Clinical Case Report

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Familial intracranial arachnoid cysts with a missense mutation (c.2576C > T) in *RERE*

A case report

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Abstract

Rationale: Arachnoid cysts are relatively common intracranial space-occupying lesions; nevertheless, familial intracranial arachnoid cysts are extremely rare, with only a few cases having been reported.

Patient concerns: The proband was a 7-year-old girl who had experienced generalized tonic-clonic seizures 5 times in the 8 days prior to admission. Nine months later, her 6-year-old younger female cousin presented to us with a 3-day history of headache.

Diagnoses: Brain magnetic resonance imaging (MRI) confirmed the diagnosis of arachnoid cyst for both of the girls.

Interventions: A cyst-peritoneal shunting and cyst fenestration were performed for the 7-year-old girl and her cousin separately. Sanger sequencing revealed a heterozygous missense mutation (c.2576C > T) in the Arginine-Glutamic Acid Dipeptide Repeats gene (*RERE*).

Outcomes: The outcome was favorable and the follow-up was uneventful.

Lessons: We hypothesize that the mutation in *RERE* may be associated with the pathogenesis of familial intracranial arachnoid cysts.

Abbreviations: CT = computed tomography, MRI = magnetic resonance imaging, *RERE* = arginine-glutamic acid dipeptide repeats gene.

Keywords: arginine-Glutamic acid dipeptide repeats gene, familial arachnoid cyst, gene, mutation

1. Introduction

Intracranial arachnoid cysts are congenital malformations that are characterized by abnormal cerebrospinal fluid collections within the arachnoidal membrane and subarachnoid space of the cisterns and major cerebral fissures.[1] Intracranial arachnoid cysts are relatively common entities accounting for approximately 1% of all intracranial space-occupying lesions.[2] However, familial intracranial arachnoid cysts are extremely rare, with only a few cases having been reported; the pathogenesis and clinical manifestations of familial intracranial arachnoid cysts are yet to be well elucidated.

Herein, we report a family with familial intracranial arachnoid cysts, and review the relevant published literature.

2. Case report

The proband was a 7-year-old girl who had experienced generalized tonic-clonic seizures 5 times in the 8 days prior to admission. The neurological examination showed no abnormalities, and the previous medical history was unremarkable. Brain magnetic resonance imaging (MRI) revealed an arachnoid cyst in the left anterior and middle cranial fossa (Fig. 1A and B). A cyst-peritoneal shunting was performed, and oral sodium valproate was administrated for 6 months postoperatively. During the follow-up period of 8 months, she was free of seizures; follow up computed tomography (CT) imaging demonstrated that the cyst was significantly reduced in size (Fig. 1C).

Nine months after the presentation of the proband, her 6-year-old younger female cousin presented to us with a 3-day history of headache. The physical examination was normal, and the previous medical history was unremarkable. Brain CT and MRI showed an arachnoid cyst in the right anterior and middle cranial fossa (Fig. 2A and B). A craniotomy with cyst fenestration was performed. Intraoperative and histopathological findings were consistent with the diagnosis of an arachnoid cyst. The postoperative course was uneventful and the headache was completely relieved. When discharged, repeated CT imaging showed that the cyst was significantly reduced in size (Fig. 2C). Both of the patients are the only child in their families; brain CT imaging was performed on their parents and no abnormalities were observed.

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Yubo Wang and Jiayue Cui contributed equally to this work.Patient consent: The patients have provided informed consent for publication of the case.

The authors have no conflicts of interest to disclose.

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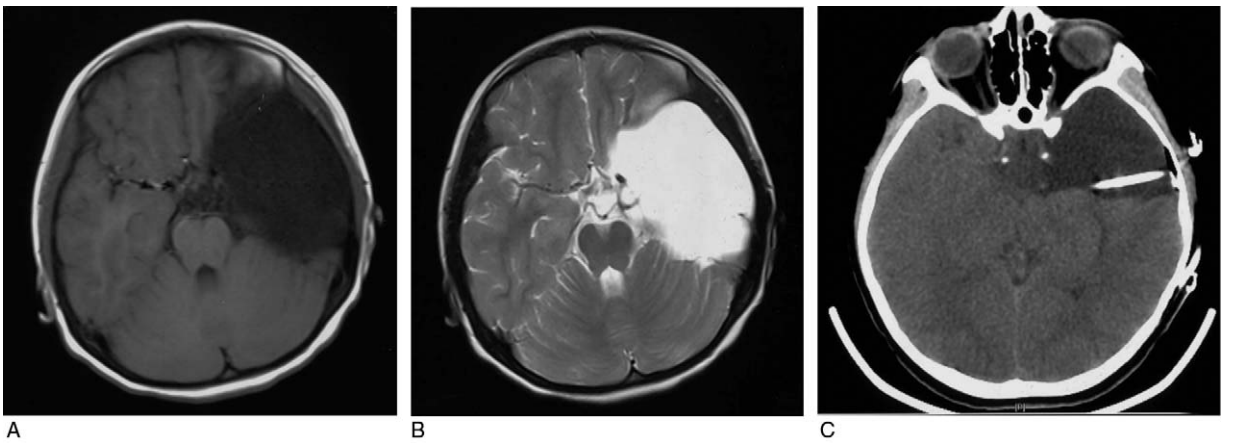

Figure 1. Radiological examination of the proband. Preoperative T1-weighted (A) and T2-weighted (B) MRI show an arachnoid cyst in the left anterior and middle cranial fossa. Follow-up CT 8 months postoperatively shows that the size of the cyst was significantly reduced (C). CT = computed tomography, MRI = magnetic resonance imaging.

Sanger sequencing revealed a heterozygous missense mutation (c.2576C > T) in the Arginine-Glutamic Acid Dipeptide Repeats gene (*RERE*) in both of the patients and their fathers.

3. Discussion

Arachnoid cysts were originally described by Bright et al in 1829, where it was proposed that the formation of arachnoid cysts may be due to the splitting of the arachnoid.[3] In the past hundred years, arachnoid cysts have been considered to be the most common intracranial space-occupying entity in the general population.[4] Arachnoid cysts are congenital and benign, and the majority of these cysts are asymptomatic and require no special attention.[4,5] The most common locations of arachnoid cysts include the middle fossa, retrocerebellar, and convexity; moreover, middle fossa cysts are reported predominantly left-sided.[5] Helland et al studied 299 patients with 305 arachnoid cysts. They noted a sex dependency for some intracranial locations of arachnoid cysts, with temporal cysts occurring more frequently in males, and cerebellopontine angle cysts occurring more frequently in females.[6] The therapeutic approaches for the treatment of arachnoid cysts include cyst-peritoneal shunting, craniotomy or endoscopic fenestration, and stereotactic aspiration. Pradilla et al believe that advances in neurosurgical techniques and neuroendoscopy continue to favor fenestration over cyst-peritoneal shunt placement as the surgical option for the treatment of arachnoid cysts.[1]

The majority of case reports of intracranial arachnoid cysts are sporadic, and only a few familial cases have been reported.[7–15] Various gene mutations and concomitant disorders have been identified in familial cases.[7–15] However, these gene mutations show great heterogeneity with no repetition. In the current case, we found a *RERE* mutation in both of the affected patients. *RERE*, located in the proximal 1p36 critical region, is a widely-expressed nuclear receptor coregulator that positively regulates retinoic acid signaling.[16] Animal experiments indicate that a *RERE* mutation might be associated with many structural and developmental birth defects. Fregeau et al found that mutations in *RERE* can cause a genetic syndrome, which was subsequently described as a neurodevelopmental disorder with or without anomalies of the brain, eye, or heart.[16] Jordan et al also reported 9 unrelated individuals with this syndrome that were caused by *RERE* mutations.[17] Notably, we found that 1 patient in Fregeau report had an arachnoid cyst in the posterior fossa,[16] and 1 patient in Jordan report had mildly prominent cerebrospinal fluid space.[17]

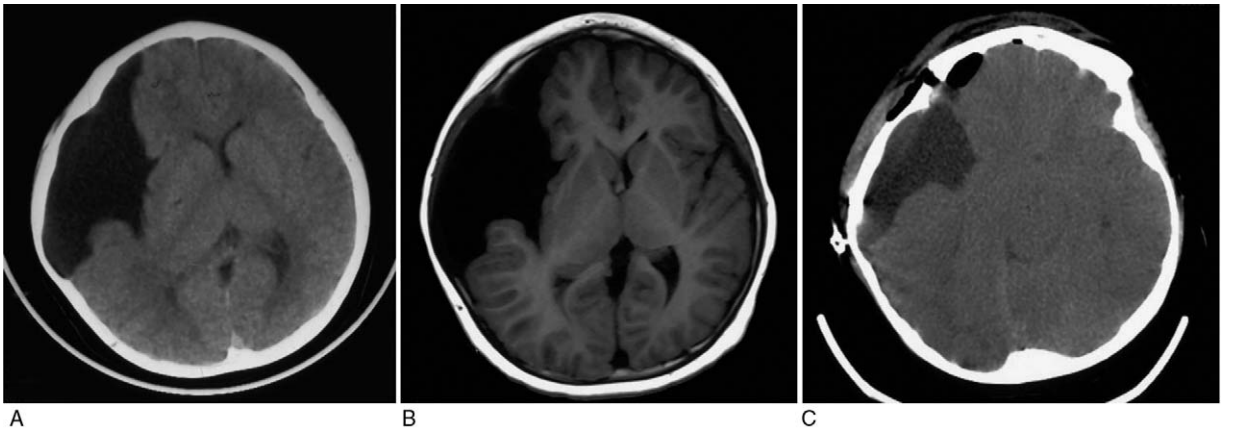

Figure 2. Radiological examination of the proband's cousin. Preoperative CT (A) and T1-weighted MRI (B) show an arachnoid cyst in the right anterior and middle cranial fossa. When discharged, a repeated CT shows that the size of the cyst was significantly reduced (C). CT = computed tomography, MRI = magnetic resonance imaging.

We speculate that *RERE* may be associated with intracranial arachnoid cysts and intracranial arachnoid cysts may be a part of the *RERE*-related genetic syndrome. Although human evidence supporting the role of *RERE* in neurodevelopmental disorders has been lacking, the association between *RERE* mutations and familial arachnoid cysts should be highlighted.

Author contributions

Conceptualization: Xinyu Hong.
Data curation: Yubo Wang, Jiayue Cui, and Xiaowei Qin.
Writing – original draft: Yubo Wang and Jiayue Cui.
Writing – review & editing: Yubo Wang, Jiayue Cui, and Xinyu Hong.

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