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Case Report

Epilepsy as the First Presentation of Arterial Tortuosity Syndrome in a Young Girl: A Case Report

Genç Bir Kızda Arteriyel Kıvrımlılık Sendromunun İlk Sunumu Olarak Epilepsi: Bir Olgu Sunumu

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ABSTRACT

Arterial tortuosity syndrome (ATS) is an extremely rare autosomal recessive connective tissue disorder characterized by tortuosity and elongation of all major arteries. We report a clinical case of a girl with this rare condition, who initially presented with epilepsy. DSA or MRA revealed a severe arterial tortuosity. EEG showed epileptiform discharge in right frontotemporal hemisphere. Here, we report the first case of ATS presenting with epilepsy. We discussed the possible clinical implications of this rare clinical presentation. Moreover, we suggest that some patients presenting with epilepsy might need serious cerebral vascular evaluation and ATS needs to be considered in the differential diagnosis.

KEYWORDS: Arterial tortuosity syndrome, Epilepsy, Digital subtraction angiography

ÖZ

Arteriyel tortüozite sendromu (ATS) tüm majör arterlerde tortüozite ve uzama ile karakterize olan çok nadir bir otozomal resesif bağ dokusu bozukluğudur. Burada, başlangıçta epilepsi ile gelen bu nadir durumun bulunduğu bir kız çocuğunun klinik olgusu sunulmaktadır. DSA ve MRA şiddetli arteriyel tortüozite gösterdi. EEG sağ frontotemporal hemisferde epileptiform deşarj gösterdi. Bu nadir klinik sunumun olası klinik sonuçlarını tartışıyoruz. Ayrıca epilepsi ile gelen bazı hastalarda ciddi serebral vasküler değerlendirme gerekebileceğini ve ayırıcı tanıda ATS'nin dikkate alınması gerektiğini belirtiyoruz.

ANAHTAR SÖZCÜKLER: Arteriyel kıvrımlılık sendromu, Epilepsi, Dijital subtraksiyon anjiyografisi

INTRODUCTION

Arterial tortuosity syndrome (ATS, OMIM #208050) is an extremely rare autosomal recessive connective tissue disorder characterized by tortuosity and elongation of all major arteries, including intracranial arteries, and its associated complications that include aneurysm formation, dilatation, and stenosis (1,8). In addition, patients often display hyperextensible skin, hypermobility of joints, and hernia (4). To our knowledge, there are no published reports on ATS presenting with epilepsy. Here, we report a clinical case of a girl with this rare condition, who initially presented with epilepsy and discuss the possible clinical implications of this rare clinical presentation.

CASE REPORT

A 10-year old girl who weighed 39 kilogram and measured 137 centimeters in height was admitted to our department with recurrent seizures. The seizures were characterized by sudden onset of staring and were often followed by vomiting or tonic stiffening of the arms. There was no history of any perinatal complications including trauma, intrauterine infections or radiation exposure, and she was born full term. On physical examination, we found that the skin was soft and there were no connective tissue manifestations, and other physical examinations were within normal limits. Routine hematological and urine tests were normal with the exception of abnormally high levels of lactic acid in the blood which measured 2.5 mmol/L. Routine chest x-ray was also normal. Dynamic electroencephalogram (EEG) monitoring showed epileptiform discharge in right frontotemporal hemisphere and magnetic resonance imaging (MRI) of the brain showed arteriovenous malformations (Figure 1A). Magnetic resonance angiogram (MRA) revealed severe abnormalities in anterior cerebral artery (Figure 1B). Further, three-dimensional digital subtraction angiography (DSA) confirmed the elongation and tortuosity in the A1 and A2 segments of the right anterior cerebral artery and a small aneurysm formation in the proximal end of anterior cerebral artery (Figure 1C,D). The findings of severe vascular malformation with tortuosity, elongation and aneurysm formation were suggestive of ATS. Hence, we recommended genetic screening for SLC2A10 gene, ultrastructural analysis of the skin and aggressive management ap-

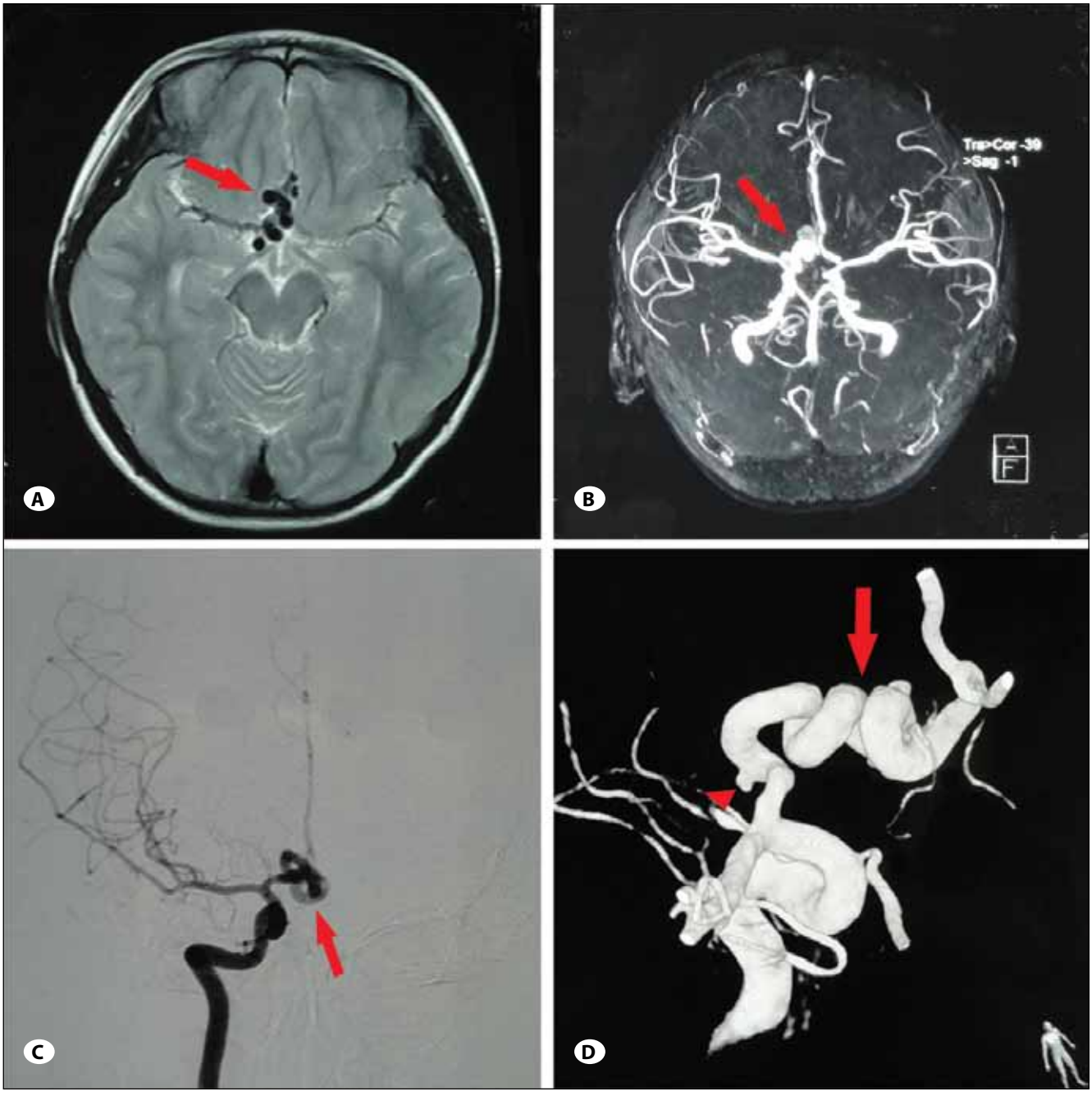

Figure 1: A) Brain MRI showed arteriovenous malformations (red arrow). **B)** MRA revealed severe abnormalities in anterior cerebral artery (red arrow). **C,D)** DSA confirmed the elongation and tortuosity in the A1 and A2 segments of right anterior cerebral artery (red arrow) and a small aneurysm formation in proximal end of anterior cerebral artery (red arrowhead).

proaches, which was declined by the patient's family due to economic concerns. Furthermore, we could not opt for surgical resection as per the wishes of the family members. Hence, we prescribed long-term antiepileptic medications to control seizures, and advised long-term regular follow-ups and recommended follow up serial imaging. It would be interesting to see how the malformation would change over the natural course of time in the long-term. No seizures were reported at 1-year follow-up.

DISCUSSION

ATS is an autosomal recessive connective tissue disorder that can affect the entire body. Patients can have a variable degree of elongation and tortuosity of the systemic vessels along with formation of aneurysms. ATS affecting the cerebral vessels have been previously reported. The angiographic images of our patient showed severe tortuosity and elongation of the right anterior cerebral artery with a small aneurysm formation

that are typical features of ATS. To the best of our knowledge, this is the first report about the association of ATS and epilepsy.

There are various possible reasons as to how ATS could be involved in the pathogenesis of epilepsy. First, genetic factors play a key role both in the pathogenesis of ATS and epilepsy (5). ATS occurs due to mutations in SLC2A10 gene, which is mapped on chromosome 20q13.1 that encodes for the 541 amino acid facilitative glucose transporter 10 (GLUT10) (5). High levels of lactic acid in our patient suggest a possible glucose metabolism disorder that could be a result of a mutation in the GLUT10. A mutation in the GLUT10 gene can lead to the upregulation of transforming growth factor-β (6), which has been identified to induce a novel putative epileptogenic signaling cascade (3). It is therefore likely that in our patient ATS was associated with a mutation in the SLC2A10 gene, which could have predisposed her to developing epilepsy. Second, Cartwright et al. showed that ATS is a risk factor for stroke (2). It is well known that epilepsy is a common complication of stroke and patients who have large sized strokes are at a higher risk of having seizures. It is possible that arterial kinking resulted in unstable blood flow to the seizure focus in our patient, which eventually led to the occurrence of epilepsy. Third, there is recently a large body of evidence describing the clinical presentation of seizures in patients with autoimmune disorders (7). It is postulated that ATS can lead to seizures likely by activating both specific and nonspecific immunity. Even though the concept of an immunological involvement in epilepsy has been gaining an increasing number of supporters, the immunoglobulin and complement levels in our patient were within normal limits, and we therefore cannot conclude what role immune system activation has in our patient manifesting with seizures. Finally, it is also possible that their coexistence of ATS and epilepsy may be purely coincidental.

CONCLUSION

To our knowledge, we report the first case of ATS presenting with epilepsy. This case provides strong evidence that, on rare occasions, epilepsy can be the first manifestation of an uncommon syndrome. We suggest that some patients presenting with epilepsy might need serious cerebral vascular evaluation and ATS need to be considered in the differential diagnosis.

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