Polymicrogyria, Large Corpus Callosum and Psychomotor Retardation in Four-Year-Old Girl: Potential Association Based on MR Findings

A Case Report and Literature Review

CATERINA BUDAI¹, GIULIA MOSCATO¹, FRANCESCO PATRUNO¹, MARCO LEONARDI¹, MONICA MAFFEI²

¹Neuroradiology Department, IRCCS Institute of Neurological Sciences, Bologna University; Bologna, Italy

²Neuroradiology Department, IRCCS Neurological Research Hospital Bologna; Bologna, Italy

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SUMMARY – *We describe a child from consanguineous parents presenting mega corpus callosum (MegaCC), polymicrogyria, psychomotor retardation with swallowing difficulties and language impairment perhaps linked to the syndrome of megalencephaly-polymicrogyria-mega corpus callosum (MEG-PMG-MegaCC). Reviewing the literature, we speculate that MegaCC, psychomotor retardation and anomalies in cortical migration are the three pathognomonic features. The presence of additional possibly associated anomalies such as megalencephaly, indicates that the spectrum of linked malformations with this rare syndrome is broad and yet to be defined.*

Introduction

The literature reports only a few cases of children presenting the association between the enlarged corpus callosum (MegaCC), polymicrogyria (PMG) and psychomotor retardation. Göhlich-Ratmann et al.¹ and Dagli et al.² respectively presented three and one paediatric patients with these abnormalities associated with megalencephaly (MEG-PMG-MegaCC; OMIM 603387). Pierson et al.³ subsequently advanced the hypothesis that this pathologic entity could also be defined without megalencephaly, through the report of a single case. Additionally, Bindu et al.⁴ published two case reports of children from consanguineous parents presenting the same pathological features, without megalencephaly and in association with posterior fossa anomalies.

We believe that this case report strengthens the hypothesis of a syndrome composed of MegaCC, abnormality in the rotation of the cortex

(especially polymicrogyria) and psychomotor retardation, not necessarily in association with megalencephaly or other additional anomalies.

Case Report

We describe the case of a four-year-old girl from Morocco, the child of healthy consanguineous parents (grade 1/32). The family history was negative; pregnancy was normal until the VIII month when the mother had an abdominal trauma, with loss of consciousness. From that moment on, she referred increased foetal movements. Childbirth was normal at 38 weeks' gestation.

The child's birth weight was 3.080 kg (10-25th percentiles), her height was 50 cm (50-75th percentiles) and her head circumference was 33 cm (10-25th percentiles); she also had an Apgar score of 9 at one and five minutes. Neonatal growth was normal. At eight months of age,

Figure 1 MRI at age 4 years. Mid-sagittal 3D T1-weighted image: diffuse enlargement of the corpus callosum, thickened in all portions to a similar degree.

Figure 2 MRI at age 4 years. Coronal IR white-matter image: bilateral incomplete opercularization and polymicrogyria of the both frontal lobes.

she had psychomotor retardation with no language development, axial hypotonia and swallowing difficulties. Diffuse cortical atrophy was interpreted at the cerebral CT scan and the first diagnostic hypothesis was infantile cerebral palsy. Consequently, motor and language rehabilitation was started.

At three years of age, the patient was seen in our neurological clinic for the first time. The neurological findings were: global psychomotor delay with good eye contact and social smile, absence of language expression with good comprehension, difficulties in mastication, dysphagia especially for liquids, diffuse hypotonia with mild right focal hypertonia. She maintained the sitting position and she had joint hyperextensibility; reflexes were mildly brisk at upper limbs. Dystonic movements of the head were sometimes noted. She also showed sporadic gaze avoidance.

At the time of hospitalization (four years of age), she presented further improved in motor development, represented by the ability to lift herself up on her knees. She also had stiffness in her limbs.

Laboratory, genetic and neurological data

– EEG (two years of age): right fronto-temporal spike-waves and fast rhythms in fronto-temporal areas.

- Fundoscopic examination: normal;
- EMG: normal;
- Neuropsychological evaluation: at the age of three years she had a Bayley scale mental score corresponding to eight months; the score was mainly reduced because of motor difficulties.
- Genetic analysis: normal 46 XX karyotype and subtelomeric rearrangements, CPK and homocysteine within normal limits, such as ARRAY CGH

Neuroradiological findings

At eight months of age, the young patient had a CT examination in Morocco, revealing “diffuse cerebral atrophy”. At 15 months, she underwent the first MRI examination (at another hospital) which showed “diffuse cerebral thickness of precentral, medium and inferior frontal gyrus, suggesting polymicrogyria. The second MRI (3T scanner GE HDxt, General Electric Healthcare, Milwaukee WI, USA) was performed at four years of age and the sequences acquired were axial FLAIR and T2-w, volumetric sagittal T1-w and coronal FSE IR, FLAIR e GRE T2*-w. There was a prominent enlargement of corpus callosum (Figure 1), with a thickness of 13.77 mm: normal thickness mean measurement in genu region for children

Figure 3 Axial FSE T2-weighted image. Diffuse polymicrogyria and enlargement of the cella media of the lateral ventricles.

and adolescents between 4 and 18 years is 8.35 mm $\pm$ 0.80 mm (SD)⁵. This enlargement was associated with a diffuse polymicrogyria in the bilateral fronto-temporo-parietal regions, without side predominance, accompanied by incomplete opercularization of both Sylvian fissures (Figures 2 and 3). The ventricular system was of normal size, with the exception of a mild enlargement of the cella media of the lateral ventricles; no signs of hydrocephalus were noted. The basal ganglia were normally represented.

Discussion

The corpus callosum (CC) is an interhemispheric linkage system. Its structural development starts between eight and 12 weeks of gestation, ending at about 20-30 weeks^{6,7}; the progress of hemispheric development directly Results in growth of the CC^{8,9}.

Unilateral brain damage leads to corresponding atrophy of the CC or a total or partial absence of the same portion^{6,7}. On the contrary, enlargement of the CC in the absence of inflammation or neoplastic infiltration is extremely rare in neurological disease. Only two syndromes show this feature: Cohen syndrome and neurofibromatosis 1 (NF-1). Cohen syndrome is an autosomal recessive disorder including non-progressive mental retardation, microcephaly, distinct dysmorphic facies, hypotonia/joint hypersensitivity and isolated neutropenia¹⁰. NF-1 is an autosomal dominant disorder due to mutation in the NF-1 gene (encoding for neurofibromin); in absence of this molecule, biochemical pathways are consequently activated resulting in aberrant cell proliferation. Resulting

abnormalities, especially in the CNS, include macrocephaly, variable mental disorders and a thickened corpus callosum⁵.

As we can see, cranial dimensions are involved in both syndromes, but with opposite characteristics. In fact, pathophysiological correlations between cranial dimensions and CC size are unclear. Likewise, precise embryologic and pathophysiologic explanations for the enlarged corpus callosum remain speculative. Gohlich and Ratmann et al.¹ hypothesized that a possible mechanism of CC enlargement could involve bi-hemispheric overgrowth or an increase in neuronal density without actual overgrowth of the hemisphere. Even though our patient has a normal cranial size, she presents MegaCC, polymicrogyria and psychomotor retardation with mainly language and swallowing impairment. As a consequence, we can speculate, like Pierson et al.³, that our patient has a disorder corresponding to the MEG- PMG-MegaCC syndrome, confirming the hypothesis that MegaCC is the pathognomonic feature, while cranial dimensions are not significant.

Other authors⁴ described two cases of children with consanguineous parents presenting the same features as ours, in association with posterior fossa anomalies and without megalencephaly.

On the basis of the very limited and recent literature, we can state that all the reported patients shared MegaCC, psychomotor retardation and anomalies in cortical migration, so we conclude that these are the three pathognomonic features for the syndrome. Additional possibly associated anomalies indicate that the spectrum of linked malformations with this rare syndrome is broad and yet to be defined.

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Monica Maffei, MD
 Department of Neuroradiology,
 IRCCS Institute of Neurological Sciences
 Via Altura, 3
 40139 Bologna, Italy
 Tel.: +39/051/6225520
 Fax: +39/051/6225785
 E-mail: marco.leonardi@centauro.it