

Unilateral nystagmus in an infant with acrocallosal syndrome

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ABSTRACT

Acrocallosal syndrome (ACS), is an extremely rare disorder characterized by the absence of corpus callosum (CC), macrocephaly, hypertelorism, pre- and postaxial polydactyly and severe motor and mental retardation. There are only 3 reports of ACS associated with ocular findings, including optic atrophy, esotropia and anophthalmus. We report on the first known Turkish case of ACS associated with unilateral nystagmus in addition to several neurologic abnormalities such as absence of the adhesio interthalamica and many others. A physically and mentally underdeveloped one year-old girl was evaluated for macrocephaly, polydactyly and left-sided nystagmus, which was not recognized until the fourth month. Magnetic resonance imaging revealed external hydrocephaly, triventricular hydrocephaly, midline brain abnormalities including partial agenesis of the CC, cavum septi pellucidi, cavum vergae, and absence of the adhesio interthalamica. The following anomalies were also noted; high arched palate, short nose with broad nasal bridge and anteverted nostrils, macrocephaly, frontal bossing, open and down turned angles of the mouth, hypertelorism, postaxial polydactyly of the left foot, hypertrichiasis, and hypertrichosis. On the basis of these findings, a diagnosis of ACS was made. In addition to neuroimaging, systemic research is needed in all patients presenting with asymmetric nystagmus as such a nystagmus may be associated with various external developmental abnormalities in addition to central nervous system involvement. Our case indicates that asymmetric nystagmus and midline brain abnormalities may also be included in the diagnostic criteria of ACS.

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In 1979 Schinzel¹ described a 3-year-old boy with a syndrome of absence of the corpus callosum (CC), macrocephaly, hypertelorism, pre- and postaxial polydactyly and severe motor and mental retardation. One year later, Schinzel called this combination of signs the acrocallosal syndrome (ACS).² Since these first reports, approximately 34 cases of ACS have been reported and nearly all patients have marked or severe retardation.³ The term acrocallosal refers to a deficit of the acra (fingers and toes) and CC. We report on a Turkish girl with ACS in association with unilateral nystagmus, external hydrocephaly, triventricular hydrocephaly, midline brain abnormalities including partial agenesis of the CC, cavum septi pellucidi,

cavum vergae, and absence of the adhesio interthalamica.

Case Report. A one-year-old girl presented with a history of macrocephaly, 6 toes at the left foot and left sided nystagmus, which was not recognized until the fourth month. She was the second child of a normal 30-year-old mother and 32-year-old father who were non-consanguineous. There were no known birth defects in the family. On ophthalmologic examination, her direct and indirect pupil reflexes were normal. She was orthophoric and cycloplegic refraction showed an insignificant hypermetropic refractive error. The

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Figure 1 - Cranial MRI showing partial agenesis of the corpus callosum.



Figure 2 - Cranial MRI showing (a) Cavum septi pellucidi (b) lateral ventriculi hydrocephaly, (c) absence of the adhesio interthalamica (d) external hydrocephaly.



Figure 3 - Clinical appearance of the patient **a)** General appearance, and **b)** Close-up view of the head. Note macrocephaly, broad nasal bridge, frontal bossing, hypertelorism, hypertrichiasis, hypertrichosis, and open and down turned angles of the mouth.

Table 1 - Midline defects in patients with ACS.

Previous reports	Defect
Gelman-Kohan et al (1991) ¹⁰	Anencephaly
Çataltepe & Tuncbilek (1992) ¹²	Anencephaly
Lurie et al (1994) ¹¹	Anencephaly
Courtens et al (1997) ³	Intestinal malrotation
Philip et al (1988) ¹⁴	An anteriorly placed anus
Moeschler et al (1988) ¹³	Decreased tracheal caliber
ACS - Acrocallosal syndrome	

patient had intermittent nystagmus only on the left eye. Amplitude was small, but frequency was fast. No headshake or abnormal head posture was observed. The remaining eye examination findings were normal except for a myelinated nerve fibre only at the half of the quarter of the superior temporal border of the optic nerve head. Magnetic resonance imaging (MRI) was carried out to evaluate possible intracranial anomalies that revealed a mild degree of external and triventricular hydrocephaly, partial agenesis of the CC, cavum septi pellucidi, cavum vergae, and absence of the adhesio interthalamica (**Figures 1 & 2**). The following anomalies were also noted; high arched palate, frontal bossing, macrocephaly, open and down turned angles of the mouth, hypertelorism, short nose with broad nasal bridge and anteverted nostrils, hypertrichiasis, hypertrichosis, and postaxial polydactyly of the left foot (**Figures 3a & 3b**). She showed generalized muscular hypotonia with psychomotor retardation with an intelligence quotient value of 65. Her body weight was 7 kg (<3rd percentile), length 80 cm (90-97 percentile), and occipitofrontal head circumference 48.5 cm (>97 percentile). She had no teeth. Other systemic and laboratory investigations revealed no abnormality. Radiographic findings showed delayed bone age. Results of metabolic screen were normal. High-resolution chromosome analyses also showed normal karyotype. Molecular studies could not be performed, however, ethylenediamine tetraacetic acid anticoagulated blood was stored at -20° for future molecular biologic investigation.

Discussion. Since the first description of ACS by Schinzel,¹ it has become evident that the clinical spectrum is broader than the first reports suggested. The pattern of multiple congenital abnormalities, including partial agenesis of the CC, macrocephaly, hypertelorism, small nose, marked growth retardation, gross motor and mental retardation, postaxial polydactyly of foot, frontal bossing in our patient is compatible with the diagnosis of ACS. Neither unilateral nystagmus nor absence of the adhesio interthalamica has been described up to date.

The known causes of the acquired horizontal unilateral nystagmus are monocular visual loss or spasmus nutans which is a combination of asymmetric nystagmus, abnormal head posture and head shake.⁴ There were neither head shake, head posture, nor intraocular pathology that might cause unilateral nystagmus in our patient. Other causes include intracranial lesions like an infarction of the lateral medulla, multiple sclerosis, intracranial hemorrhages or infections.⁵ The MRI findings excluded these mentioned lesions, while disclosing other intracranial anomalies, and after detailed systemic investigation, a diagnosis of ACS was

established in our case. There are only 3 reports of ACS associated with ocular findings, including optic atrophy, esotropia and anophthalmus.⁶⁻⁸

Acrocallosal syndrome could be a developmental field defect: a primary field defect with predominantly midline formation defect as defined by Opitz.⁹ Reviewing the findings described in reported ACS patients,^{3,10-13} we ascertained a large number of midline anomalies (**Table 1**). Acrocallosal syndrome may be the result of various midline developmental processes early in embryogenesis, causing CNS defects (agenesis of the CC, Dandy-Walker malformation, anencephaly), cleft lip, congenital heart defect, hypospadias and so forth.¹⁴ Courtens et al³ reported that the delineation of ACS has changed with time, as it became evident that the clinical spectrum was wider and more variable than those (midline defects) described by the first reports.

In our case, the cause of the unilateral nystagmus might be midline brain abnormalities. Furthermore, due to hydrocephalus of ventriculi, the medial longitudinal fasciculus, which is a small compact tract near the midline and ventral to the fourth ventriculus and has a relationship between bilateral vestibular connections, might have been affected asymmetrically. To the best of our knowledge no case of ACS has been reported previously in association with unilateral nystagmus, midline abnormalities of the brain and hydrocephalus.

There are many similarities between our patient and the earlier reported cases.¹⁻³ Courtens et al³ recently defined minimal diagnostic criteria (presence of 3 of the 4 following symptoms: agenesis or partial agenesis of the CC, minor craniofacial anomalies, psychomotor retardation and polydactyly), which should lead one to suspect the diagnosis of ACS. Our patient's findings were consistent with Courtens' criteria and sufficient for the diagnosis of ACS. Various authors have called attention to the similarities between ACS and Greig cephalopolysyndactyly syndrome (GCPS) and have proposed that they were the same entity.^{15,16} However, ACS differs from GCPS in that hypotonia, severe mental retardation and partial or total agenesis of CC are the 3 major findings for the former while pedunculated postminimus digits together with severe syndactyly of hands and feet are the major findings for the latter.¹⁵ Koenig et al¹⁷ reported that intracerebral cysts are a common finding in ACS, and may serve in differentiating ACS from GCPS. However, we suggest that intracerebral cysts are not the major criteria for the diagnosis of ACS, because they have been seen only in 25% of the previously published cases of ACS. Some previous reports have described cases with developmental delay and congenital cerebral abnormalities in infants who had been exposed to vasoactive drugs in utero, such as cocaine, heroin,

and amphetamine. These infants also had ophthalmological abnormalities including strabismus, nystagmus, agenesis of CC and other abnormalities like congenital hydrocephaly.¹⁸ Our patient had no history of prenatal exposure to any vasoactive drugs.

In conclusion, besides neuroimaging, systemic research is also needed in all patients presenting with asymmetric nystagmus because such nystagmus may be associated with various external developmental abnormalities in addition to CNS involvement. On the other hand, our case indicates that asymmetric nystagmus and midline brain abnormalities might also be included in the diagnostic criteria for ACS.

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