Rare disease

Unilateral facial palsy in an infant: an unusual presentation of familial multiple cerebral cavernous malformation

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Summary

Cerebral cavernous malformation (CCM) in infants tends to have genetic predisposition. These cavernomas have a progressive course of events and associated neurological symptoms with increase in age. They most commonly present with seizure and syndrome of increased intracranial pressure comprising of headache, vomiting and focal neurological signs. We describe a case of a 7-month-old infant who presented with an acute onset of right facial paralysis with a background of familial CCM. The CT and MRI scan revealed fresh haemorrhage in the right cerebellar and pontine cavernomas with surrounding oedema and no evidence of obstructive hydrocephalus. These two cavernomas re-bled in a week duration causing episodes of incessant crying and irritability. After discussing the pros and cons of treatment, owing to stable clinical status, the patient is currently been managed conservatively.

BACKGROUND

Familial cerebral cavernous malformation (CCM) is a rare condition with genetic predisposition. The presentation varies and sometimes the symptoms and signs may be subtle in the paediatric age group. We describe this rare occurrence in an infant with a review of literature. The management of these patients may pose a challenge and clinicians should be aware of this clinical entity.

CASE PRESENTATION

A 7-month-old male infant presented with a 2-day history of right-sided facial weakness noted by the parents. He was found to be irritable and cried excessively without any specific trigger factor over the same period. He has a background of multiple cavernomas in the brain diagnosed at 2 months of age. He had no history of any infection or trauma prior to the current presentation.

When he was 2 months of age, he underwent a posterior fossa craniotomy and excision of a 4 cm cavernoma in the cerebellum and insertion of a ventriculo-peritoneal (VP) at the same stage for obstructive hydrocephalus. A follow-up CT and MRI brain showed multiple supratentorial and infratentorial cavernomas and a decrease in the size of the cerebellar lesion (figure 1). His father was diagnosed to have the same condition when he was 18 years of age when he presented with seizure. There was no other family member known to have this condition. It was at this stage he was diagnosed to have familial CCM.

On examination, he was alert and irritable. Cranial nerve examination revealed a right upper motor neuron facial paralysis. There was no papilloedema. The rest of the neurological examination was normal.

INVESTIGATIONS

CT brain revealed fresh haemorrhage in the right pontine and cerebellar region (figure 2) with no evidence of

hydrocephalus. Subsequent MRI (figure 3) revealed multiple cerebral cavernomas in the supratentorial and infratentorial compartments. MRI brain using susceptibility-weighted imaging (figure 4) demonstrated lesions which were otherwise not picked up on T1 and T2 sequence.

DIFFERENTIAL DIAGNOSIS

- Neoplasm
- Bell's paralysis
- Vascular malformation

TREATMENT

He was admitted for observation and a low-dose dexamethasone was started. During this period, his facial weakness remained unchanged and he was discharged with a view for a follow-up MRI brain.

OUTCOME AND FOLLOW-UP

He represented the following week with episodes of arching towards the right side accompanied by excessive unconsolable crying episodes lasting for a few minutes, several times a day. There was no history of seizures associated with these crying episodes. Subsequent CT brain (figure 5) revealed a rehaemorrhage in the pontine and cerebellar region. Neurological examination remained unchanged and dexamethasone was re-started. After detailed discussion with parents explaining the treatment options, they opted for conservative management. However, surgical removal of the cerebellar lesion was planned in case of neurological deterioration.

DISCUSSION

In paediatric population, CCM tends to have a prevalence of 0.35–0.53%.¹ In familial cases, it is inherited in an autosomal dominant manner² and carries a higher risk of haemorrhage. Cavernomas also tend to grow in size and

Figure 1 (A) An axial view of contrast CT brain at 2 months postoperatively showed a hyperdensity area on the right cerebellum consistent with the remaining cavernoma; (B) A T2 coronal and (C and D) an axial view of MRI brain with susceptibility-weighted imaging showed multiloculated area of mixed signal hypointensity and hyperintensity area in keeping with haemosiderin (full arrow).

Figure 2 An axial view of CT brain showed a right cerebellar cavernoma (full arrow), with evidence of fresh haemorrhage on the right pontine region near the cerebello-pontine angle (dashed arrow).

this has been attributed to the higher tendency of paediatric cavernomas undergoing repeated intralésional microhaemorrhages.¹ A molecular genetic testing is confirmatory of the diagnosis. The mutations associated with the familial CCM are any one of these three genes (*KRIT1*, *CCM2* and *PDCD10*). Morrison and Akers² described in detail the natural history and molecular genetics associated with this lesion. The most common attribution will be mutations in *KRIT1*/*CCM1*, followed by *CCM2* and *PDCD10*/*CCM3*.² *KRIT1*, however, has the least severe clinical phenotype but has more common skin lesions.³ *CCM3* mutation carries a higher risk of haemorrhage and present earlier than *CCM1* and *CCM2*.⁴ In our case, his father was diagnosed with the same condition at the age of 18. Blood samples were sent for genetic analysis to determine the mutational type.

Patients with familial cases usually have multiloculated cavernomas in different areas, either supratentorial or infratentorial and can be small enough that they remain asymptomatic and therefore only require radiological surveillance.²⁻⁴ Symptomatic episodes such as recurrent seizures can be treated conservatively, unless surgically accessible specific lesion is responsible for seizures that are disabling.¹⁻² Azam *et al*⁵ described a 50 h old infant, who

Figure 3 An axial view of T1-weighted (A) and a sagittal view of T1 fluid-attenuated inversion recovery (FLAIR) (B) MRI brain showed cavernomas in both supratentorial and infratentorial area.

Figure 4 (A–C) An axial view of MRI susceptibility-weighted imaging sequence on different slices demonstrating multiple cavernoma within the supratentorial brain. They are predominantly within the superficial and deep white matter, the left temporal and the right occipital lobe (full arrow). In infratentorial area (D), there is a mixed signal intensity on the right cerebellar peduncle and on the left side of the pons, in keeping with fluid/haemorrhage at different level. A marked hyper intense halo noted within the right side of the pons which could represent an acute lesion (dashed arrow).

Figure 5 A non-contrast CT brain of axial (A and B) and sagittal (C) view showed a re-haemorrhage in both right cerebellar and pontine regions as evidenced by an increased of hyperdensity area (full arrow).

presented with seizure and was found to have two separate cavernomas; right frontal lobe and adjacent to right lateral ventricle. This infant was treated with antiepileptic medication. Conservative approach should not be the main treatment as paediatric cavernoma naturally manifest with an increase in size, repeated haemorrhages and recurrence of seizures from cerebral irritation or cranial nerve palsy, as illustrated in our case. Ideally, any surgical treatment should be performed electively, with the luxury of careful surgical planning and appropriate family counselling regarding the options of surgery and conservative management.⁶ However, these with acute hydrocephalus and brain stem compression needing surgery; which was the case in this child's initial presentation. A few reported cases have described patients who presented with obstructive hydrocephalus secondary to haemorrhage from cavernomas requiring an external ventricular drainage followed by VP shunt and excision of cavernomas.^{7 8} Several studies have concluded that, in patients with symptomatic lesions abutting the pial surface, those who have had repeated haemorrhages causing progressive neurological deterioration, who have experienced acute

haemorrhages outside the lesion's capsule, or who have a significant mass effect after haemorrhage within the lesion itself, should undergo surgical treatment with the goal of cure.^{9 10} Complete resection definitively eliminates further haemorrhagic risk.^{1 11}

Hence to summarise, familial multiple cavernous malformations are rare and there is consensus that treatment needs to be symptomatic. Diagnosis is relatively easy and, in a symptomatic child with a family history, a CT scan alone may be enough in making the diagnosis. Considering the radiation exposure through CT, MRI brain may be performed to obtain details about the precise number and location of cavernomas. In non-accessible eloquent areas, conservative management is followed due to the high risk incurred with surgical treatment. More recently, radiosurgery is being considered as an alternative treatment modality though the long-term results are still not available.

The index case illustrates the difficulty in the management of these patients. The patient had a strong family history and had presented with a bleed prior to the index presentation. As these patients have multiple cavernomas

in different parts of the brain, surgery is clearly not an option and it is not possible to remove all of them. Moreover, de novo cavernomas are known to form in patients with a genetic predisposition.

Learning points

- ▶ Treatment of familial cerebral cavernous malformation (CCM) in infants remains a dilemma but the most important step is establishing an early diagnosis.
- ▶ Depending on the severity of the initial diagnosis, treatment options range from radiological surveillance to surgical excision.
- ▶ Patients who present with recurrent bleeds may be candidates for surgery balancing risks versus benefits.
- ▶ Genetic test is mandatory in elucidating specific mutation involving one of the three genes (*KRIT1*, *CCM2* and *PDCD10*).
- ▶ De novo cavernomas are known to form in patients with a genetic predisposition.

Competing interests None.

Patient consent Obtained.

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