

Familial Cavernous Angioma of the Brain Stem Dominantly Inherited in Hispanics

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A 23-year-old Hispanic woman whose mother had died of a brain hemorrhage developed signs and symptoms of a brain stem lesion. These gradually progressed over the next 30 years. Her computed tomographic and magnetic resonance imaging scans show features typical of a cavernous angioma in the brain stem. Her daughter had a transient right hemiparesis at age 25, and at age 28 noted periorbital pain with twitching of the forehead and jaw. The daughter's computed tomographic and magnetic resonance imaging scans likewise suggest cavernous angioma of the brain stem. There has been only one other report of familial cavernous angioma of the brain stem, and that also involved a Hispanic family. Hispanics have a known predisposition to familial cavernous angioma, and this diagnosis should be considered when more than one person in a family develops brain stem symptoms. (*Neurosurgery* 24:102-105, 1989)

Key words: Brain stem, Cavernous angioma, Computerized tomography, Hereditary disorders, Magnetic resonance imaging, Vascular malformation

Cavernous angiomas of the brain are vascular malformations in any part of the brain made up of irregular sinusoidal channels, generally without intervening neural parenchyma, large feeding arteries, or large draining veins. They may involve any part of the nervous system, and present with seizures, focal signs, or hemorrhage (16). Although rarely visualized in angiography, they are easily demonstrated by computed tomography (CT) or by magnetic resonance imaging (MRI) (13). They are often inherited in a Mendelian autosomal dominant pattern (11). We report the findings in a Hispanic woman and her daughter, both of whom have brain stem lesions on CT and MRI typical of cavernous angiomas.

CASE REPORTS

Case II-2

This 53-year-old Hispanic woman, the daughter of Case I-1 and mother of Case III-1 was well until 1959, when in the third month of her pregnancy at age 23, she became clumsy in the right hand. Two months later she abruptly developed vertigo, vomiting, diplopia, dysarthria, ataxia with falling to the left, and numbness of the left arm and face and both legs. Examination revealed medial and lateral gaze paresis in the right eye, and nystagmus on gaze up and right. Deep tendon reflexes in the biceps, triceps, brachioradialis, patellar, and Achilles tendons were 2+ and symmetric. Skull x-ray, electroencephalogram, and cerebrospinal fluid examination were normal, and she improved substantially but not completely within 3 months. She was thought to have multiple sclerosis.

In 1961 she developed rotatory nystagmus and hyperreflexia. Examination in 1965 revealed a head-tilt to the left, and oculopalatal myoclonus with synchronous movements of the face, jaw, tongue, and diaphragm. Bilateral internuclear ophthalmoplegia was noted in 1968, and in 1973 she developed myoclonic eye closure, aggravated in upward gaze and opposed by frontalis overactivity. In 1975 she was found to have seesaw nystagmus on downward gaze and up-beat nystagmus when she attempted to converge, and in 1976 she developed impaired hearing on the left.

A CT scan (Fig. 1A) in 1984 showed an elongated lesion of high density extending from the low pons to the quadrigeminal plate, with numerous coarse punctate calcifications, little mass effect, and no surrounding edema. There was slight enhancement after contrast administration. MRI (Fig. 1, B, C, and D) revealed a $3.7 \times 3 \times 3$ cm mass in the right half of the brain stem beneath the floor of the 4th ventricle, extending from the pontomedullary junction to the level of the superior cerebellar peduncle and collicular plate. The lesion was well circumscribed with a low signal intensity rim compatible with hemosiderin. The interior of the mass had similar low signal intensity areas, plus high signal intensity foci compatible with subacute hemorrhage. A similar smaller focal lesion was seen in the right occipital lobe. There was no significant mass effect and no hydrocephalus; the cerebellar vermis and hemispheres were atrophic.

Case III-1

This 28-year-old Hispanic woman, the only child of Case II-2, was well until age 25, when she felt weak in the right arm and leg for 7 days and then recovered.

Her CT scan (Fig. 2A) showed a high-density, enhancing pontine lesion compatible with cavernous angioma. When examined 2 years later in the fifth month of pregnancy, she had mild slowing of finger tapping and hand rolling, hyperreflexia, and an extensor plantar response, all on the right. Mental state, cranial nerve examination, and sensory function were all normal.

Her pregnancy was uneventful, with normal vaginal delivery of an apparently healthy baby girl, who has not been examined neurologically or radiographically. Two months later she began to notice pain around the left eye, twitching of the frontalis muscle, and spasm of the jaw muscles on the left, occurring in 5-minute episodes, and occasionally subsiding for weeks at a time. There were no new abnormalities in her neurological examination. MRI of the brain (Fig. 2, B, C, and D) showed a $2.5 \times 2.5 \times 2$ cm lesion in the brain stem extending from the left middle cerebellar peduncle to the left cerebral peduncle. There were punctate areas of high signal

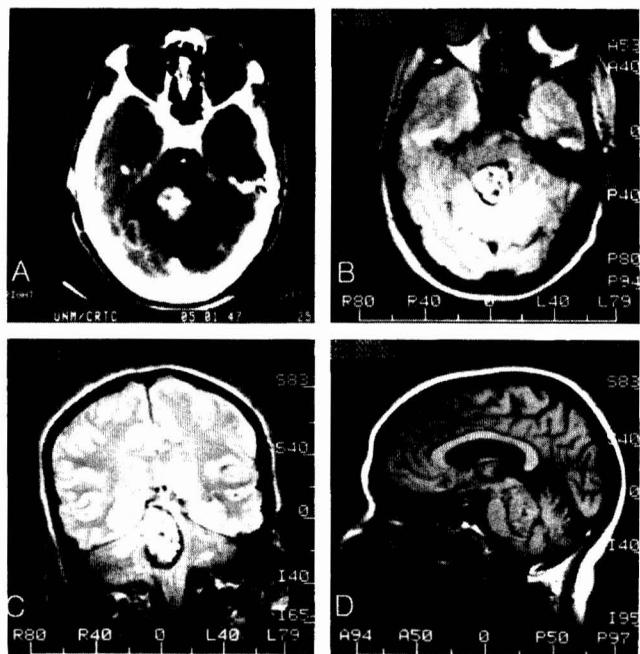


FIG. 1. Case II-2. *A*, CT scan showing high-density right brain stem lesion with punctate calcification. *B*, *C*, and *D*, MRI showing right brain stem lesion with regions of high signal intensity compatible with recent hemorrhage and low-signal areas typical of hemosiderin. Cerebellum is atrophic.

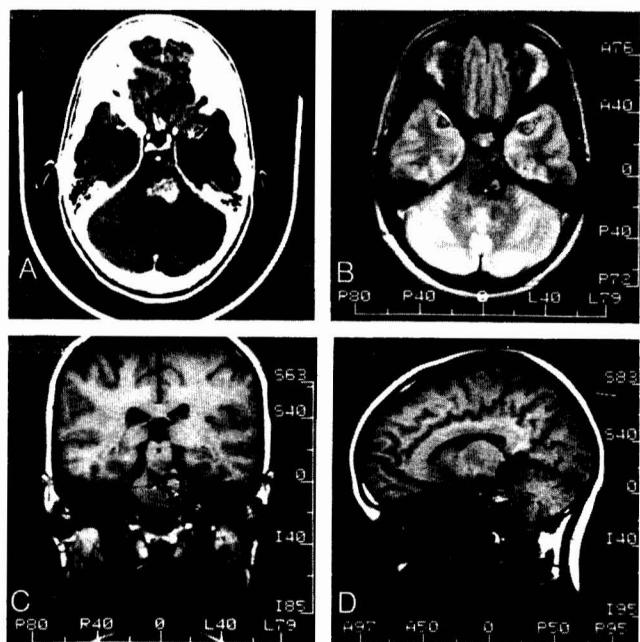


FIG. 2. Case III-1. *A*, CT scan showing high-density, enhancing lesion in left pons. *B*, *C*, and *D*, MRI shows left brain stem lesion with punctate areas of high signal intensity suggesting recent hemorrhage, and large areas of low signal intensity compatible with hemosiderin from old hemorrhage.

intensity suggesting small hemorrhages, plus large areas of low signal intensity typical of hemosiderin, suggesting old hemorrhage. There was no mass effect to suggest recent bleeding.

Case I-1

All that is known of this Hispanic woman, the mother of Case II-2, is that she became ill after giving birth to Case II-3 and died several months later. The family was told death was from brain hemorrhage.

Case II-1

This woman is an older sister of Case II-2 and has no neurological symptoms. She is said to have an abnormal CT scan.

Case II-3

This patient is a younger brother of Case II-2. He reportedly has seizures and an abnormal CT scan.

DISCUSSION

These cases are typical of familial cavernous angioma, a Mendelian autosomal dominant inherited disorder designated by McKusick Number 11686 (11). This is the second known occurrence of familial cavernous angioma of the brain stem. The prior cases involved two Hispanic brothers (1).

The younger brother had the abrupt onset of a right hemipontine syndrome at age 8. When examined at age 26, he had right paresis of the 5th, 6th, and 7th nerves, oculopalatal myoclonus, and no oculomotor response to caloric stimuli; he had impaired hearing, left hemiparesis, hemianesthesia, and hemiataxia, and reduced sweating on the right half of the body. Lumbar puncture, pneumoencephalogram, and carotid and vertebral angiography had been normal at the onset of his symptoms, and he was felt to have had a localized brain stem infarct in childhood. He died suddenly at age 35 of an acute alcohol overdose, and a cavernous angioma was found in the right brain stem tegmentum, extending from the upper medulla to the lower midbrain, and into the right cerebellar hemisphere.

At age 38, the older brother suddenly noted occipital headache, vertigo, tinnitus, and hearing loss. Examination revealed right 5th, bilateral 6th, and right 7th nerve palsies with horizontal and rotatory nystagmus and saccadic pursuit; hearing was impaired bilaterally, and he had weakness, ataxia, and anesthesia on the left side. Pneumoencephalography showed enlargement of the right pons; vertebral and carotid angiograms were normal. He was felt to have a brain stem glioma and was treated with radiation and chemotherapy. After the death and postmortem examination of his brother 3 years later, CT scanning, which had just become available, showed a contrast-enhancing lesion of the right pons compatible with a cavernous angioma. Further inquiry regarding the family revealed that this patient's son had seizures and a calcified, angiographically negative temporal lobe lesion, compatible with cavernous angioma on CT scan. In addition, the mother of the two affected brothers was said to have died suddenly with a severe headache.

This presentation brings to 15 the total number of reported families with familial cavernous angioma of the brain (1, 2, 4-6, 9, 12, 14), of which 10 are Hispanic (1, 4, 9, 14). The inheritance pattern in every instance is compatible with autosomal dominance.

Pathologically, these lesions may be multiple and may bleed, calcify, or thrombose. Although the 4 cases discussed here all involved the brain stem, posterior fossa lesions were present in only 20 of the 138 cases reviewed by Simard et al. (16), whereas there were 23 patients with frontal lesions, 29 with parietal, 10 with occipital, 37 with temporal, 22 with

deep, and 11 with multiple lesions. Savoardo et al. (15) reported 36 cases, of which 33 were supratentorial, 1 involved the pons, 1 was in the cerebellum, and 1 was attached to the dura in the posterior fossa. In the review by McCormick et al. (10) of 80 cavernous angiomas, 21 involved the posterior fossa (11 in the cerebellum and 10 in the brain stem), while 59 were supratentorial.

Patients may present with seizures, hemorrhage, focal signs, or hydrocephalus; erroneous diagnoses, including multiple sclerosis, neoplasm, and encephalitis, are common (16). The possibility of a long, fluctuating course simulating multiple sclerosis was emphasized by Stahl et al. (17) who described 6 patients with symptom durations ranging from 1 to 16 years. Many of these lesions, however, are clinically silent. In 10 previously reported, pathologically proven brain stem cases, the patients all presented with typical focal features, and most pursued a prolonged but ultimately fatal clinical course (16). When these 10 and our 4 patients are combined, the ratio of men to women is 1:1 and the age at onset of symptoms ranges from 8 to 55 years, with a mean of 34 years.

Angiography in cavernous angioma is usually normal or shows a nonspecific mass effect, and only rarely demonstrates abnormal blood vessels; such cases have been termed "occult vascular malformation" or "cryptic arteriovenous malformations" (7). Fortunately, these lesions are readily seen by CT and MRI. CT may be more sensitive in demonstrating small foci of enhancement or calcification, but MRI appears the more useful procedure for demonstrating posterior fossa lesions and foci of hemorrhage (7, 9, 13).

The prognosis for patients with familial cavernous angioma is hard to determine. Simard et al. (16) reviewed 138 cases, all pathologically confirmed by biopsy or autopsy. None of these was asymptomatic; 49 presented with seizures, and 8 of these died. Of 23 who were followed after surgery, 12 were seizure free, 9 were "satisfactory," and 2 had persistent seizures. Forty patients presented with hemorrhage, and 11 died, 2 postoperatively and 9 without surgery. Twenty-nine who survived surgery had a satisfactory postoperative course. Another 49 patients had signs and symptoms of a focal lesion, and there were 7 deaths in this group, all patients with relentlessly progressive brainstem lesions; 2 of the 7 expired with acute hemorrhagic infarction. Of 19 patients who presented with nonspecific mass effect, most fared well after biopsy or resection.

In contrast to the report by Simard et al., in which all cases were pathologically confirmed and virtually all were symptomatic, Mason et al. (9) reported a family studied by CT and MRI after the index case was pathologically confirmed. In this family, 5 of 10 patients with lesions demonstrated by imaging techniques were totally asymptomatic, as were several known obligate carriers. The 5 symptomatic patients all had easily controlled seizures, and there were no known deaths attributable to angiomas.

Hayman et al. (4) described 22 persons in a large kindred. Some were symptomatic, some had asymptomatic lesions demonstrated by CT, and some were known by genetic analysis to be obligate carriers. Of the 22, 7 had hemorrhage, 7 had focal deficits, and 4 had seizures, but 3 had no problem except headache, and 8 were totally asymptomatic. There were 4 sudden deaths, presumably from hemorrhage. Seven persons at risk were followed by CT scanning over a 5-year period, and new lesions appeared in 3 whose scans had been previously normal.

In the two families with brain stem lesions that we review here, there were 2 sudden deaths, presumably from hemorrhage. Of the 4 individuals with brain stem lesions, 3 had

severe disability, and 2 other family members had seizures. Only 1 person with an abnormal CT scan was asymptomatic.

While cavernous angiomas seem prone to small recurrent hemorrhages that may be seen in follow-up CT scans (4), these are rarely catastrophic, and may be clinically silent. By contrast, in arteriovenous malformation, the risk of significant bleeding is estimated at 2 to 3% per year, with 10% mortality and 30% morbidity for each bleeding episode (8), and the 20-year outcome in arteriovenous malformation has been projected to include seizures in 18% of patients, focal deficit in 27%, hemorrhage in 42%, and death in 29% (3).

The treatment of cavernous angioma varies with the site and the symptoms. Accessible lesions with focal deficits or hemorrhage can be excised, and since the hemosiderin surrounding the lesions appears to be epileptogenic, surgery may help control intractable seizures (14). Follow-up CT or MRI studies should be obtained to identify newly emerging lesions (4).

When more than one member of a family has cavernous angioma, all first-degree relatives should have CT or MRI studies, and those with similar lesions should receive genetic counseling (4). With the widespread use of CT or MRI, the number of cases recognized is likely to increase rapidly.

Cavernous angioma should be considered in the differential diagnosis of brain stem lesions, especially if the patient is Hispanic or has a family history of cerebral hemorrhage, seizures, or focal neurological deficit. Angiography is often unrevealing; CT scanning or MRI examination should be carried out, and appropriate therapy and counseling should be provided.

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COMMENT

The article entitled, "Familial Cavernous Angioma of the Brain Stem Dominantly Inherited in Hispanics" alludes to two important features of this condition. They are the facts that cavernous malformations are often transmitted in an autosomal dominant fashion and, secondly, that this lesion has some predilection for the brain stem. The article's goal is

to stress the coexistence of these two features. The author has analyzed a Hispanic family in which the proposita had gradually progressing symptoms suggestive of brain stem involvement for 30 years. Her CT and MRI scans showed a cavernous angioma in the brain stem. Her daughter also developed signs and symptoms of brain stem lesion and her CT scan suggests a cavernous angioma. The author, Dr. Bicknell, has been interested in the topic of familial cavernous angiomas for some time. There seems to be a predominance of Hispanic families throughout the literature, even though it is my feeling that this predilection may not be statistically significant. It is also important to note that the classic neuroradiological work-up may not be very helpful in the case of cavernous malformations, because they tend to be occult to angiography. Finally, the author properly states that the prognosis for this patient is hard to determine. We agree with the author on the necessity of recommending a CT or MRI scan for all first-degree relatives of patients in whom more than one family members has a cavernous malformation.

In summary, this article points out two important features of this unusual lesion, and stresses that with the advent of MRI, the diagnosis becomes certainly easier, and as a consequence of this, in the case of the familial disease, genetic counseling becomes an important option.

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Intrasellar Balloon Inflation for Treatment of Symptomatic Empty Sella Syndrome

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Intrasellar extradural placement of a detachable vascular balloon via a transsphenoidal approach was performed successfully in a patient with primary empty sella syndrome, relieving headache and visual field defect. This technique offers an alternative approach to other methods of treating symptomatic empty sella syndrome that require packing of the sella with fat, muscle, cartilage, or bone. (*Neurosurgery* 24:105-109, 1989)

Key words: Empty sella, Extradural balloon, Transsphenoidal surgery

Empty sella syndrome is an anatomic variant in which the subarachnoid space herniates through the diaphragma sellae. While empty sella syndrome remains asymptomatic in most patients, its presence in association with visual disturbances, headaches, or rhinorrhea prompts consideration for surgical therapy (7-9). When visual field defects predominate, surgical therapy is directed at altering the relationship of the optic chiasm, which is thought to sag into the empty sella. This process of propping up the optic chiasm has been termed *chiasmapexy* and has been accomplished transcranially by inserting muscle, cartilage, or a silicone sponge under the optic chiasm (4, 10), or transsphenoidally by packing the sella with fat, muscle, or cartilage to raise the optic chiasm (1, 5, 11).

More recently, packing of a symptomatic empty sella by transsphenoidal placement of a detachable vascular balloon has been described (3). We report an additional example of this approach with successful correction of a visual field deficit and relief of headaches secondary to empty sella syndrome.

CASE HISTORY

A 30-year-old man presented to the Cook County Hospital emergency room with complaints of increasing headaches and visual disturbances. He described severe retro-orbital headaches that had worsened progressively over the prior 3 months and decreasing vision, primarily in the right eye for 2 months. He denied any other neurological or endocrinological symp-