

Prenatal diagnosis of absence of the septum pellucidum associated with septo-optic dysplasia

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ABSTRACT

Septo-optic dysplasia (SOD; De Morsier syndrome) is a rare congenital disorder characterized by the absence of the septum pellucidum (SP), hypoplasia of the optic chiasma and nerves, and various types of hypothalamic–pituitary dysfunction. We report on two fetuses with absence of the SP diagnosed by ultrasound examination at 29 and 30 gestational weeks. In the first case the diagnosis of SOD was suspected in utero and confirmed postnatally; to the best of our knowledge this is the first report of the prenatal diagnosis of SOD. In the second case absence of the SP appeared to be isolated and no visual or endocrine impairment were detected after birth. Copyright © 2004 ISUOG. Published by John Wiley & Sons, Ltd.

CASE REPORTS

Case 1

A healthy 17 year-old primigravid woman was referred at 29 weeks of gestation on suspicion of fetal holoprosencephaly. Sonographic examination, using an Aloka 5500 (Aloka, Decines Charpieu, France) ultrasound machine equipped with 6-MHz abdominal and transvaginal probes, revealed isolated absence of the septum pellucidum (SP): the lateral ventricles had square fused frontal horns (Figure 1). There was no ventriculomegaly, the thalami were not fused, and the corpus callosum, fornix, anterior cerebral artery and falx cerebri were normal, thus excluding holoprosencephaly (Figure 2). Cerebral gyration appeared normal for gestational age, the Sylvian fissure and callosomarginal, central and temporal sulci all being observed. Fetal MRI confirmed the sonographic findings and showed hypoplasia of the optic chiasma (Figure 3). There was no evidence of cortical

dysplasia. The possibility of septo-optic dysplasia (SOD; De Morsier syndrome) was raised and maternal serum and urinary estriol tests were performed, which revealed very low levels. Since estriol arises from placental aromatization of androgens of fetal adrenal origin¹, these low levels were consistent with the diagnosis of fetal adrenal insufficiency, probably secondary to adrenocorticotrophic hormone (ACTH) deficiency and hypopituitarism. These biological results, along with the ultrasound and magnetic resonance imaging (MRI) findings, were consistent with the diagnosis of fetal SOD but the mother refused cordocentesis for further fetal endocrine assessment. Despite counseling about a poor outcome, she did not ask for a termination of pregnancy, which would have been permitted, according to French law, and a full-term 2960-g male infant was delivered. Postnatal investigations ascertained the diagnosis of SOD with hypopituitarism and blindness. The infant had growth hormone, ACTH and thyroid stimulating hormone deficiency. At the time of writing the child was 4 years old, and was developmentally delayed and blind.

Case 2

A healthy 31 year-old primigravid woman was referred for a first sonogram at 30 weeks of gestation when her pregnancy was discovered. On sonography only the very anterior part of the SP was seen, with no posterior part, the frontal horns being fused at this level (Figure 4). The atrium of the lateral ventricles was 10 mm wide. Holoprosencephaly was ruled out since the corpus callosum was normal in length (37 mm), and the anterior cerebral arteries, the columns of the fornix and the falx cerebri were also normal. The gyration was normal for gestational age. The optic nerves were 3 mm in diameter, which is standard for this gestational age. There was no microcephaly nor dysmorphic features. The

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Figure 1 Ultrasound image (transabdominal axial plane) showing absence of the septum pellucidum with fused frontal horns (Case 1).



Figure 2 Ultrasound image (transvaginal sagittal plane) showing normal corpus callosum (Case 1).

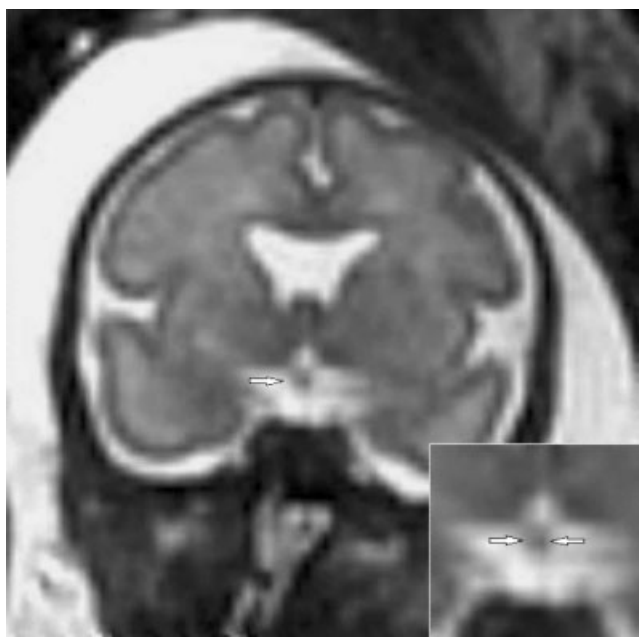


Figure 3 Magnetic resonance image (coronal plane) showing hypoplastic optic chiasma (between arrows) (Case 1).



Figure 4 Ultrasound image (transabdominal coronal plane) showing absence of the septum pellucidum and fused frontal horns with visible corpus callosum (Case 2).

possibility of SOD was raised. Fetal MRI confirmed the sonographic examination and revealed a normal optic chiasma. Maternal serum and urinary estriol tests were within the normal ranges. Fetal measurements of growth hormone, ACTH, and prolactin in blood obtained by cordocentesis were within the normal ranges. Although SOD could not be excluded with certainty, the diagnosis was thought to be unlikely and a full-term 2885-g male infant was delivered. At the time of writing the infant was 3 months old and had no features suggestive of hypopituitarism or impaired vision. His development was normal.

DISCUSSION

Absence of the SP is a rare congenital brain malformation (1/50 000). It may be one manifestation of a broad spectrum of developmental anomalies detectable by ultrasound, or it may be associated with cytoarchitectural disturbances of cortical layers undetectable by ultrasound or MRI². The malformation may also occur without associated brain anomalies^{2,3}. Absence or dysgenesis of the SP at ultrasound examination is a clue to the prenatal diagnosis of SOD, which also includes optic nerve dysgenesis and endocrinological deficiencies. Potential defects of the central midline of the brain are associated with SOD⁴ and bilateral cleft lip and palate can also be present^{5,6}. Recently, the term SOD-Plus was suggested to describe SOD associated with any cortical dysplasia^{7,8}; in such cases, it is common to observe developmental delay. Absence of the SP may also be due to secondary mechanisms, such as hydrocephalus or valproic acid embryopathy⁹. In SOD, optic nerve hypoplasia can be unilateral or bilateral and results in a variable degree of visual impairment¹⁰. The onset and extent of hormonal disorders in SOD patients vary considerably¹¹. Absent SP with communicating square frontal horns may indicate SOD or lobar holoprosencephaly, and may even be an isolated anomaly. If the anterior corpus callosum,

falx cerebri and anterior cerebral arteries are normal in shape/position this is suggestive of absence of SP without holoprosencephaly, in which case SOD is then suspected. A detailed ultrasound examination should check the optic nerves and look for other associated midline defects and schizencephaly. MRI should look for hypoplastic optic chiasma, schizencephaly or cortical dysplasia. In the presence of one or more of these features, the diagnosis of SOD is to be strongly suspected and should be confirmed by the presence of maternal and fetal endocrinological deficiencies. However, although pituitary hormone deficiency is one of the characteristics of SOD, it is found in only 50–90% of patients¹² and is usually diagnosed at a mean age of 4–5 years¹¹. In our first case, very low maternal serum and urinary estriol levels suggested fetal adrenal insufficiency¹³. In the context of midline malformation of the forebrain, this was suggestive of ACTH insufficiency¹, and pointed to a likely diagnosis of SOD. In the second case, maternal serum and urinary estriol levels were normal, suggesting normal adrenal function and ACTH production in the fetus. Furthermore, growth hormone, ACTH and prolactin levels in fetal blood sampled by cordocentesis were in the normal range^{14,15}.

Prenatal endocrine data for the condition are scarce and have been obtained mainly from umbilical cords of human abortuses and preterm infants. Although normal fetal pituitary function and normal appearance of the optic chiasma on fetal MRI cannot rule out SOD, the diagnosis in such cases is unlikely; one should consider an isolated absence of the SP, even if this diagnosis and the normal development of a healthy child cannot be confirmed before birth. Absence of the SP can be diagnosed by ultrasound from 20 weeks onwards, but some associated forebrain malformations and especially cortical dysplasia will not be detectable by ultrasound or MRI before 30–32 weeks. The prognosis of apparently isolated absence of the SP is controversial because it may be associated with cytoarchitectural disturbances of cortical layers not yet detectable by MRI^{2,5}, but absence of the SP may have no association with psychological deficit or epileptic seizures². Prenatal diagnosis of SOD is certainly important for early examination and treatment at birth. It is impossible to determine the severity of the disease before birth and we know that there is the potential risk of development of endocrine deficiencies in later life. However, the possibility of

SOD-Plus must be carefully investigated by ultrasound and MRI, since it is generally associated with developmental delay. Parents should be informed of all the differential diagnoses.

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