CASE REPORT

Commissural malformations: Beyond the corpus callosum

Malformations commissurales : au-delà du corps calleux

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Summary
Corpus callosum agenesis is frequently only the tip of the iceberg in midline commissural anomalies. Agenesis or hypogenesis of the remaining commissures including the anterior and hippocampal commissures should be excluded. Magnetic resonance imaging is the most sensitive imaging modality to identify commissural anomalies. Diffusion tensor imaging can be helpful to identify hypogenetic or absent commissures even in the preterm neonate.

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Corpus callosum; Commissures; Malformations; Diffusion tensor imaging

Introduction

Anomalies or abnormalities of the corpus callosum (CC) are well-known and frequently described cerebral malforma-
tions. Agenesis of the CC ranges in occurrence from seven per 1000 in the general population to three per 100 in the developmentally delayed population [3]. Developmental CC agenesis should be differentiated from secondary destruction of an initially normally developed CC as can be observed in trauma, infarction, hemorrhage and in several metabolic diseases. Developmental CC agenesis is associated with many congenital syndromes involving the development of the midline structures and/or forebrain. In developmental...
CC agenesis the delicate balance between various guidance molecules and chemorepellant molecules as well as their interaction with the receptors is disturbed. This may result in a failure of commissural axons to develop or to cross the midline [6]. Several commissures connect both cerebral hemispheres. The CC is the largest interhemispheric commissure, additional crossing white matter tracts include the anterior commissure (AC) and the hippocampal commissure (HC). Because CC agenesis is frequently associated with additional anomalies, the remaining midline commissures such as the AC and the HC should be carefully studied [1,2].

We present the imaging findings using anatomical magnetic resonance imaging (MRI) and diffusion tensor imaging (DTI) in a child with a commissural anomaly involving the CC, AC and HC.

**Case Report**

Routine ultrasound (US) examination of the head in a preterm (36 weeks of gestation) girl had revealed a complete agenesis of the CC. Further diagnostic work up was done on day seven of life by MRI and DTI to exclude additional malformations or focal lesions. Clinically the child was doing well, neurological examination was age appropriate. Imaging was performed on a 3 Tesla MRI unit (General Electric Medical Systems, Millwaukee, USA) according to the standard departmental protocol which includes sagittal and axial T2-weighted fast spin-echo (TR/TE, 6250/102 ms, field-of-view 180 mm, slice thickness 2.5 mm, matrix 512 × 384, averages: 2), axial T1-weighted spin-echo (TR/TE, 700/17 ms; field-of-view, 180 mm; slice thickness, 3; matrix, 256 × 224; averages, 2), axial T2*-weighted gradient-echo (TR/TE, 650/45 ms; field-of-view, 200 mm; slice thickness, 4 mm; matrix, 320 × 160; averages, 2). The diffusion tensor was sampled by repeating a diffusion-weighted single-shot spin-echo echo-planar sequence along six different geometric directions. Diffusion sensitization was achieved with two-balanced diffusion gradients centered around the 180° radio-frequency pulse. An effective b-value of 800 s/mm² was used for each of the six diffusion-encoding directions. An additional measurement without diffusion weighting (b = 0 s/mm²) was added. Scan parameter were TR/TE, 12000/91 ms; field-of-view, 220 mm; slice thickness, 3 mm; matrix, 128 × 128; average, 1. A total of 22 contiguous axial sections were acquired, covering the caudal medulla up to the vertex. Isotropic diffusion-weighted, apparent diffusion coefficient (ADC) and fractional anisotropy (FA) maps were generated using standard post-processing software (Functool; GE healthcare). Anatomical MRI images and FA maps were studied for the presence or absence of the following commissures: CC, AC and HC by two pediatric neuroradiologists in consensus.

MRI confirmed US diagnosis of a complete agenesis of the CC (Fig. 1[a,b]) with all classical imaging features previously described in the literature [1]. The mediolateral sulci are orientated perpendicular to the third ventricle, the roof of the third ventricle is elevated, the lateral ventricles run parallel in their course and are laterIALIZED on axial imaging and mildly dilated in the posterior aspect (colpocephaly). In addition, on coronal imaging the anterior horns of the ventricles reveal a "trident" configuration due to the medial impression of the ventricles by the anterior-posterior course of the well developed, T2-hypointense, Probst’s bundles and

**Figure 1**

(A) Sagittal, coronal T2-weighted MRI of the brain: midsagittal MRI reveals complete absence of the corpus callosum. Significantly hypoplastic anterior commissure visible along the superior lamina terminalis (arrow). Coronal images reveal the Probst’s bundles along the medial surface of the lateral ventricles (arrowheads) and the malrotated hippocampi (small arrows). (B) Axial T2-weighted MRI of the brain: no corpus callosum visible with colpocephaly and prominent interhemispheric III ventricle. (C) Axial fractional anisotropy maps of the brain: Probst’s bundles are easily identified as hyperintense bands of white matter along the medial surface of the lateral ventricles (arrows). The corticospinal tract (arrowheads) and the optic radiations (small arrows) are also displayed as hyperintense bundles.

(A) Séquences IRM T2 coronale et sagittale : la coupe sagittale médiane révèle l’absence complète de corps callosum. La commissure antérieure hypoplastique est visible le long de la lame terminale supérieure (flèche) ; les images coronales révèlent des faisceaux de Probst le long de la surface interne des ventricules latéraux (têtes de flèche) et une malrotation des hippocampes (petites flèches). (B) IRM en coupe axiale T2 du cerveau : pas de corps callosum visible avec colpocephalie et troisième ventricule interhémisphérique proéminent. (C) Cartographies d’anisotropie fractionnelle dans le plan axial : les faisceaux de Probst sont clairement identifiés comme des bandes hyperintenses de substance blanche le long de la surface interne des ventricules latéraux (flèches). Le faisceau corticospinal (têtes de flèche) et les radiations optiques (petites flèches) sont également visibles.
the everted cingulated gyri. There is no cingulate sulcus. The hippocampi are malrotated and appear vertical in orientation. The AC can faintly be detected along the superior lamina terminalis and is highly hypoplastic. No HC could be identified. The optic chiasm appeared normal. No additional malformations, in particular migrational anomalies were noted. The circle of Willis was intact. The volume of white matter appeared age appropriate.

DTI confirmed the complete agenesis of the CC (Fig. 1[c]). In addition, no AC or HC could be identified. The Probst’s bundles were easily identified as hyperintense bands on FA-maps that run medially to the lateral ventricles. The optic tract and radiation was also easily identified as FA-hyperintense tracts.

Discussion

The CC is the principal commissure connecting both cerebral hemispheres. Normal and abnormal development of the CC have been the focus of many studies. Recent advances in molecular, histological and immunohistochemical techniques resulted in the identification of commissural regulatory genes and guidance molecules. Ren et al. [6] carefully analyzed the callosal formation in the developing human fetal brain and compared their results with results of DTI. They concluded that multiple interacting mechanisms and molecules are required for midline commissure formation. The subcallosal sling, the midline glial populations and pioneering axons work together to guide axons across the midline. In addition, Northern blot analysis has shown that callosal fibers require multiple guidance mechanisms at molecular and cellular level in order to cross the midline properly [6].

Previous studies of Raybaud et al. [5], Hetts et al. [2] and Kueker et al. [4] also concluded that an agenesis of the CC is part of a spectrum of commissural anomalies. The AC and HC can also be simultaneously hypoplastic or absent. Hetts et al. showed that abnormalities of the AC is seen in 71% of agegnesis of the CC and in 67% of cases with a hypogenesis of the CC. Abnormalities of the HC were seen in 95% of patients with agenesis of the CC and in 88% of children with a hypoplastic CC [2]. In addition, not all patients with an agenesis of the CC will show Probst’s bundles [7]. Consequently, in cases of agenesis or hypogenesis of the CC, hypo- or agenesis of the additional commissures should be excluded. Agenesis of the CC is rarely a single malformation. Nowadays, maldevelopment of the commissures are categorized as part of the phenotypic spectrum of commissural anomalies. In our patient, the complete agenesis of the CC was accompanied by a nearly complete absence of the AC and HC. No additional anomalies were identified, no migrational disturbances, no callosal lipoma. The prognostic value of the degree of CC agenesis and the impact of coexisting AC and/or HC, absence or hypoplasia on neurocognitive outcome is not yet determined. Kueker et al. discussed that the combined absence of multiple commissures may represent a more severe form of cerebral malformation than CC agenesis alone. Further, prospective studies are mandatory. DTI with sensitive identification of the presence, absence or anomalous course of white matter tracts/commissures may be very helpful in answering these questions. In our case, DTI confirmed the absence of the three major commissures and also allowed to identify the Probst’s bundles in a preterm neonate.

Conclusion

Agenesis of the CC is frequently part of a more complex malformation involving multiple commissures and should accordingly be referred to commissural anomaly. If the CC is missing or hypoplastic, the remaining commissures should be evaluated. DTI can adequately detect the lack of commissures even in a preterm neonate. Further prospective studies are mandatory to determine the prognostic value of an exact identification of the severity of commissural anomalies.

References