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# Visual System Abnormalities in a Case of Nonsyndromic, Complete, Isolated Corpus Callosum Agenesis

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The corpus callosum (CC) is the largest white matter structure of the human brain involved in interhemispheric signal connections. Corpus callosum agenesis (CCA) is a brain malformation that can occur isolated or in conjunction with other congenital or developmental defects. It can be either complete or partial and can occur as an isolated disorder or as a part of other syndromes, such as Arnold–Chiari malformation, Dandy–Walker syndrome, De Morsier syndrome, schizencephaly, and holoprosencephaly (1). When a CCA occurs in a syndromic condition, due to chromosomal anomalies (2), relevant ocular findings are marked optic nerve pallor, optic nerve hypoplasia, or chiasmal defects (1). In the isolated condition, minimal ocular findings have been reported (3).

In this report, we describe ocular motility, macular, and visual pathway morphofunctional abnormalities detected in a 26-year-old man (G.M.), which were stand-alone signs of CCA condition.

Five months after birth, the patient underwent cytogenetic analysis and no numerical or structural chromosomal abnormalities were found (karyotype 46, XY). During growth and until present, in the absence of systemic or neurological signs and symptoms, genetic investigations were not performed.

Based on the reported reduced visual acuity (VA) in his right eye (RE), presumably for a history of amblyopia, the following evaluations were performed. Visual function revealed a best-corrected VA 20/32 in RE with a refraction of +4 D sphere and +1.50 D cylinder axis 50° and 20/20 in the left eye (LE) with a refraction of +5.25 D sphere and +0.25 D cylinder axis 80°; near vision was J7 and J3 character in RE and LE, respectively; color vision (assessed by Ishihara charts) was reduced (1/22) in both eyes (OU); kinetic visual field examination showed a centrocecal scotoma in RE and exclusion of blind spot from the I2 isopter in LE.

The orthoptic examination revealed a hypofunction of superior oblique muscle in LE and hypofunction of inferior oblique muscle in RE and hypofunction of medial rectus muscle in OU (RE > LE). In primary gaze, we observed a condition of divergent strabismus. In the far vision, an exotropia of 16 prismatic diopters (PD) with fixation of the LE and concomitant slight vertical misalignment was found, whereas in the near vision, an exotropia of 25 PD with fixation of LE was detected. In upgaze, alphabetic position and anomalous head position turned toward right were found. Stereopsis was absent. Pendular nystagmus was detected in OU, with fine amplitude and high velocity in primary position in RE and fine amplitude, slow velocity in the extreme positions of gaze with reduction of the same in convergence in LE. Pupils' reflexes were normal at the direct and consensual light stimulus.

Anterior segment findings were within normal limits; the fundus examination showed signs of slight macular retinal pigmented epithelium (RPE) dystrophy in LE and light pallor of the temporal side of optic nerve in OU (see **Supplemental Digital Content**, Figure, http://links.lww.com/WNO/A609).

The macular, retinal ganglion cells (RGC) and visual pathways' function was assessed using multifocal electroretinogram (mfERG), pattern electroretinogram (PERG), and visual evoked potential (VEP) recordings, respectively, by using recently published methods (4).

Due to the patient's instable fixation, no reliable mfERG responses were recorded. PERG P50-N95 amplitudes were reduced, and VEP 100 implicit time and N75-P100 amplitudes were delayed and reduced, respectively, in OU (reported on SDC1 and in Fig. 1A, respectively).

The morphological evaluation of the central retinal area and of the optic nerve was performed by swept source optical coherence tomography (SS-OCT) (DRI OCT Triton, Topcon Tokyo, Japan), with good reliability despite the presence of nystagmus, by using a recently published method (4). As presented on Figure 1B, the macular profile showed

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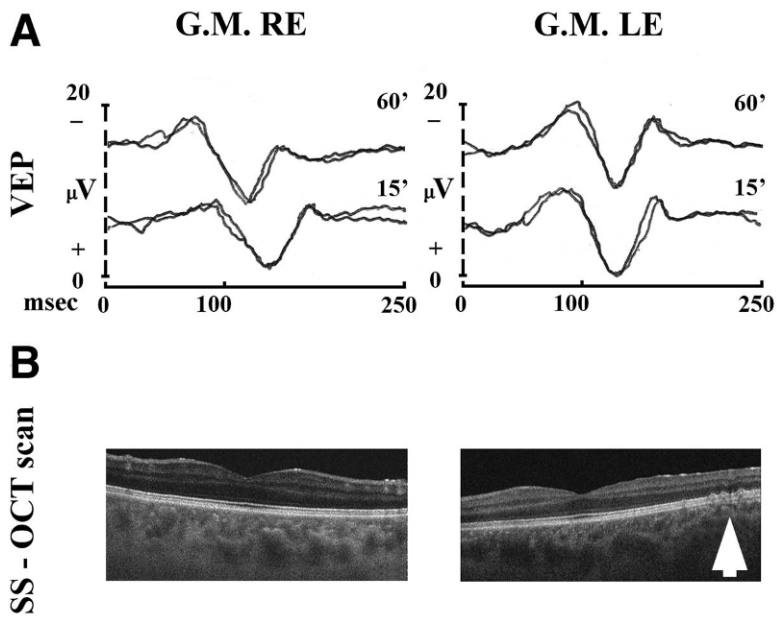


**FIG. 1.** VEP (**A**) recordings and macular (**B**) analyses by SS-OCT performed in a patient (G.M.) affected by isolated CCA. VEP were recorded in response to 60′ and 15′ checks of visual stimulation to evaluate the neural conduction along the large and small axons of the visual pathways, respectively. Delayed P100 implicit times (15′ VEP P100 implicit time was more delayed in RE than in LE) and reduced N75-P100 amplitudes were detected in OU. Normal macular morphology was seen in RE, whereas slight macular abnormalities, suggesting macular dystrophy, were detected in LE (see *arrow*).

normal inner and outer retinal layers morphology with hyper-reflectivity of the internal limiting membrane in RE. In LE, the macular profile appeared quite irregular for the presence of hyper-reflectivity and irregular band at the level of the internal limiting membrane in the inferior-temporal sector and irregular and hyper-reflective deposits at the level of RPE—choriocapillary such as macular drusen in the temporal sector of the macular region. As showed on SDC1, reduced retinal nerve fiber layer thickness was detected exclusively in the inferior-nasal sector in RE.

The presence of abnormal VEP responses suggested performing an MRI that failed to detect alterations of optic nerves and chiasma but showed a complete absence of the CC with the concomitant typical features, as showed in detail in Figure 2.

In summary, in the reported case, in association to isolated CCA, we observed reduced VA in RE, abnormal color vision, RGC and visual pathways dysfunction, pendular nystagmus in OU, and slight RPE macular dystrophy in LE. Our findings suggested that the reduced VA in RE could be ascribed to anisometric amblyopia with a concomitant dysfunction of RGC and of the neural conduction along the visual pathways (greater than LE).

Considering the lack of similar findings in the available literature, the observed visual pathways dysfunction in our patients with isolated CCA may suggest a novel interesting feature of optic nerve and of RGC neurodegeneration.

Regarding the observed ocular motility deficits (pendular nystagmus and ocular muscles hypofunctions), we agree with the already reported finding in isolated CCA (3). For instance, Ramelli et al (3) observed one case of pendular nystagmus in a cohort of 6 CCA-affected children. Pendular nystagmus, rarely seen associated to CCA, is usually observed in demyelinating disorders and other deficits, such as pharmacological intoxication, metabolic, genetic, and granulomatous disorders.

Moreover, in our case, we also observed unexpected signs of macular dystrophy, generally seen in aged subject. Macular impairment has been already described only in one case with CCA but associated with hippocampi hypoplasia concomitant with multiple genetic defects, suggesting for a novel neuro-ophthalmic syndrome (5).

In conclusion, we are aware that the fully documented visual system involvement in isolated CCA represents a novel report, and therefore, all that observed needs to be confirmed in a larger cohort of similar patients.

STATEMENT OF AUTHORSHIP

Conception and design: V. Parisi. Acquisition of data: L. Barbano, G. Antonelli, E. Tinelli. Analysis and interpretation of data: V. Parisi, L. Ziccardi. Drafting the manuscript: L. Barbano, V. Parisi, L. Ziccardi. Revising the manuscript for intellectual content: V. Parisi, L. Ziccardi. Final approval of the completed manuscript: L. Barbano, G. Antonelli, L. Ziccardi, E. Tinelli, V. Parisi.

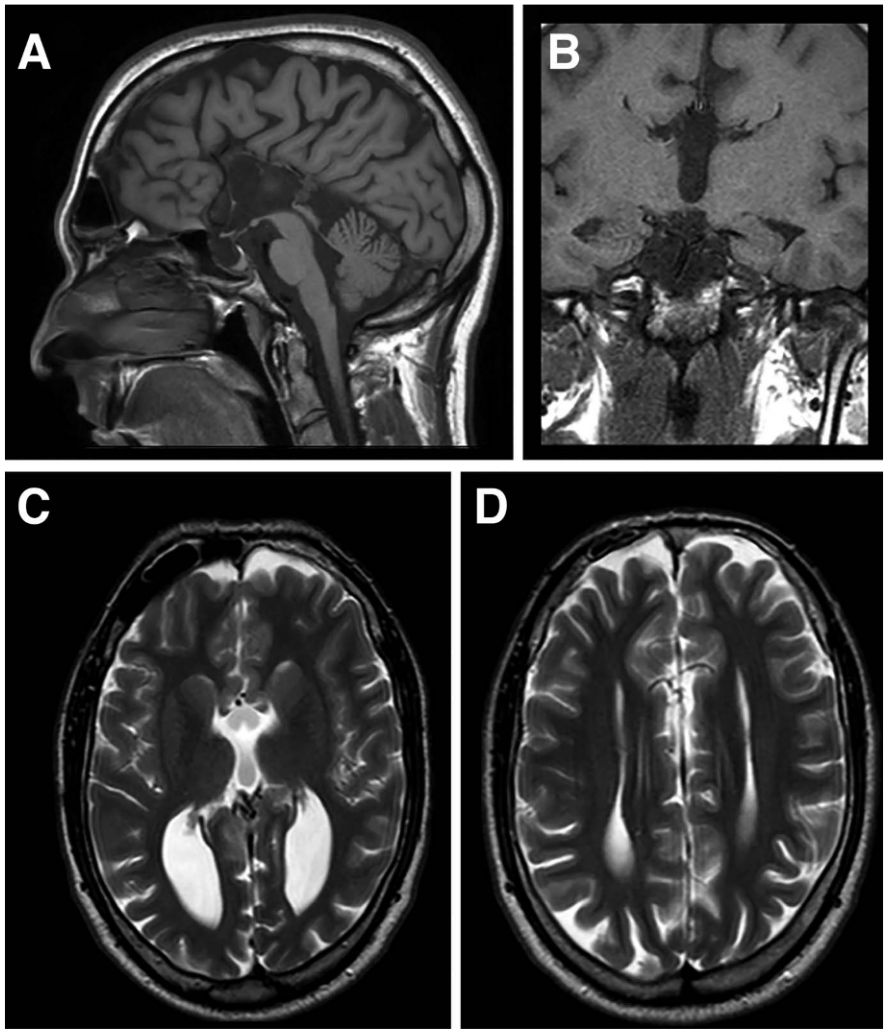


**FIG. 2.** Main MRI findings of the patient G.M. **A**. T1 sagittal image shows complete agenesis of the CC; the third ventricle was dilated. The herniation of chiasmatic cistern was also evident. **B**. T1 coronal image showed classical "viking helmet" of the lateral ventricles; third ventricle communicating with the interhemispheric fissure. **C** and **D**. T2 axial images showed colpocephaly and parallel lateral ventricles.

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