Antenatal diagnosis of complete agenesis of the corpus callosum: study of two cases

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INTRODUCTION

The corpus callosum (CC) is a slice of white substance (bundles of nerve fibres) that unites the two cerebral hemispheres [1].It plays a central role in the transfer of information between the left and right hemispheres of the brain: it is the coordinator between both of them [1].
CC malformations are frequent brain defects that can occur either in isolation or in combination with other malformations, sometimes constituting a congenital syndrome.
In this study we will report two observations of complete agenesis of the corpus callosum (CACC) diagnosed during antenatal period.

OBSERVATIONS

Case 1: a 32-year-old patient with a history of antiphospholipid antibody syndrome,gravida 1 Para 1 currently pregnant at 31 Weeks GA, pregnancy is conducted under low molecular weight heparin 0.6 IU *2/day, was referred by her doctor for the discovery of dilatation of the lateral ventricles at a term of 31Weeks GA. The current prenatal assessment was unremarkable: morphological ultrasound performed at 22 WG was normal, there was no gestational diabetes, First term serum screening showed a low risk for chromosomal aberrations (trisomy 21, 13, and 18).
Ultrasound findings on admission objectified a male fetus carrying a CACC, colpocephaly, lateral ventricular dilatation measured at 17mm, absence of cavum lucidum, an ascent of the 3rd ventricle (figure 1), There were no other detectable anomalies in particular no anomaly of the posterior fossa. No intra uterine growth restriction was detected.
Pregnancy was followed normally, the patient delivered at 37WG+ 2-day term by cesarean section for a globally narrow pelvis. The newborn delivered was male, his birth weight was 3165 g, his Apgar score was respectively 9-10-10 at 1st, 5th and 10th minute, he had good axial and peripheral tone, good height, and no abnormalities at his first clinical examination at the age of two months.

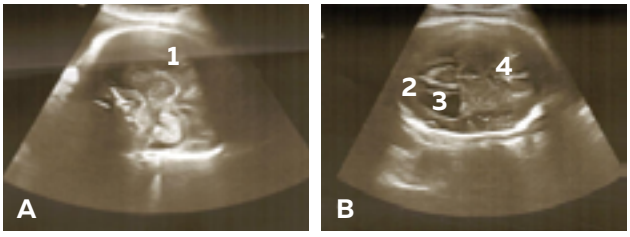

Figure 1 : A+B :
A : Mid-sagittal section of the brain, 1 : Complete agenesis of the corpuscallosum,
B : trans ventricular cut, 2 : colpocephaly, 3 : dilation of the lateral ventricles, 4 : absence of cavum lucidum

Case 2: A 39-year-old patient with no significant medical background history, Gravida 1 Para 0, was referred to our department for follow up of biamniotic bichorian twin pregnancy. Cervical cystic hygroma was discovered in twin B by her doctor at a term of 12 Weeks GA +4 days. An ultrasound performed at our department confirmed the presence of a 4 cm long axis hygroma without any other evident abnormalities at this age. Amniocentesis carried out at 18 Weeks GA concluded to a normal karyotype for both fetuses. The sick fetus is male, the other is female. A morphological ultrasound performed at 21 Weeks GA showed a bi amniotic bichorian twin pregnancy, the female fetus was normal, whereas the male fetus had a CACC, colpocephaly, prefrontal edema, cervical cystic hygroma, a single umbilical artery with no other detectable morphological abnormalities. . The same findings were found in a fetal MRI. Given the advanced maternal age and the increased risk of abortion after a gesture of embryonic reduction, the collegial decision of carrying on the pregnancy was taken. At 38 Weeks GA, the patient gave birth by cesarean section, to two newborns: the female, in a good health, had an APGAR score of 9 at 1st minute and 10 at 5th minute, and weighed 2700g, the male, had an APGAR score of 6/8/8 at respectively 1, 5 and 10 minutes, he weighed 2200g, clinical examination at birth found facial dysmorphism, a 5 cm long axis cervical cystic hygroma, without any other detectable abnormalities. The male newborn died after 20 days because of severe apnea in NICU.

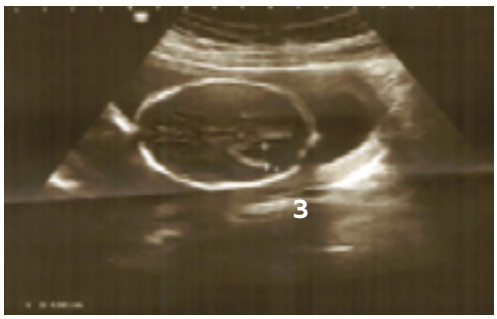

Figure 2 : Ultrasound: Trans ventricular section of the brain

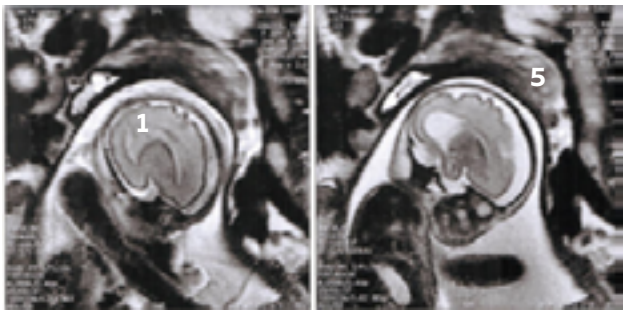

Figure 2 : MRI : Mid-sagittal section of the brain : Complete agenesis of the corpuscallosum and cervical cystic hygroma (5)

DISCUSSION

Cerebral hemispheres are connected by neuronal fibers organized in larger tracts i.e., anterior and posterior commissures, hippocampal commissure and the fornix. The largest of them is the corpus callosum (CC). It is the largest white matter structure of the human brain, which is located at the bottom of the longitudinal fissure, also serving as the cover for the lateral ventricles. It consists of axons that pass signals to various regions of the contralateral hemisphere cortex [1]. Functionally, the corpus callosum allows the transfer of information from one hemisphere to another and the coordination of responses from each hemisphere. Its development begins around the tenth week of gestation and ends at 20 weeks of gestation [2]. The prevalence of ACC in the general population varies depending on the sources and is probably underestimated often due to the asymptomatic course. The usual range is 1:5000 to 1:4000 (0.020–0.025%) [1], although higher prevalence (0.2–0.7%) is also reported [3-4]. In subjects with impaired neurodevelopment, this defect is present in even up to 1–3% of a given group [4-5]. The gender distribution of the ACC indicates a predominance of male subjects (63% vs. 37%) and this is the case for our two fetuses [6]. Fetal development of this structure may be interrupted by various genetic factors and maternal alcohol abuse [7]. The most frequent causes of corpus callosum agenesis (ACC) are gene mutations that are related to pathways of axon guidance, ciliary development, cell adhesion, proliferation, differentiation and migration. The presence of Probst bundles is a common evidence of abnormal commissure formation. These bundles are packs of longitudinally (rather than transversely) oriented neurons. As a result, they are unable to fulfill their role of connecting both hemispheres. The genetic cause is identifiable for 30–45% of ACC cases, with approximately 10% of them having chromosomal abnormalities and the remaining 20–35% being single gene mutations [8]. In our reported cases, patients do not report the notion of infection or alcohol or drug use during pregnancy, toxoplasmosis and rubella serology are negative.Imaging techniques and morphometrics provide evidence of multiple levels of callosal developmental anomalies from thinning to complete agenesis. The absence of all parts of CC is identified as complete ACC, as opposed to the absence of some parts (partial ACC). This malformation may be an isolated abnormality, but it may be also a component of syndromes composed of various neurological pathologies. Clinical pictures are very variable: from severe intellectual deficiency to normal intellectual development. The complete and isolated agenesis of the corpus callosum is generally of good prognosis in about 80% of cases. In this case the child generally remains neurologically asymptomatic and has apparent normal intelligence. However, these fundamental deficits are expressed in various domains of cognitive, behavioral and social functioning [9-10]. Patients affected by this abnormality present with a varying range of symptoms, some being severely impaired, while others may not even be aware of the abnormality since it does not interfere with their normal functioning. The antenatal diagnosis of corpus callosum agenesis is based on the morphological ultrasound performed during the second trimester of pregnancy. This diagnosis is based on direct but essentially indirect ultrasound criteria. The direct criterion is the absence of CC on a median sagittal section of the fetal brain. Indirect criteria are seen on a trans-ventricular section showing the absence of visualization of the cavum septum pellucidum, ventriculomegaly and colpocephaly (tear-like dilatation of the ventricle occipital horn) [11-12].These indirect signs become more visible at the end of the second trimester of pregnancy and are absent or barely visible in a significant proportion of cases if the screening ultrasound is performed in the middle of the dedicated screening period (22-24 WG) [13-14],as in the case of our first patient who had no morphological abnormalities on her screening ultrasound done at 22 WG but all the indirect signs were present on an ultrasound done at 31 WG. In a retrospective study published in 2008 by Glass HC including 630 cases of agenesis and hypoplasia of the corpus callosum diagnosed in the postpartum period, advanced maternal age (≥ 40 years) was associated with an increased risk of ACC especially in infants with a chromosomal disorder when paternal age was not significantly associated with a risk of ACC after adjusting for maternal age. In infants with detected chromosomal abnormality, advanced maternal age was associated with a six-fold risk for ACC (RR 5.9; 95% CI 1.8–19.3) from a baseline age 25–29 years old. There was also a trend for increased risk of corpus callosum hypoplasia in this age group (RR 3.5; 95% CI, 0.9–14.1). For cases without chromosomal abnormalities, the effect of advanced maternal age, adjusted for paternal age, was considerably smaller [15]. D. PALADINI et al. published in 2013 a retrospective study involving 54 cases of children suffering from corpus callosum agenesis who received a three-dimensional ultrasound scan during

their antenatal life and whose objective is to evaluate the presence and degree of appearance of signs of corpus callosum agenesis (ACC) according to gestational age and to determine the percentage of cases in which each sign is present at 24 WG. They found that prior to 24 WG, ventriculomegaly was present in 26.5% of ACC cases and colpocephaly was present in 20.6% of cases, so they concluded that most of the indirect signs of ACC are either absent or barely visible at the time of the second trimester screening ultrasound [16].As a result, ACC may evade diagnosis on the screening ultrasound before 24WG if the CC has not been searched in a median sagittal section of the brain. The prognosis is determined primarily by the associated malformations. Agenesis of the corpus callosum is associated with the following intracranial anomalies (in decreasing order of frequency), interhemispheric cyst with hydrocephalus, Dandy-Walker malformation, neuronal migration disorder, agenesis of the inferior vermis, encephalocele, lipoma of the interhemispheric fissure. Newborns with isolated agenesis of the corpus callosum without any significant neurologic sequelae have the best prognosis. Newborns with agenesis of corpus callosum associated with the neuronal migration disorder with or without Dandy-Walker malformation have the worst prognosis.

CONCLUSION

Although the precise incidence of ACC is unknown, it seems to be a rare condition. It may be suspected at the time of the routine anomaly scan due to the presence of indirect features, or diagnosed on direct visualization. However, in isolation it may remain undetected. The finding should trigger detailed assessment to establish whether it is isolated, or if there are associated ultrasound abnormalities. When available, fetal MRI is indicated, allowing confirmation of the finding and assessment of coexisting brain abnormalities. It poses a significant diagnostic challenge as the outcome is variable, depending on whether there are coexisting abnormalities and on the underlying cause; however, even in isolated ACC, outcomes vary. These uncertainties mean that antenatal counseling is difficult and further large prospective studies are needed. Given this, both antenatal and postnatal follow-up should be considered when this diagnosis is performed.

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