cerebrovascular malformations. They are the second most frequent vascular malformation after DVAs, and are approximately as frequent as AVMs. It is thought that cavernous malformations become symptomatic more frequently than either DVAs or capillary telangiectasias.

Because cavernous malformations are usually angiographically occult, it was not until the introduction of MRI that these lesions could be readily detected and diagnosed.

Thus, most of our current understanding regarding the clinical presentation and natural history of cavernous malformations comes from case series published over the last 20 years.²⁻⁶ In general, these studies are retrospective studies, prospective-observational studies, or a combination of these two types of studies. It should be noted that these studies are not population-based studies but instead rely upon patients referred to tertiary neurosurgical centers. Interpretations of these studies should take into account referral biases that may potentially exist.

Patients may present with initial signs and symptoms of cavernous malformations over a wide range of ages. Patients less than 1-year-old have suffered clinical symptoms secondary to these lesions.² The initial clinical

presentation of symptomatic cavernous malformations has been documented in patients over 80 years old.² Generally, patients first present with symptoms between the ages of 20 and 50 years.²⁻⁶ The mean age of all patients at initial presentation is approximately 35 years.

Both male and female subjects may present with cavernous malformations. In most studies, both sexes are equally represented.^{2,4} In one study, however, female subjects were more frequently observed to possess symptomatic cavernous malformations than male subjects.⁵ Because these are not population-based studies, definitive answers are not available. A reasonable interpretation of the data is that there does not seem to be any difference in the proportion of male and female subjects presenting with the disease.

Cavernous malformations come to medical attention after patients experience any number of clinical symptoms. Symptomatic lesions present with signs and symptoms that can generally be referred to their location. Asymptomatic lesions also come to medical attention. Although the majority of cavernous malformations come to medical attention because they are symptomatic, up to 20% are discovered incidentally.²⁻⁵

Cavernous malformations have been observed throughout the CNS.^{2-5,27-29} They occur intracranially, as either intraaxial or extraaxial lesions. Intraaxial lesions are more common and are either supratentorial or infratentorial.²⁻⁵ Supratentorial lesions have been observed in cortical areas, including the frontal, temporal, parietal, and occipital lobes, as well as the insular cortex (Fig. 1). Lesions have been described in the corpus callosum, thalamus, and basal ganglia. Infratentorial lesions have been discovered in both the brainstem and cerebellum (Fig. 2). Approximately 65% to 80% of cavernous malformations that come to medical attention are supratentorial and 20% to 35% are infratentorial.

Most studies have shown that patients with symptomatic cerebral cavernous malformations present with headaches, seizures, focal neurologic deficit, or intracranial hemorrhage.²⁻⁵ Many patients will present with more than one sign or symptom. Headaches have been reported in 6% to 65% of patients when they first come to medical attention. Seizures have been reported as an initial symptom in 23% to 52% of patients. Focal neurologic deficits are observed in 20% to 45% of affected individuals. Intracerebral hemorrhage generally occurs in 13% to 25% of patients presenting with cavernous malformations, although some series have documented hemorrhage in 50% to 60% of patients.³⁰

A correlation between lesion location and presenting symptoms has been observed.²⁻⁵ Patients with lesions located superficially in the cerebral hemispheres more frequently present with seizures. In comparison, patients with lesions located in deep structures such as the brainstem generally present with focal neurologic deficits.

Cavernous malformations may occur in the spinal cord and vertebrae.²⁷⁻³² Spinal cavernous malformations occur in the vertebral body, as extradural, as intradural-extradural, or intradural-intradural masses.²⁷⁻²⁹

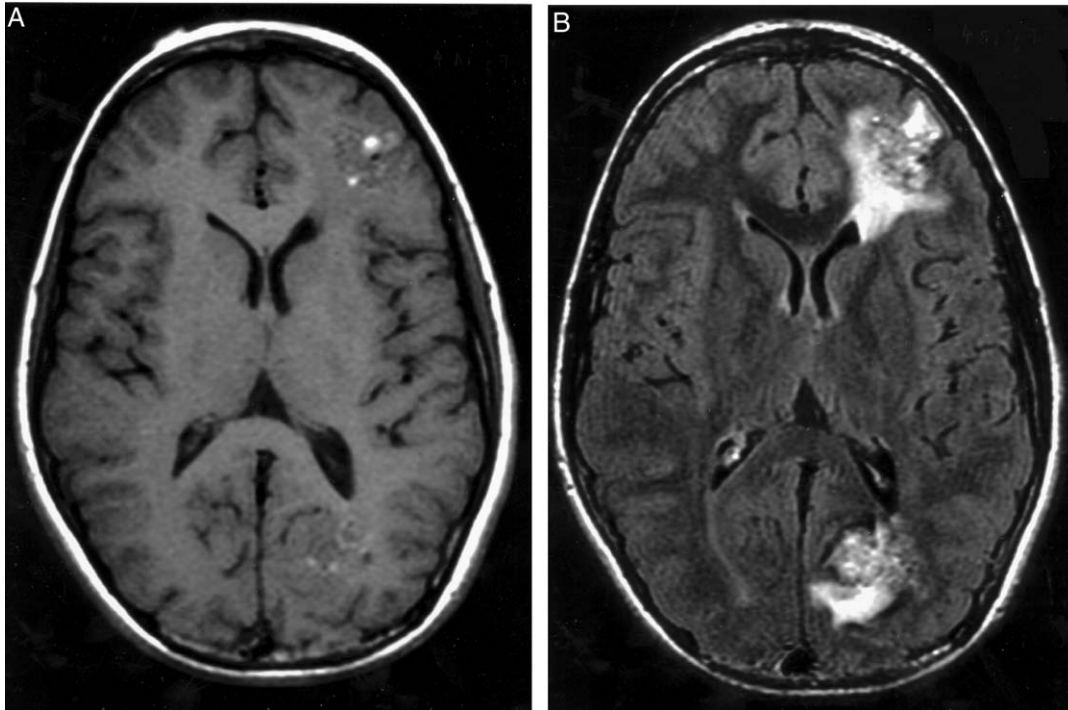


FIGURE 1. A, T1-weighted axial MRI. Complex isointense and hyperintense signal is observed in both a left frontal and left occipital lesion found in a 13-year-old male who presented with seizures. Investigation revealed 4 supratentorial lesions: 1 in the left frontal lobe (shown), 1 in the left occipital lobe (shown) and 2 lesions in deep white matter tracts (not shown). Because the patient's seizures were intractable to medical therapy the patient underwent successful surgical resection of the lesions. These hypointense and hyperintense lesions are most consistent with type 2 lesions. (Radiology section.) B, Flair image, axial MRI. Isointense to hyperintense signal is identified in the 2 supratentorial lesions. Associated edema is observed surrounding the left frontal lesion.

The cervical, thoracic, and lumbar areas of the spinal cord may be affected. Spinal cord cavernous malformations are less frequently observed than intracranial lesions. Both sexes may be affected. Patients with these vascular anomalies commonly present between the ages of 30 and 40 years.²⁷⁻²⁹

Similar to intracerebral cavernous malformations, patients with spinal cord cavernous malformations present with myriad signs and symptoms of their lesion. Vertebral body lesions cause pain, paraparesis, or bowel and bladder dysfunction. Cavernous malformations of the spinal cord can cause paraparesis, radiculopathy, paresthesias, and myelopathy. Patients with spinal cavernous malformations may present with either slowly progressive symptoms or a rapid, acute onset of symptoms.

Unusual presentations of cavernous malformations have been seen. Extradural cavernous malformations of the middle fossa, specifically the cavernous sinus, have been reported.^{33,34} Patients with these lesions presented with symptoms referable to the location of the lesion in the cavernous sinus and included visual acuity deficits, visual field deficits, and extraocular muscle palsies. Cavernous malformations around the pineal gland have been detected after patients presented with headache,

nausea, vomiting, and Parinaud's sign.^{35,36} Patients with intracerebral cavernous malformations have presented with signs and symptoms of superficial siderosis including progressive sensorineural hearing loss, ataxia, and myelopathy.³⁷

Patients may be affected with either solitary or multiple cavernous malformations. Approximately 20% to 30% of patients will harbor more than one cavernous malformation at presentation.²⁻⁵ When patients do possess multiple lesions, generally 3 to 4 lesions are discovered in the neuraxis. These lesions are located throughout the CNS, both intracranially and in the spinal cord. Both sexes can have multiple lesions. Patients with a family history of cavernous malformations are more likely to present with multiple lesions.⁵ Interestingly, an observation has been made that patients with intramedullary spinal cord cavernous malformations may have an increased risk of harboring multiple lesions compared with other patients.²⁹

NATURAL HISTORY

Cavernous malformations are clinically dynamic lesions. After initial presentation, cavernous malformations have been observed to cause new neurologic events.

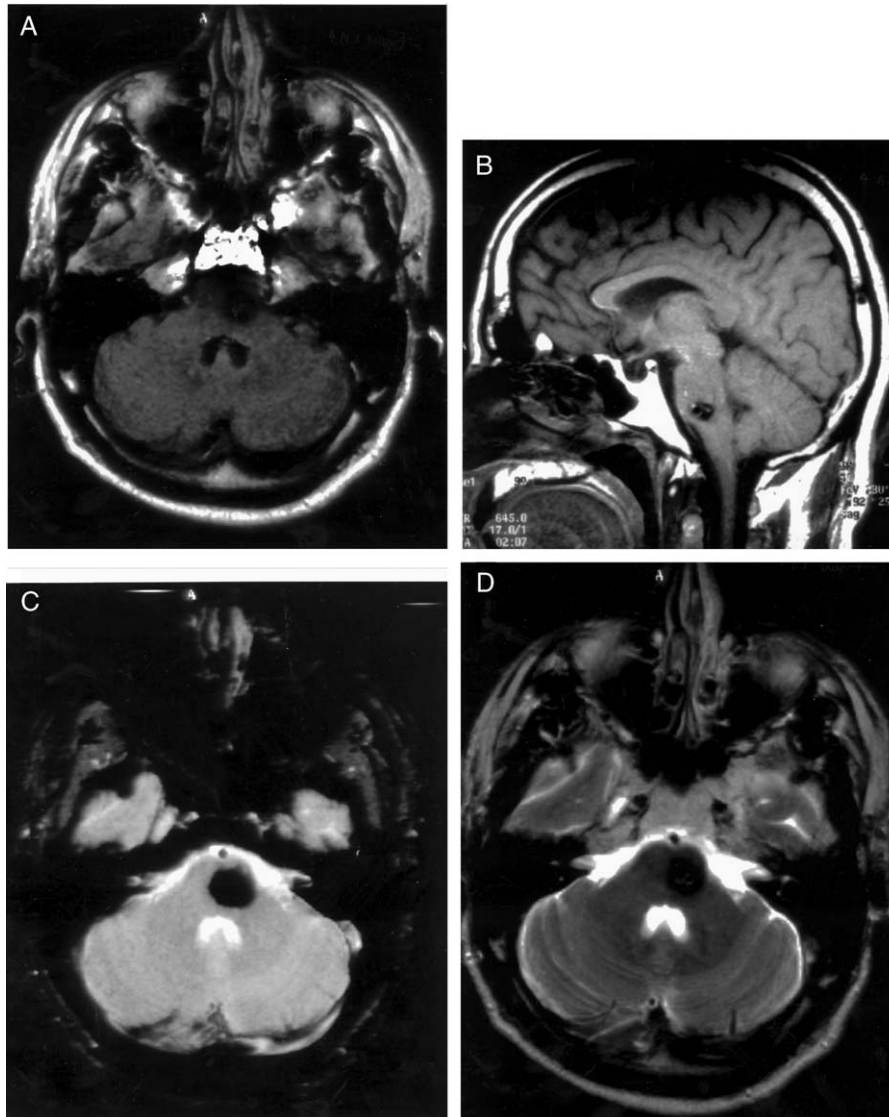


FIGURE 2. A, T1-weighted axial MRI. Hypointense signal is observed in a lesion in the left pons. This 42-year-old man presented 15 months before this scan with headache and diplopia. The hypointense signal observed in multiple imaging sequences is indicative of the presence of a chronic lesion with resolving hemorrhage and hemosiderin staining both in and around the lesion. (Radiology section, type 3 lesions.) B, Sagittal T1 weighted MRI demonstrates hypointense signal present in a lesion in the pons. C, Axial T2-weighted MRI demonstrates hypointense signal present in a lesion in the pons. D, Axial hemosiderin-sensitive gradient echo MRI demonstrates hypointense signal present in a lesion in the pons.

New clinically appreciable events that have been observed include additional seizures, new onset seizures, worsening focal deficits, and extralesional hemorrhages. Numerous studies have analyzed cohorts of patients with cavernous malformations to determine the rate at which these lesions cause new symptoms.²⁻⁵ These studies have also attempted to identify potential risk factors associated with symptomatic lesions.

Hemorrhage is a frequent cause of clinical deterioration in patients with cavernous malformations. A wide range of hemorrhage rates has been reported in these

patients. Annual rates of hemorrhage between 0.25% and 13% per patient-year have been observed.^{2,8,3,4,5,26} Studies reporting on prospective rates of hemorrhage observe a rate of hemorrhage between 2.6% and 6.5% per year.²⁻⁵

Seizures are a frequent symptom observed at initial presentation in patients with cavernous malformations. Seizure recurrence has been documented as a significant cause of morbidity in these patients. New onset seizures also occur in patients who were initially seizure free. In a recent study, the prospective seizure risk was

approximately 5% per patient-year.⁵ In this same study, the risk of new onset seizure was 2.5% per patient-year.⁵ Approximately 5% to 10% of patients who were initially seizure free experienced a seizure at some point during the study.

Risk factors associated with symptomatic cavernous malformations have been investigated. One report has identified an infratentorial location of the cavernous malformation as being associated with an increased risk of hemorrhage or new focal neurologic deficit.⁴ Two studies have observed that female patients were more likely to experience a second hemorrhage than male patients.^{2,5} Patients with familial forms of the disease have been observed to experience an increased risk of clinically significant hemorrhage.⁸ This is most likely related to the fact that patients with familial disease generally possess multiple lesions, however, and not that there exists an increased risk of hemorrhage per lesion in these patients.

RADIOLOGY

Numerous imaging modalities have been used to analyze cavernous malformations including angiography, computed tomography (CT), and MRI. In these studies, in particular MRI studies, distinct radiographic characteristics of cavernous malformations have been discovered. These have allowed clinicians and investigators to identify the lesions in the CNS and have enabled them to distinguish cavernous malformations from other cerebrovascular abnormalities.

Historically, neither CT nor angiography has been successful in identifying cavernous malformations. CT scanning has a sensitivity of detecting the cavernous malformation in approximately 70% of cases.⁷ With CT scanning, the lesion, when observed, is generally hyperdense on the precontrast study, rarely enhances with contrast and may suggest a mass lesion due to displacement of the surrounding blood vessels.

Cerebral angiography has a sensitivity of detecting some type of imaging abnormality in approximately 60% of cases.⁷ This abnormality may include a small capillary vascular blush or venous pooling. Cerebral angiography may disclose avascular regions. Cerebral angiography may suggest a mass lesion if displacement of surrounding blood vessels is noted.

MRI has been shown to be the most effective imaging modality for cavernous malformations of the CNS.^{7,8} On the basis of radiologic findings that have been correlated with pathologic investigations, an MRI classification system for cavernous malformations has been developed.⁸ This classification systems categorizes cavernous malformations into 1 of 4 distinct types of lesion based upon their MRI appearance and correlated pathologic findings.

The first type of lesion (type 1) described in the classification system is the cavernous malformation in which subacute hemorrhage has occurred. This lesion is surrounded by hemosiderin and gliotic brain. On T₁

weighted (T₁) MRI, it has a hyperintense core and on T₂ weighted (T₂) MRI it has a hyperintense or hypointense core surrounded by a hypointense rim. Pathologically, type 2 lesions have loculated areas of hemorrhage, thrombosed vessels, hemosiderin-stained brain, and areas of calcification. On T₁ imaging, these lesions have a reticulated core of hypointense and hyperintense signals. On T₂ imaging, the core of the lesion is both hypointense and hyperintense and surrounded by a hypointense ring. Type 3 lesions are chronic lesions with resolving hemorrhage and hemosiderin staining both in and around the lesions. T₁ imaging identifies the lesion as possessing hypointense or isointense signals. T₂ images reveal a hypointense lesion with a hypointense rim. In gradient echo MRI imaging, the type 3 lesion is hypointense. Type 4 lesions may be very small cavernous malformations or may actually be capillary telangiectasias. These lesions are poorly visualized by T₁ or T₂ imaging. Gradient echo imaging reveals them to be small punctate hypointense lesions.

In addition to being clinical dynamic lesions, cavernous malformations have been observed to be radiographically dynamic lesions as well.⁸ In patients with documented familial forms of the disease, new lesions have been observed to appear in approximately 30% of patients over a mean follow-up period of 2 years. During this follow-up period, cavernous malformations have been observed to undergo significant changes in signal characteristics (10% of patients) and size (4% of patients). The appearance of new lesions, change in lesion volume and change in signal characteristics has been documented in sporadic forms of the disease also.

GENETICS AND MOLECULAR BIOLOGY

Over the last 20 years, significant advancements have been made towards understanding the molecular causes of cavernous malformations. It has been recognized for numerous years that these lesions could occur sporadically or as an inherited trait in particular families.³⁸⁻⁴⁰ In 1988, it was shown that the disease could be transmitted as an autosomal dominant trait in some Hispanic American families.⁴¹ One genetic locus (CCM1) potentially responsible for familial cavernous malformations was subsequently mapped to chromosome 7q and the mutated gene identified.^{11,42-44} Genetic heterogeneity of the disease had been observed, however. Additional loci implicated in certain familial manifestations of the disease were then mapped to chromosomes 7p13-15 (CCM2) and 3q25-27 (CCM3).^{10,45} The genes mutated in families linked to CCM2 and CCM3 were recently identified.^{12-14,46}

In 1999, the CCM1 gene located on chromosome 7q was identified as Krev interaction trapped gene 1 (KRIT1).^{11,47-49} KRIT1 was originally identified through its interaction with the Ras family GTPase, krev1/rap1, in a yeast 2hybrid screen.⁵⁰ Several groups later identified additional 5' coding exons in the KRIT1 gene.^{51,52} The full-length protein is now thought to be encoded by 16

exons and to comprise 736 amino acids. Frame-shift mutations, nonsense mutations, missense mutations, mutations in invariant splice junctions, and deletion mutations have all been implicated as causes of familial forms of the disease.

Initially it was thought that the protein product of KRIT1, *krit1* was involved in GTPase signal transduction cascades and that it functioned as a tumor suppressor.⁵⁰ It was interesting to note that experiments involving the full-length *krit1* failed to reveal any interaction between *krit1* and *krev1/rap1*, however.^{53,54} Instead, it was discovered that the full-length protein showed a strong interaction with integrin cytoplasmic domain-associated protein 1 (*icap1 α*), a protein thought to associate with the cytoplasmic tail of $\beta 1$ integrin. Apparently, the new codons in the 5' end of KRIT1 encode a NPXY motif that allows *krit1* to interact with *icap1 α* .

The interactions between *krit1* and *icap1 α* were further investigated in a series of reports.⁵³⁻⁵⁵ Additional experiments revealed that induced expression of *krit1* limited the ability of *icap1 α* to interact with $\beta 1$ integrin. It has been postulated that truncating mutations of *krit1* found in families affected by cavernous malformations could limit the ability of *krit1* to interact with *icap1 α* . This would permit *icap1 α* to more effectively associate with $\beta 1$ integrin, alter $\beta 1$ integrin-mediated angiogenesis, and initiate the formation of cavernous malformations.

The gene accounting for familial forms of the disease that are linked to the CCM2 locus has recently been identified as *MGC4607*.^{12,46} Nonsense, frameshift, missense, and splice site mutations have been observed in this gene.^{12,13,46} The protein product from this gene has been named "malcavernin".¹² Malcavernin also contains a phosphotyrosine-binding domain that is thought to mediate interaction with *krit1* and create a membrane-associated complex.⁵⁶ Experiments have been performed that link this complex to the p38 mitogen-activated protein kinase signaling cascade.⁵⁶ It has therefore been postulated that dysregulation of mitogen-activated protein kinase signaling cascade may be implicated in cavernous malformation development.⁵⁶

The gene mutated in CCM3 has been identified as programmed cell death 10 gene or TF-1 cell apoptosis-related protein (*TFAR15*).^{14,57} Deletion, nonsense, and splicing mutations were detected in 8 families with the disease.¹⁴ Per report, the transcripts from this gene were first identified after being induced by apoptotic stimulation of the TF-1 premyloid cell line.^{14,57} The role programmed cell death 10 gene plays in initiating cavernous malformations is currently unknown.

CLINICAL MANAGEMENT

In general, except in the exceedingly rare situation in which a patient presents in poor clinical condition, the clinician has the opportunity to apply a logical, progressive approach to diagnosis and treatment of these lesions. All patients with cavernous malformations should under-

go an extensive and thorough clinical and radiologic workup. At presentation, all patients should have their entire neuraxis evaluated by MRI. Both brain and spine MRI are required to identify additional asymptomatic cerebral and spinal lesions. The purpose of this workup is to document a baseline neurologic and radiologic examination. This permits a more accurate determination of additional clinical or radiologic events that may occur.

The possibility that a patient presenting with cavernous malformations has a family history should be investigated, especially if multiplicity of lesions is confirmed. This screening is important because the natural history of familial forms of the disease may be more aggressive than sporadic disease. If a familial form of the disease is suspected, it suggests that additional members of the patient's family should undergo clinical and radiologic examination to determine whether they are affected.

Treatment options for cavernous malformations include conservative management, medical management of symptoms associated with the lesion such as seizures, surgical resection or stereotactic radiation. Guidelines exist for guiding the therapy of a patient with cavernous malformations. Each patient who presents with the condition is unique, however. The therapies proposed to a patient must take this into account and should be specifically designed and tailored for each individual.

Patients presenting with incidental lesions should be managed conservatively. In fact, only a subset of patients presenting with asymptomatic lesions will eventually experience symptoms associated with their lesion. Surgery and stereotactic radiation are not indicated for these patients and should be deferred. These patients should be followed with intermittent examinations and MRI imaging to document any changes in the lesion or the development of additional lesions.

The majority of patients with cavernomas that are initially symptomatic present with seizures and do not experience a clinical significant hemorrhage or a progressive neurologic deficit. These patients are usually managed conservatively with intermittent clinical and imaging surveillance at yearly intervals, unless special situations arise. Medical management of seizures is strongly recommended and is best carried out with the help of a neurologist familiar with current anticonvulsant therapeutic strategies.

The indications for surgical resection or stereotactic radiation have recently changed. Previously, there was only consensus favoring the resection of readily accessible, supratentorial cavernomas that were symptomatic. Presently, however, there is a more proactive approach regarding the management of patients in view of the cumulative risk of hemorrhage and onset of new seizures. This proactive approach applies to both supratentorial and brainstem lesions and involves surgical or stereotactic radiation therapies.

In patients with epilepsy that is refractory to medical therapy or lesions that have caused additional

morbidity secondary to additional hemorrhage, surgical resection or stereotactic radiation should be considered. In patients with epilepsy refractory to medical management, surgical resection of the cortical or subcortical lesions should be considered. Successful surgical cure of seizure activity can be obtained if the lesion is in the cerebral hemispheres in an area that correlates with electroencephalographic data that localizes seizure origin or seizure activity to the same area. Surgical resection of cavernous malformations may even be attempted if the lesion is in the eloquent cortex where resection could risk morbidity to the patient if the lesion is causing substantial morbidity due to intractable seizure activity. Regarding the management of young patients with recent onset seizures, based on evidence in the literature, we believe that surgery is a reasonable treatment option if the seizures are associated with a single lesion considered to be the epileptic focus.⁵⁸

Lesions in the diencephalon or brainstem are usually associated with focal neurologic deficits. These lesions present a higher risk of neurologic deficit when symptomatic hemorrhage occurs. In patients with cavernous malformations located in the brainstem, additional brainstem hemorrhages may be catastrophic. Treatment options for these lesions are more problematic, however. There exists no medical therapy for these lesions and surgical resection is inherently more dangerous secondary to their deep location. Although successful surgical resection of cavernomas located in the diencephalon or brainstem has been reported, controversy still exists about the choice of surgical resection versus stereotactic radiosurgery in the management of these lesions.⁵⁹⁻⁶⁴ In general, surgery may be attempted if the lesion is a high-risk lesion that has already demonstrated a propensity to rebleed and approaches a pial surface.⁶⁴

The role of stereotactic radiation in the treatment of symptomatic cavernous malformations is more controversial and is evolving.⁶⁵⁻⁷³ Originally, radiation therapy was associated with substantial morbidity secondary to radiation-induced edema.⁶⁵ Current protocols utilizing lower doses of radiation and more exact targeting of the radiation are now being employed. These protocols have shown reasonably good outcomes for lesions that were thought to be surgically unresectable, high-risk lesions.^{68,72-74} These lesions had already rebled but were considered surgically unresectable secondary to their location. In these lesions, stereotactic radiation was thought to considerably reduce the risk of rebleeding, especially 2 years after therapy. Stereotactic radiation has also been employed to treat symptomatic cortical cavernous malformations that were initiating seizures.^{67,72} These lesions were deemed surgically unresectable, generally due to their location in the eloquent cortex. Stereotactic radiation reduced the incidence of seizure in approximately 50% of patients with minimal side effects. In general, however, we believe that because of underlying genetic defects, radiosurgery should be avoided in familial cases.

CONCLUSIONS

Cavernous malformations are a type of cerebrovascular abnormality. These lesions are distinct from cerebral aneurysms, AVMs, venous malformations, and capillary telangiectasias. They may present incidentally or because of specific signs or symptoms referable to the lesion. These lesions have a unique pathology, clinical presentation, natural history, radiologic imaging characteristics, and genetic causes. Familial forms of the disease are not uncommon and it is important to recognize them. Numerous treatment options for cavernous malformations exist. Potential treatments include conservative therapy, surgical resection, and radiation therapy. Treatments have to be individually customized to the patient's lesions, nature of presentation and course of the disease.

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