Clinical History:

A two-month-old boy was admitted to the hospital due to irritability. The infant presented with prolapse of the forehead, flat nasal bridge, hypotelorism, plane posterior skull, microcephaly, small anterior fontanelle, median cleft lip-palate, generalized hypotonia, syndactyly of the 4th and 5th finger of the left lower extremity.

Imaging Findings:

Due to the clinical phenotype, a brain magnetic resonance imaging (MRI) was performed and revealed semi-lobar holoprosencephaly. The cerebral lobes were present, but fused anteriorly and at the thalami (Fig. 1). There was agenesis of the genu and the body of corpus callosum (Fig. 2). The electroencephalogram was normal. Laboratory analysis revealed hyponatremia, low urine specific gravity, high serum and low urine osmolality. These findings in absence of dehydration were suggestive of partial central diabetes insipidus. Low plasma antidiuretic hormone levels were found. An MRI of the hypothalamo-pituitary axis was normal, depicting on T1-weighted images a normal pituitary stalk and a normal pituitary gland with intermediate signal of the anterior lobe and a bright posterior lobe (Fig. 3). After subcutaneous desmopressin administration the patient showed normal serum levels of Na+, increased urine and decrease in serum osmolality. Molecular karyotype as well as genetic testing on HPE revealed no causative factors.

Discussion:

Holoprosencephaly (HPE) results from failure of the prosencephalon (embryonic forebrain) to differentiate into the cerebral hemispheres and lateral ventricles between the fourth and eighth week of gestation [1]. HPE has been graded as alobar, semilobar, and lobar types. In the alobar type there is no cleavage of the forebrain into hemispheres. There is a single ventricle; the thalami are fused and the corpus callosum, falx cerebri, optic tracts, and olfactory bulbs are absent. In semilobar HPE, the hemispheres have a tendency to separate, the ventricles are partly segmented, and the thalami are fused incompletely. In lobar HPE, the cerebral hemispheres are separated by a distinct interhemispheric fissure and the septum pellucidum is absent [1, 2]. HPE is often associated with median facial anomalies, including: proboscis, cyclopia, cleft lip and/or palate, ocular hypotelorism, solitary median maxillary central incisor [3, 4]. Additionally these children also have systemic problems, with poor feeding, hypothalamic/pituitary dysfunction and developmental delay [5]. The aetiology of HPE is heterogeneous. The majority of cases have a normal karyotype, although this anomaly can be accompanied by disorders such as trisomy 13, trisomy 18, triploidy, various deletions, and duplications, as well as gene mutations including SHH, PTCH, TGIF, TDGF1, ZIC2, SIX3, GLI2, or FAST 1. Abnormal karyotype occurs in 37% of affected patients. Although the
malformation is rather sporadic, familiar occurrence has been reported [6-8]. Prenatal diagnosis of lobar HPE is difficult; however, by ultrasound, the earliest diagnosis of alobar HPE was made at 9 weeks of gestational age, of semilobar HPE at 11 weeks, and of lobar HPE at 21 weeks of gestational age. Hoffman-Tretin reported two cases of sonographically diagnosed fusion of the anterior horns of the ventricular system at 27 and 32 weeks of gestation [9]. Futhermore, fetal MR may be an additional useful imaging tool if the diagnosis is suspected on ultrasound. The prenatal diagnosis of lobar HPE is difficult because it relies mainly on the absence of the cavum septum pellucidum together with variable enlargement of the lateral ventricles. These findings are also associated with agenesis of the corpus callosum and septooptic dysplasia. Prognosis of affected patients depends on the severity of the abnormalities of the central nervous system.

**Differential Diagnosis List:** Semi-lobar holoprosencephaly.

**Final Diagnosis:** Semi-lobar holoprosencephaly.

**References:**


Figure 1

Description: Abnormal face and median cleft lip-palate. Origin: Child Health Department, Medical School, University of Ioannina, Greece.
Description: Axial T2-weighted image depicts frontal interhemispheric and mid-thalamic fusion (arrow).
Origin: Department of Clinical Radiology, Medical School of Ioannina, Greece.
Description: Sagittal T1-weighted image demonstrates the absence of the genu and the body of corpus callosum while it shows normal high signal of the neurohypophysis (arrows). Origin: Department of Clinical Radiology, Medical School of Ioannina, Greece.