

## Fatal giant pediatric intracranial cavernous angioma

Funda Çorapçioğlu<sup>1</sup>, Gür Akansel<sup>2</sup>, Erdem Gönüllü<sup>1</sup>, Kürşat Yıldız<sup>3</sup>, Volkan Etuş<sup>4</sup>

Departments of <sup>1</sup>Pediatrics, <sup>2</sup>Radiology, <sup>3</sup>Pathology, and <sup>4</sup>Neurosurgery, Kocaeli University Faculty of Medicine, Kocaeli, Turkey

**SUMMARY:** Çorapçioğlu F, Akansel G, Gönüllü E, Yıldız K, Etuş V. Fatal giant pediatric intracranial cavernous angioma. Turk J Pediatr 2006; 48: 89-92.

Cavernous angioma is a benign vascular lesion that may occur in the central nervous system. The symptoms of raised intracranial pressure or consciousness alteration are usually related to acute hemorrhage. A previously healthy four-year-old girl was admitted with sudden loss of consciousness, vomiting and clonic seizures. Her Glasgow coma score (GCS) was 7 at presentation (5m 1v 1e). Anisocoria and mydriasis were present on the right. Computerized tomography revealed a giant spherical, hyperdense intraaxial left frontoparietal lesion. The findings of surrounding vasogenic edema and compression of the adjacent lateral ventricle were seen on computerized tomography (CT). She was taken to operation and the mass was grossly excised. The GCS remained unchanged. A diagnosis of brain death was made. A cavernous hemangioma was diagnosed with pathologic examination. In conclusion, a cavernous angioma may occasionally follow a rapid and fatal course by causing gross hemorrhage in the pediatric age group. Early recognition by CT or magnetic resonance imaging (MRI) and prompt surgical evacuation are necessary.

*Key words:* intracranial cavernous angioma, children, fatal cavernoma.

Cavernous angioma (cavernoma) (CA) is a benign vascular lesion that may occur at any site within the central nervous system (CNS) as well as other organs such as the liver or skin<sup>1</sup>. Twenty-five percent of the CNS CAs are seen in pediatric patients<sup>2</sup>. Although the clinical progress is usually protracted because of slow growth, rapid fatal outcome is occasionally encountered. We report such a case to illustrate the need for awareness of vascular lesions as cause of rapidly increased intracranial pressure and a sudden alteration in consciousness in an acutely ill child.

### Case Report

A previously healthy four-year-old girl was admitted to the emergency room with a sudden loss of consciousness, vomiting and clonic seizures involving the right upper and lower extremity. Her history revealed headache for the last two days and vomiting for the last 10 hours. She had no such complaints in the past.

Her body weight and height were at the 50<sup>th</sup> percentile for age, body temperature 36.6°C, pulse 80 beats/min and the respiratory rate 24/min. The blood pressure (113/87 mmHg) was

higher than +2 SD for age. Her Glasgow coma score (GCS) was 7 at presentation (5m 1v 1e). Anisocoria and mydriasis were present on the right. The pupil reflexes were normal on the left but absent on the right. Clonic movement of the right upper and lower extremity was seen. The muscle tone was increased.

Computerized tomography (CT) revealed a spherical, hyperdense intraaxial left frontoparietal lesion measuring 40x40x35 mm. The lesion included peripheral areas of speckled calcification (Fig. 1). The findings of surrounding vasogenic edema and compression of the adjacent lateral ventricle were seen on CT (Fig. 2).

The patient was taken to the operating room with a GCS decreased to 3 (e1 m1 v1). During surgery, the hemispheres were grossly edematous. Grey-black appearance of the left frontoparietal lobes was noted. The hematoma was evacuated and the mass was grossly excised. The GCS remained unchanged. EEG showed no electrical activity. A diagnosis of brain death was made.

Pathologic examination showed a soft, fragile beige-brown mass with occasional superficial orange stains and a similar cut surface. Microscopically, there were hematomas of

varying age as well as areas of hematoma organization, hyalinization and dystrophic calcification. A cavernous hemangioma was diagnosed with these findings (Fig. 3).

### Discussion

Cavernous angioma (CA) is a vascular malformation that is defined in histologic terms by blood-filled cavities covered by a single layer of endothelium. The intervening tissue includes microglia but no neural elements<sup>1-3</sup>.

The etiology of CAs is unknown. A minority of cases are hereditary with high penetrance, autosomal dominant transmission. A gene (CCM1) causing familial disease has been

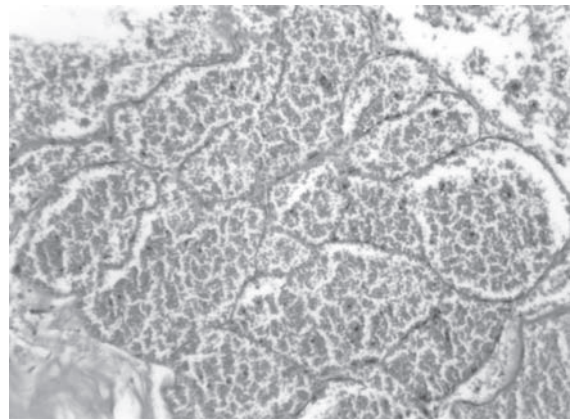


Fig. 3. Markedly dilated congested blood vessels lined by a thin layer of endothelial cells. Hyalinized dense stroma appears at upper right quadrant (hematoxylin-eosin, x40).

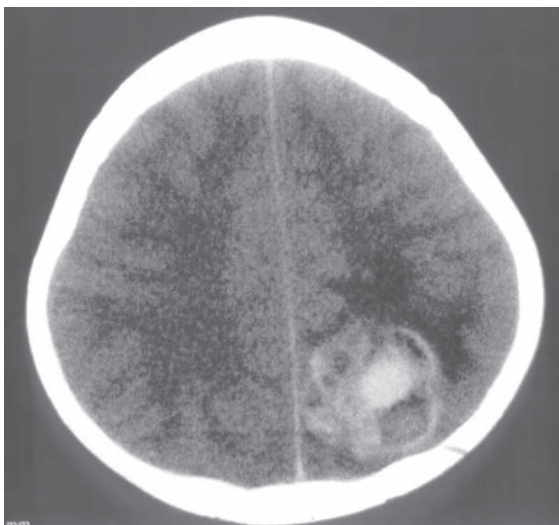


Fig. 1. Axial computerized tomography (CT) scan shows a left frontoparietal hemorrhagic intraaxial lesion.

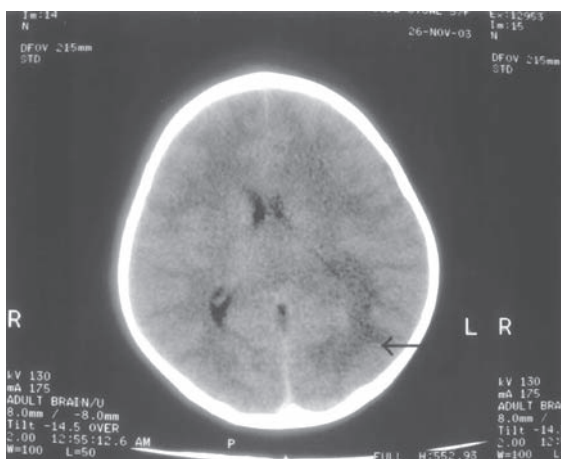


Fig. 2. Surrounding vasogenic edema, mass effect and compression of the adjacent lateral ventricle (arrow).

mapped to chromosome 7q21 (F) and the CCM1 gene was identified as coding for Krev-1 interaction trapped 1 (KRIT1) protein, which was shown to be a modulator of beta1 integrin signal transduction<sup>4-6</sup>.

One fourth of these lesions occur in the pediatric age group, and CAs are one of the two main causes of spontaneous intracerebral hemorrhage in children with ruptured arteriovenous malformations<sup>2,7</sup>. A bimodal distribution in the pediatric age group has been observed by many investigators, ranging from the first year to three years for the first peak and 11 to 17 years for the second peak<sup>7-11</sup>. The reason for the bimodal distribution is unknown.

The clinical presentation of pediatric cerebral cavernomas is variable. They may be asymptomatic or induce acute or chronic symptoms related to hemorrhage, mass effect, or epileptogenicity<sup>7</sup>. The most common presentation is seizures (70%), followed by neurological signs due to mass effect or acute hemorrhage<sup>7,12</sup>. In the pediatric age group, a higher incidence of hemorrhage is usually reported, estimated between 36% and 78% of symptomatic cases compared to 8% to 37% for adult patients. Focal neurological deficits with or without symptoms of raised intracranial pressure or consciousness alteration are usually related to acute hemorrhage<sup>7</sup>. Bleeding from a CA may be intraparenchymal or subarachnoidal, depending on the location of the lesion<sup>12,13</sup>. In the presented case, the main causes of death were acute hemorrhage and herniation. On the other hand, seizure and status epilepticus may have been the other causes of death.

The size of CA varies from a few millimeters to 2-3 centimeters. Usually CAs reach a larger size in children but giant CAs are rare<sup>7,14-16</sup>. Initially smaller lesions may grow during follow-up, in some instances relatively rapidly<sup>17</sup>. Due to the increase in complexity along with size, the lesion may resemble a glial tumor<sup>15</sup>.

Cavernomas are usually not detected angiographically, hence grouped with "occult" vascular malformations. CT is less sensitive than magnetic resonance imaging (MRI) for the detection of cerebral cavernomas, especially when multiple and small<sup>18</sup>. However, in a recent review, Mottolese et al.<sup>7</sup> advocated CT especially in the emergency setting because cerebral CT always shows at least one lesion in every symptomatic child and CT findings are suggestive of diagnosis in most cases. Among the symptomatic group, the cavernomas presenting with acute hemorrhagic complications are the most frequent and appear on plain CT scan as a hyperdense hematoma with a spherical shape, sharp and regular margins, and minimal or no perilesional edema. Punctate or large calcifications may be seen as well as big cystic areas. Differential diagnosis from other intraaxial lesions may be difficult, especially on CT findings alone<sup>7</sup>. Large lesions with calcifications and cysts may be misdiagnosed as ependymomas or oligodendrogliomas<sup>19</sup>. Although mass effect is usually less than expected for the size of the lesion, it can be severe as in our case.

Fatal outcome due to hemorrhage from CA is rare<sup>20,21</sup>. van Rybroek et al.<sup>20</sup> reported a 13-year-old patient who died due to hemorrhage from choroid plexus CA. Three such pediatric cases were reported out of 65 autopsies in another report<sup>21</sup>. On the other hand, Kupersmith et al.<sup>22</sup> observed a significant morbidity due to CAs in 8% of their series. Also shown in their study was a greater likelihood of hemorrhage for lesions greater than 10 mm in diameter. Initial presentation with hemorrhage was not associated with a greater risk for rebleeding.

In children, surgery is clearly indicated in case of acute hemorrhage or focal neurological deficits. It is especially recommended for infratentorial CAs, even if clinically silent, due to their high risk of bleeding<sup>7</sup>.

In conclusion, an intracranial cavernous angioma may occasionally follow a rapid and fatal course by causing gross hemorrhage in

the pediatric age group. Early recognition by CT or MRI and prompt surgical evacuation are necessary.

#### REFERENCES

1. Moran NF, Fish DR, Kitchen N, Shorvon S, Kendall BE, Stevens JM. Supratentorial cavernous hemangiomas and epilepsy: a review of the literature and case series. *J Neurol Neurosurg Psychiatry* 1999; 66: 561-568.
2. Hsu FP, Rigamonti D, Huhn SL. Epidemiology of cavernous malformations. In: Awad IA, Barrow DL (eds). *Cavernous Malformations*. Park Ridge: AANS Publications Committee; 1993: 13-23.
3. Curling OD, Kelly DL, Elster AD, Craven TE. An analysis of the natural history of cavernous angiomas. *J Neurosurg* 1991; 75: 702-708.
4. Cave-Riant F, Denier C, Labauge P, et al. Spectrum and expression analysis of KRIT1 mutation in 121 consecutive and unrelated patients with cerebellar cavernous malformations. *Eur J Hum Genet* 2002; 10: 733-740.
5. Gunel M, Laurans MS, Shin D, et al. KRIT1, a gene mutated in cerebral cavernous malformation, encodes a microtubule-associated protein. *Proc Natl Acad Sci USA* 2002; 99: 10677-10682.
6. Gunel M, Awad IA, Anson J, Lifton RP. Mapping a gene causing cerebral cavernous malformation to 7q11.2-q21. *Proc Natl Acad Sci USA* 1995; 92: 6620-6624.
7. Mottolese C, Hermier M, Stan H, et al. Central nervous system cavernomas in the pediatric age group. *Neurosurg Rev* 2001; 24: 55-71.
8. Edwards MS, Baumgartner JE, Wilson CB. Cavernous and other cryptic vascular malformations in the pediatric age group. In: Awad IA, Barrow DL (eds). *Cavernous Malformations*. Park Ridge: AANS Publications Committee; 1993: 163-183, 185-186.
9. Fortuna A, Ferrante L, Mastronardi L, Acqui M, d'Addetta R. Cerebral cavernous angioma in children. *Childs Nerv Syst* 1989; 5: 201-207.
10. Cavalheiro S, Braga FM. Cavernous hemangiomas. In: Choux M, Di Rocco C, Hockley AD, Walker ML (eds). *Pediatric Neurosurgery*. London: Churchill-Livingstone; 1999: 691-701.
11. Gangemi M, Longatti P, Maiuri F, Cinalli G, Carteri A. Cerebral cavernous angiomas in the first year of life. *Neurosurgery* 1989; 25: 465-468; discussion 468-469.
12. Scott RM. Brainstem cavernous angiomas in children. *Pediatr Neurosurg* 1990; 16: 281-286.
13. Scott RM, Barnes P, Kupsky W, Adelman LS. Cavernous angiomas of the central nervous system in children. *J Neurosurg* 1992; 76: 38-46.
14. Anderson RC, Connolly ES Jr, Ozduman K, et al. Clinicopathological review: giant intraventricular cavernous malformation. *Neurosurgery* 2003; 53: 374-378.
15. Chicani CF, Miller NR, Tamargo RJ. Giant cavernous malformation of the occipital lobe. *J Neuroophthalmol* 2003; 23: 151-153.
16. Hayashi T, Fukui M, Shyojima K, Utsunomiya H, Kawasaki K. Giant cerebellar hemangioma in an infant. *Childs Nerv Syst* 1985; 1: 230-233.

17. Stacey RJ, Ashkan K, Edwards JM. Rapid growth in a cavernoma. *Br J Neurosurg* 2000; 14: 585-588.
18. Perl J, Ross JS. Diagnostic imaging of cavernous malformations. In: Awad IA, Barrow DL (eds). *Cavernous Malformations*. Park Ridge: AANS Publications Committee; 1993: 37-48.
19. Steinberg GK, Marks MP. Lesions mimicking cavernous malformations. In: Awad IA, Barrow DL (eds). *Cavernous Malformations*. Park Ridge: AANS Publications Committee; 1993: 151-162.
20. van Rybroek JJ, Moore SA. Sudden death from choroid plexus vascular malformation hemorrhage: case report and review of the literature. *Clin Neuropathol* 1990; 9: 39-45.
21. Schejbal V, Oellig WP. Sudden death of children by hemorrhage from a cerebral angioma. *Klin Padiatr* 1979; 191: 498-500.
22. Kupersmith MJ, Kalish H, Epstein F, et al. Natural history of brainstem cavernous malformations. *Neurosurgery* 2001; 48: 47-53.