Unusual association of diseases/symptoms

Familial cerebral cavernomas due to a *KRIT1* mutation presenting with epilepsySanjeev Rajakulendran,¹ Sreeman Andole,² Angus Kennedy¹¹Department of Neurology, Chelsea and Westminster Hospital, Barnet Hospital, Barnet, UK;²Department of General Medicine and Geriatrics, Chelsea and Westminster Hospital, Barnet Hospital, Barnet, UK**Correspondence to** Dr Sreeman Narayan Andole, sreeman@doctors.org.uk**Summary**

The authors present the case of a 25-year-old individual who presented acutely following a generalised tonic-clonic seizure. Brain MRI of the individual demonstrated the classical appearance of multiple cerebral cavernous haemangiomas (cavernomas). There was an autosomal dominant family history. Genetic testing identified a truncating mutation in the *KRIT1* gene in the individual and confirmed the diagnosis of familial cerebral cavernomas as the cause of epilepsy in the family.

BACKGROUND

The case illustrates a number of important points. First, it underpins the importance of obtaining a detailed family history in patients who present with seizures. Although pure monogenic forms of epilepsy are rare, genetic testing may be available and should be considered. Second, it highlights the role and value of brain imaging (particularly MRI) in the management and investigation of patients with epilepsy. In addition, this case illustrates the classical MRI appearances of cerebral cavernomas.

CASE PRESENTATION

A 25-year-old right-handed man presented acutely following one witnessed generalised tonic-clonic seizure of 2 min duration followed by a period of postictal confusion. Prior to his seizure, he described difficulty in concentrating and visual disturbance. Subsequent neurological examination was unremarkable. He had no relevant medical history. On further questioning, it came to light that his sister was being treated for epilepsy as a result of multiple cerebral cavernomas and that the proband's father also had lifelong epilepsy.

INVESTIGATIONS

Initial investigations including blood tests, an ECG and a chest x-ray were all normal. A CT scan of his head revealed multiple high signal lesions in the temporal lobes, the left frontal cortex and above the third ventricle (figure 1A,B). Subsequent MRI demonstrated the classical appearances of multiple cavernous haemangiomas (figure 1C,D). Genetic analysis of the proband identified a four base pair deletion in exon 13 of the *KRIT1* gene (c.1201_1204delCAAA). This is predicted to result in a premature termination of the KRIT1 protein (p.Gln401ThrfsX10) and is therefore likely to be pathogenic.

TREATMENT

The patient was started on sodium valproate following his acute presentation.

OUTCOME AND FOLLOW-UP

He has been seizure free for 8 months.

DISCUSSION

The presence of cerebral cavernomas in both siblings and the presence of epilepsy in their father suggested a diagnosis of familial cerebral cavernous haemangiomas. Genetic screening of the *KRIT1* gene identified a causative mutation in the patient and confirmed the diagnosis. Cavernomas are vascular anomalies consisting of closely packed capillaries which are devoid of intervening brain parenchyma. The majority of cavernomas in this dominantly inherited disorder are supratentorial. Although approximately 25% are asymptomatic throughout life, affected individuals may present with headaches, seizures and focal neurological deficits depending on the size and location of the cavernomas. To date three genes have been associated with familial cavernomas: *KRIT1* (CCM1, chromosome 7q), *CCM2* (MGC4607, chromosome 7q) and *CCM3* (PDCD10, chromosome 3q).¹⁻³ Although their exact functions are unclear, they are all thought to play a role in angiogenesis.

Learning points

- ▶ In the assessment of individuals who present with a seizure, a family history is important to elicit as the genetic predisposition to epilepsy is substantial.
- ▶ Genetic tests are available for a number of monogenic forms of epilepsy and should be considered in discussion with the patient.
- ▶ Brain imaging (particularly MRI) is important in excluding structural causes of epilepsy.
- ▶ Although rare, cerebral cavernomas may present with seizures.

Competing interests None.

Patient consent Obtained.

Figure 1 CT (A and B) and MRI (C and D) scans demonstrating the appearance and locations of the cavernomas in the individual.

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