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Neoplasm

Multiple dynamic cavernous malformations in a girl: long-term follow-up☆

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Abstract

Background: Cavernous malformations have generally been viewed as fairly benign vascular lesions with low potential for causing massive hemorrhage.
Case Description: We present an interesting case of multiple CMs, several of which were formed de novo and exhibited aggressive biological behavior resulting in recurrent episodes of intracranial hemorrhage over a 10-year period. This case illustrates a dynamic and aggressive form of CMs. Recent advances in our understanding of the molecular pathogenesis of CMs implicate genetics as an important pathogenic factor, which is the most likely etiology of this patient's presentation.
Conclusion: Special challenges exist in managing young children with multiple, highly aggressive CMs.

Keywords: Cavernous malformation; Natural history; Hemorrhage; De novo formation; Vascular malformation

1. Introduction

Cavernous malformations are low-flow, benign vascular lesions that affect 0.4% to 0.8% of the population [10,11]. However, their potential for a more aggressive course has also been recognized. We will describe this unique case of multiple hemorrhages of CMs by outlining the patient's initial presentation, radiologic findings, and histopathologic findings over a 10-year follow-up period. We will conclude with a discussion of recent advances in their potential for serious complications.

2. Case Report

2.1. History and operative interventions

In May 1996, when this patient was a 6-month-old baby girl, she was transferred to our hospital for evaluation of inconsolable crying and vomiting. Emergency CT scan of the head revealed 2 small hematomas in the left parietooccipital lobe, which were thought to be CMs. The patient recovered well after conservative therapy. Two months later, the patient's symptoms recurred and a repeat CT scan showed rebleeding of the same CMs. This was also treated conservatively.

Two years later, this patient presented with a more severe, third episode of intracranial hemorrhage that was associated with somnolence and required admission to our neurosurgical intensive care unit. In addition to the enlarging hematoma in the left parietooccipital lobe, CT scan also demonstrated a separate, expanding hematoma in the left cerebellum as well as a smaller hemorrhage originating from the right frontal lobe. Despite significantly elevated intracranial pressure, there was no imminent threat of herniation; hence, con-

Abbreviations: AVM, arteriovenous malformation; CECs, cavernous malformation endothelial cells; CMs, cavernous malformations; CT, computed tomography; DSA, digital subtraction angiography; MR, magnetic resonance; VEGF, vascular endothelial growth factor; VM, venous malformation.

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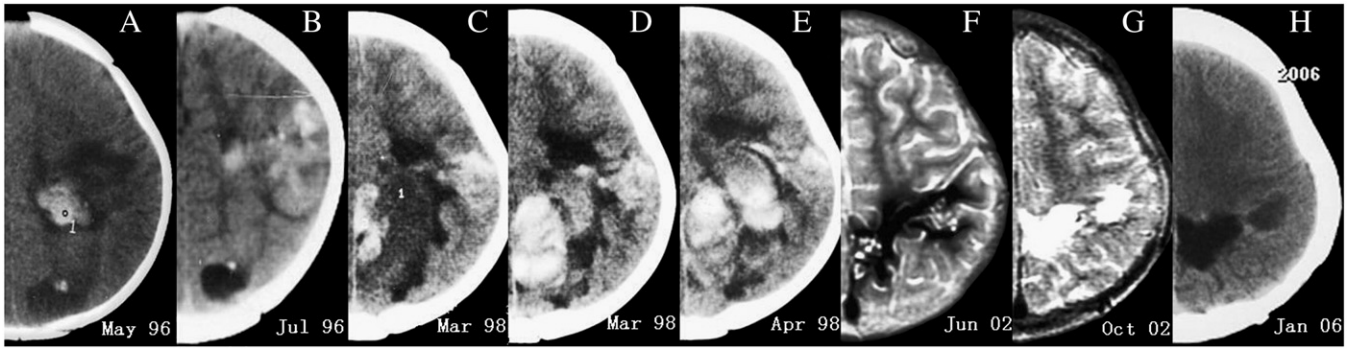

Fig. 1. CT (A-E, H) and MR (F, G) manifestations of 2 hemorrhagic CMs in the left parietooccipital lobe. Initial CT scan (A) revealed 2 small hematomas in the left parietooccipital lobe, with the parietal one enlarging 2 months later (B). Rehemorrhage of this CM occurred 2 years later (C). At that time, continuous enlargement of the occipital lesion was found (D, E). MR (F) was performed after absorption of the hematoma. Postoperative MR (G) and CT (H) showed complete resection of the CMs.

servative therapy was once again followed. The patient eventually recovered well except for mild gait ataxia.

Further investigations were pursued once the patient was stabilized from her acute illness. Digital subtraction angiography of the brain was unremarkable. Von Hippel-Lindau disease was effectively ruled out by a normal abdominal CT scan, as well as a normal dilated fundoscopic examination. A familial cause was also explored but denied.

The left cerebellum CM was resected in March 2001. This was followed by resection of the remaining 2 CMs in the parietooccipital lobe in July 2002 under neuronavigation. In January 2006, however, this patient underwent episode of brain hemorrhage derived from a suspected CM in the left frontal lobe that was not seen in previous CT or MR images. After the hematoma was absorbed, a third operation was recommended to the patient's family, although the patient's family remains hesitant and will likely opt for continued surveillance and follow-up.

The patient is currently 11 years old, developmentally normal, and otherwise well except for mild gait ataxia. She presents almost all forms of CM biological behavior, including the de novo formation of the left frontal CM, the concurrent overt hemorrhages of the CMs in the left parietal-occipital lobe and left cerebellum, and the dynamic changes from de novo formation, maturation, to total calcification of the right frontal CM. Serial CT and MR images of the 5 lesions over a 10-year period are presented in chronological order (Figs. 1-4, Table 1).

2.2. Histopathologic findings

The pathologic specimens of the left parietooccipital and left cerebellar vascular lesions revealed CMs with typical histopathologic features. These specimens were composed of dilated, thin-walled vascular channels consisting of endothelium and collagen, filled with blood and thrombi, without intervening neural parenchyma within the bulk of lesion. We did not find any significant difference in

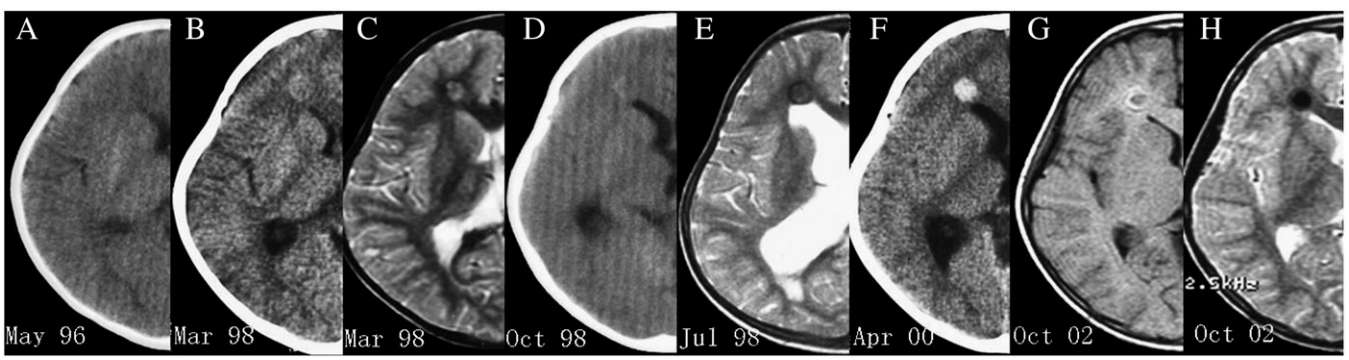

Fig. 2. The formation and signal change of a CM in the right frontal lobe on CT and MR images. Nothing abnormal was found in the right frontal lobe on initial CT scan (A). Two years later, a lesion of slightly high density was found near the anterior horn of the lateral ventricle (B). The MR (C) confirmed this finding, but this lesion did not demonstrate features consistent with a typical CM. After the absorption of the small hematoma, the lesion becomes unclear as to its identity on CT scan (D), although T2-weighted MR images (E) show a lesion with a low-signal ring, which is typical of CM. The CT (F) shows several intralesional hemorrhages. Obvious low-signal change is found both on T1- and T2-weighted MR images (G, H), which we believe is due to intralesional calcification, a consequence of the lesion aging.