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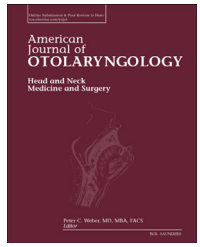

Acute pediatric facial nerve paralysis as the first indication for familial cerebral cavernoma: Case presentation and literature review☆,☆☆,★

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ABSTRACT

Familial cerebral cavernoma is an autosomal dominant phenotype with incomplete clinical and neuroimaging penetrance. The most common clinical manifestations include seizures and cerebral hemorrhage. We present the case of a 7-year-old boy who developed acute onset facial nerve paralysis secondary to previously unknown familial cerebral cavernoma. Genetic workup revealed a *KRIT1* gene deletion which was later confirmed in the patient's asymptomatic father and younger brother.

1. Introduction

Facial nerve paralysis (FNP) occurs less frequently in children than in adults. Nevertheless, its presentation understandably causes the child and the family tremendous angst. The literature varies on the most common etiology of FNP in the pediatric population based on two main factors: date of publication and geographic location of data collection. While earlier studies suggest Bell's palsy to be the cause of up to 62% of the cases [1], recent reports have sought to identify more specific etiologies. More recent studies have shown infection and trauma to be the two leading causes of pediatric FNP [2]. In regions endemic of Lyme disease, however, up to 50% of pediatric FNP are attributable to infection by *Borrelia burgdorferi* [3]. Less frequent etiologies, such as congenital and neoplastic causes, do occur and should always be kept in a patient's differential diagnosis. In this article, we report what we believe to be a rare case of a child who presented with FNP secondary to familial cerebral cavernous malformation (CCM).

Cavernous malformations (also called cavernous venous malformations, cavernous hemangiomas, and cavernomas) are 'blackberry-like,' 'popcorn-like' dark bluish lesions composed of enlarged, blood-filled capillary sinuses, lined with a single layer of endothelium and void of any neural tissue [4]. Pediatric CCMs are not rare and appear with prevalence of about 0.37–0.53% [5]. These lesions represent 5–15% of all CNS vascular malformations and are second only to arteriovenous malformations as main causes of spontaneous intracerebral

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bleeding in children. Clinical manifestations typically include seizures, headaches, and neurological deficit, mostly due to acute hemorrhage [4]. We present a case of pediatric CCM resulting in right cerebellar peduncular hemorrhage at the level of the intraparenhymal seventh cranial nerve manifesting as acute right-sided FNP.

2. Case

A 7-year-old previously healthy Caucasian male presented from an outside institution with a four-day history of emesis and right-sided facial pain with acute onset mild ataxia and incomplete facial nerve paralysis (House-Brackmann (HB) III/VI). At an outside institution, a CT head exam revealed a 1.2 cm rounded hyperdense acute hemorrhagic lesion in the right middle cerebellar peduncle and dorsal pons region (Fig. 1). Upon arrival, MR brain imaging showed mild edema and mass effect associated with the brainstem intraparenchymal hematoma, and multiple additional, chronic-appearing hemorrhages. The patient was admitted to the pediatric intensive care unit and placed on IV steroids. Nausea and emesis improved over the next two days and the patient was discharged on a steroid taper. No change in facial nerve function was appreciated while in the hospital.

MR acquired 5 weeks after the onset of symptoms (not shown) revealed evolution of blood products within the subacute brainstem hematoma, with similar mild local mass effect and mild edema. Due to the multiple intraparenchymal hemorrhages, a genetic workup was performed. This analysis revealed a *CCM1/KRIT1* gene deletion and the patient was diagnosed with familial cerebral cavernous malformation. Despite steroids, the patient's facial nerve paralysis worsened and became complete over the next month. An audiogram performed approximately 7 weeks following the onset of symptoms revealed a moderate to severe sensorineural hearing loss on the right side—distortion product otoacoustic emissions (DPOAEs) were present, robust, and repeatable in both ears. Because the patient demonstrated incomplete eye closure, the decision was made to perform an upper eyelid gold weight placement and a lateral tarsal strip procedure. Following this procedure, we noted, unexpectedly, that the patient began to demonstrate significant improvement. Repeat MR imaging, performed just over four months following initial presentation, revealed resolved mass effect and edema associated with the brainstem hematoma, and no new hemorrhages. The patient's facial nerve function had gradually improved to HB grade II with complete eye closure. Ultimately, over 8 months following initial onset of symptoms, the gold weight was removed. During the final visit, the patient had a repeat audiogram that revealed a return of normal hearing.

3. Discussion

We have presented the case of a young boy diagnosed with familial cerebral cavernoma (FCC) presenting with facial nerve paralysis. CCMs are slow-flow vascular anomalies void of any neural tissue with an estimated prevalence of 0.3%–0.5% of the population. Patients typically present between the second and fifth decades of life and symptoms can range from headaches to focal neurological deficits. Seizures are the most common, however, and represent 40%–60% of patients.

While sporadic cases of CCM are typically associated with a single lesion, the familial form is characterized by multiple lesions. FCC is inherited in an autosomal dominant fashion with incomplete clinical and neuroimaging penetrance—hemorrhages may be subclinical. It accounts for up to 50% of CCMs observed in Hispanic-American patients [6] and 10–40% of CCMs in non-Hispanics [7]. Approximately 78% of cases have mutations in *CCM1/KRIT1* (7q), *CCM2/MGC4607* (7p), and *CCM3/PDCD10* (3q) genes with *CCM1* and *CCM3* being the most common [6]. While the function of these genes remains incompletely defined, current understanding suggests they play an important role in angiogenesis throughout embryonic development and vascular maintenance in the postnatal stages [8]. *CCM1*, which is at minimum partially deleted in our patient, consists of 16 coding exons. The likely pathophysiological mechanism associated with defective *CCM1* gene allele is hypothesized to be loss of function due to mRNA decay [7]. Clinical penetrance is observed in about 60%–88% of cases involving *CCM1* defects [8]. Incomplete penetrance is evident in our patient's family with his father and younger brother having *CCM1/KRIT1* mutations without any clinical or neuroimaging evidence of cavernomas. The patient's paternal grandfather did die suddenly in his thirties of unknown causes; however, any connection to a CCM-related bleed is purely speculative.

Because the majority of CCMs in non-Hispanic patients are not familial in origin, it may be falsely assumed that a patient with no symptomatic relatives automatically represents a sporadic case. However, data suggest that up to 75% of patients with multiple lesions on MR imaging have at least one parent who is genetically affected but has remained clinically asymptomatic [9]. Even MR studies of asymptomatic carriers may show no lesions due to the incomplete neuroimaging penetrance of FCC [6]. Therefore, a high index of suspicion should be maintained in cases with multiple lesions. Genetic testing is the preferred method for ascertaining the nature of the disease in such instances.

Overall, patients with CCMs have a 50–70% estimated lifetime risk of hemorrhage, epilepsy, and other neurological sequelae [9]. Specifically, patients with brainstem CCMs have an estimated 2–21% annual hemorrhage risk. Those patients

Fig. 1 – Axial CT and MR images obtained at presentation show acute and old parenchymal hemorrhages. (A) CT image through the posterior fossa shows acute, hyperdense hematoma within the right dorsal pons and middle cerebellar peduncle. (B) Corresponding T2-weighted FLAIR image shows central T2-hypointense signal of the acute hematoma, mild surrounding T2-hyperintense edema, and mild mass effect on the fourth ventricle. Gradient-recalled echo images through the pons (C) and temporal lobes (D, E) show prominent susceptibility effect within the brainstem hematoma and a focus of susceptibility effect within each temporal lobe (arrows). There was no edema or mass effect associated with the foci of susceptibility effect within the temporal and left occipital lobes (not shown), consistent with old blood products.