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Case study

Perisylvian polymicrogyria, infantile spasms and arthrogryposis: The severe end of the spectrum of congenital bilateral perisylvian polymicrogyria

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ABSTRACT

Congenital bilateral perisylvian polymicrogyria (CBPP) is the most frequent type of polymicrogyria in children. A 3-month-old male patient is described here with the combination of CBPP, infantile spasms and arthrogryposis. Only four patients have been reported earlier in the literature with this combination. Three of them had epilepsy. These patients represent the more severe phenotype of CBPP, characterized by early onset of symptoms, epilepsy, mental retardation, pseudobulbar palsy and arthrogryposis.

1. Introduction

Polymicrogyria is a malformation of cortical development resulting in an irregular cortex with multiple small, partly fused gyri, divided by shallow sulci. Polymicrogyria can be focal, diffuse, unilateral or bilateral. Different types with specific topographic distribution were described illustrating a clinical, etiological and histological heterogenicity. Polymicrogyria can occur as a single isolated anomaly or a familial case, or as part of a congenital anomalies/mental retardation syndrome. The incidence of polymicrogyria is not known but currently the diagnosis is made more frequently because of advances in magnetic resonance imaging (MRI).[1,2] Congenital bilateral perisylvian polymicrogyria (CBPP) is the most frequent type.

We report a 3-month-old male patient with the combination of congenital bilateral perisylvian polymicrogyria, infantile spasms and arthrogryposis.

2. Case history

The proband is the second child of non-consanguineous healthy parents. Family history was unremarkable. At 20

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weeks gestation intra-uterine growth retardation was noticed. He was born after induction of labour at 42 weeks. Birth weight, length and head circumference were at the third percentile. Clinical examination at birth showed arthrogryposis of both wrists and fingers. Protrusion of the tongue was seen. Severe feeding difficulties and excessive drooling due to weak sucking were seen in the first weeks of life. Nevertheless, initial development was normal with eye pursuit at four weeks and social smile at six weeks. At age three months he presented with infantile spasms. At that time he was found to have microcephaly (head circumference 38 cm, third percentile = 38,2 cm). Weight and length were in the third percentile. Arthrogryposis, protrusion of the tongue and drooling were noticed again. Arms and legs were hypertonic, the trunk was hypotonic with excessive head lag. The rest of the clinical examination was normal. Routine blood and urine tests as well as the results of metabolic screening were normal. Serum antibodies against CMV were negative. Ultrasound of the heart was normal. Karyotype was normal (46,XY). Cerebral MRI showed bilateral perisylvian polymicrogyria (Fig. 1). The EEG showed a spike focus in the right frontal lobe and background slowing but no hypsarrythmia. Clinically the seizures were suggestive of infantile spasms. Treatment with vigabatrine (160 mg/kg/d in 2 gifts) was started. The infantile spasms stopped but he kept having attacks existing of a short cry followed by clonic activity of both legs. The arms didn't participate anymore. After topimarate (6 mg/kg/d in 2 gifts) was started, he became seizure free. However, infantile spasms reoccurred one month later. The topamirate dose was doubled and nitrazepam and valproate were added, without success. Finally seizures were controlled under treatment with corticotropin (ACTH).

3. Discussion

Congenital bilateral perisylvian polymicrogyria (CBPP) is a recognizable neuronal migration disorder. Bilateral, generalized types of polymicrogyria are often hereditary. It can be part of a congenital anomalies/mental retardation syndrome, and was reported in patients with Aicardi syndrome, Walker-Warburg syndrome and Prader–Willi syndrome.[1,3,4] CBPP was also seen in patients with chromosomal abnormalities, including patients with 22q11 deletion.[1,5,6] Familial occurrence of CBPP was reported in the literature in 28 families. All patterns of inheritance were seen with different penetrance,[1,5,6] although in the majority of the families (75%) X-linked inheritance was found. In the series reported by Villard, male predominance of 60% was seen and males were more severely affected than females.[7] Linkage analysis in five families revealed a locus on the distal part of the long arm of chromosome X in the Xq28 region. The responsible gene has not been identified yet.[1,6,7] Focal asymmetric polymicrogyria tend to be more acquired.[1–3,5,8,9] It occurs later during the organization phase of cerebral development between the 16th and 24th week of gestation[1,2,5] and can be seen f.e. after intra-uterine infection (CMV), hypoperfusion of the placenta, twin to twin transfusion syndrome, maternal drug-intake, maternal carbon monoxide inhalation. Bilateral, generalized types of polymicrogyria are mostly unlayered. The external molecular layer is continuous and does not follow the profile of the convolutions. The underlying neurons have radial (or vertical) distribution but no laminar organization[5]. In focal, asymmetric polymicrogyria the cortex exists usually of only four layers (molecular, outer cellular, cell sparse, and inner cellular) instead of the six layers in the normal cortex[9]. Four-layered and unlayered polymicrogyria can co-occur in contiguous cortical areas, indicating that they may compromise a single spectrum.[5]

The diagnosis of CBPP is based on the typical MRI findings.[1–3,6,9,10] The cerebral cortex is abnormally thickened and infolded on the borders and in the depth of the sylvian fissures, with multiple small gyri in the depth of the sylvian fissures. In addition, the sylvian fissures are more vertically oriented and extend more posteriorly up to the parietal lobes. CBPP is usually symmetric but varies in extent among patients.[1,9]

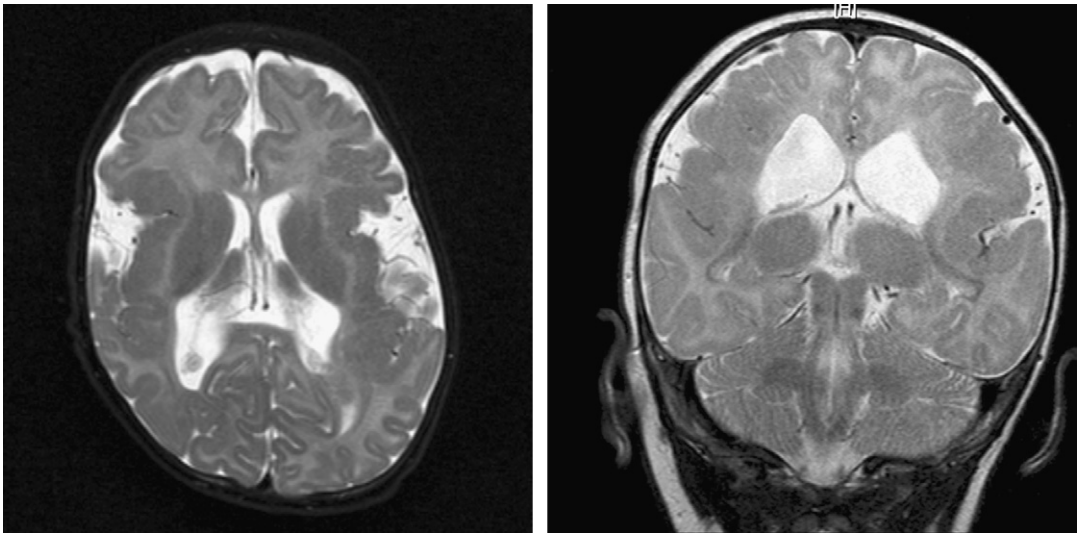

Fig. 1 – Cerebral MRI at the age of 3 months. Extended symmetric polymicrogyria with irregular thickened and abnormally infolded cortex bilaterally on the borders and in the depth of the broad Sylvian fissures as seen in bilateral perisylvian polymicrogyria.