Paediatr Croat. 2012;56:79-82

ACROCALLOSAL SYNDROME WITH UNILATERAL CEREBELLAR HYPOPLASIA

ARZU EKICI, COSKUN YARAR, AYTEN YAKUT, KURSAT BORA CARMAN, SUZAN SAYLISOY*

Acrocallosal syndrome is a rare disorder characterized by craniofacial anomalies, polydactyly, agenesis or hypoplasia of the corpus callosum and psychomotor retardation. We report on a case of acrocallosal syndrome with dysmorphic features, macrocephaly, duplicated hallux, agenesis of corpus callosum and unilateral cerebellar hypoplasia.

Descriptors: ACROCALLOSAL SYNDROME; AGENESIS OF CORPUS CALLOSUM; MACROCEPHALY; HALLUX - abnormalities; CEREBELLUM - abnormalities

INTRODUCTION

Acrocallosal syndrome (ACS) is an autosomal recessive disorder described by Schinzel in 1979 (2). The main characteristics are craniofacial abnormalities, distinctive digital malformations, agenesis of corpus callosum and psychomotor retardation (1). Here we present a 13-month-old boy with ACS and unilateral cerebellar hypoplasia.

CASE REPORT

A 13-month-old boy was admitted to our hospital with developmental delay and relative macrocephaly. He was born by cesarean section after a normal pregnancy at 38 weeks of gestation. His birth weight was 2100 g. His family history revealed that he was the first child and that his parents were first-degree relatives. He was hospitalized because of feeding difficulty during neonatal period, and had undergone operation for cleft lip at the age of 12 months.

Physical and neurologic examination revealed head circumference of 47 cm (25 percentile), height of 66 cm (<5 percentile) and weight of 5.7 kg (<5 percentile). Therefore, we concluded that he manifested growth retardation. He was unable to control head and had no meaningful words. He exhibited dysmorphic features such as large head with prominent forehead and cephalic veins, hypertelorism, high arched palate, cleft palate, thick lip, depressed and broad nasal bridge, anteverted nostrils and low-set ears. Anterior fontanelle was 4x5 cm in diameter. There was an incision scar on the lip left after corrective operation. His hair was thin and curly (Figure 1). His muscle tone was hypotonic and deep tendon reflexes were brisk. He demonstrated bilateral positive Babinski reflex. Right inguinal hernia and

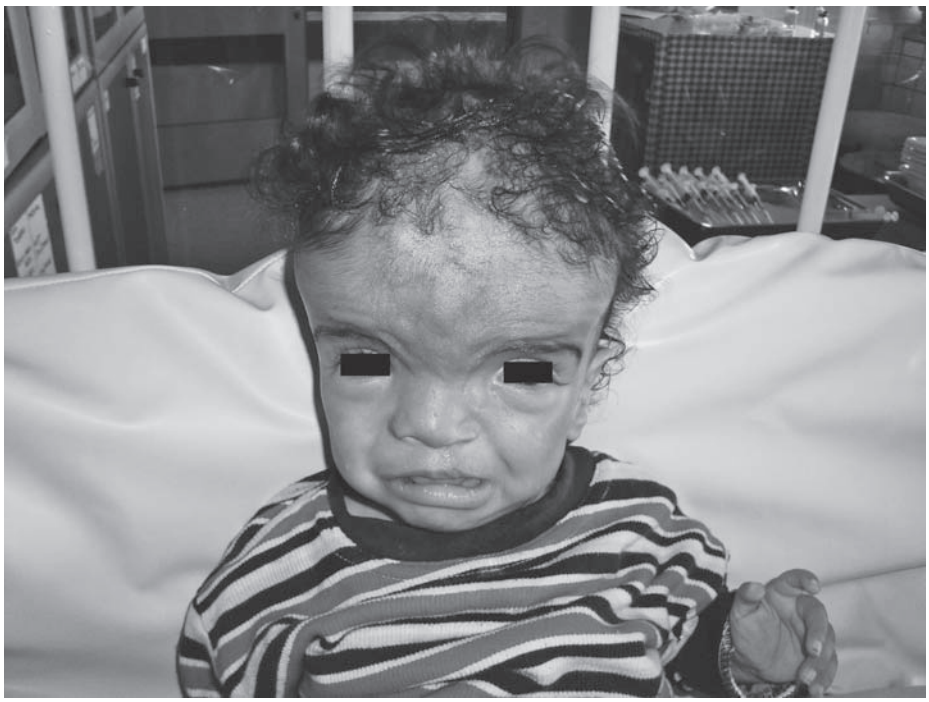

Figure 1. *Phenotypic appearance of the patient*
Slika 1. *Fenotipski izgled bolesnika*

* Eskişehir Osmangazi University

Correspondence to:
Arzu Ekici, MD, Eskişehir Osmangazi University, Medical School, Department of Child Neurology, Hasan Polatkan Avenue Eskisehir, Turkey, E-mail: drarzuekici@gmail.com

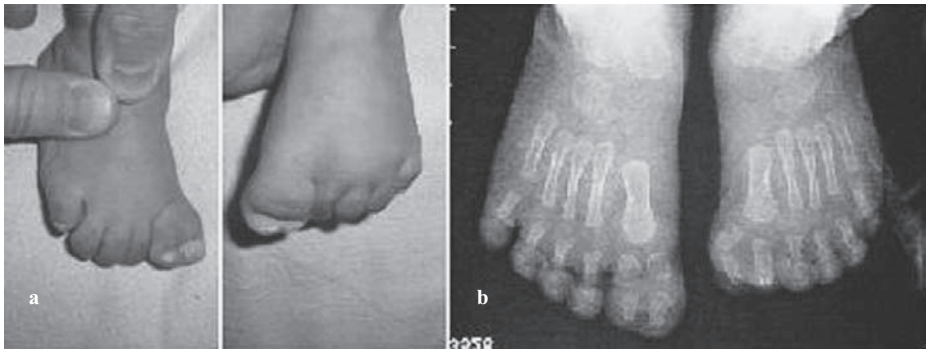

Figure 2. *a) Feets of the patient showing bilateral duplicated hallux b) Radiographs of the feet: Bilateral duplication of hallucal phalanges*
Slika 2. *(a) Obostrani duplicirani haluks na bolesnikovim stopalima; (b) rendgenogrami stopala: obostrano duplicirane falange haluksa*

bilateral duplicated hallux were observed (Figure 2a and 2b).

Laboratory investigations including toxoplasmosis, rubella, cytomegalovirus, herpes virus (TORCH) screening, blood and urine amino acid screens, and thyroid-stimulating hormone produced normal results. Cytogenetic analysis of peripheral blood indicated normal 46,XX karyotype. Abdominal ultrasonography and echocardiography also produced normal results. The Denver Developmental Screening Test-II revealed a delay in all fields.

Radiographies of the feet and skull demonstrated bilateral duplication of hallucal phalanges, silver beaten appearance of the skull and frontal bossing (Figure 3). Cranial magnetic resonance imaging (MRI) showed agenesis of the corpus callosum and left cerebellar hypoplasia (Figure 4).

DISCUSSION

Acrocallosal syndrome is a multiple congenital anomaly syndrome that mainly affects the central nervous system, facial midline structures and skeleton (3). It is an autosomal recessive inherited disorder; its candidate gene is located on chromosome 12p (4, 5). The variable clinical spectrum of the ACS is interpreted as a pleiotropic gene effect (4).

Diagnostic criteria of ACS have been defined by Courtens et al (6) as follows: (a) total or partial absence of the corpus callosum; (b) minor craniofacial anomalies (prominent forehead, hypertelorism, short nose with anteverted nostrils, large anterior fontanelle); (c) moderate to severe psychomotor retardation (with hypotonia); and (d) polydactyly. The presence of three of these four criteria together with other associated findings could lead one to suspect the diagnosis of ACS (6). In our case, there were agenesis of corpus callosum, craniofacial anomalies, neuromotor development delay, hypotonia and bilateral hallux duplication. Therefore, all four criteria were present including other associated features.

Patients with ACS have various, nonpathognomonic facial dysmorphic features such as broad and prominent forehead, macrocephaly, hypertelorism, down slanting palpebral fissure, deep-set eyes, posteriorly angulated malformed ears, short philtrum, small nose, depressed nasal bridge, anteverted nostrils, high arched palate, cleft palate, thick lip and bifid uvula (3, 7). This variety of facial features results in diagnostic difficulty. Our patient had multiple dysmorphic features (prominent broad forehead, hypertelorism, high arched palate, cleft palate, thick lip,

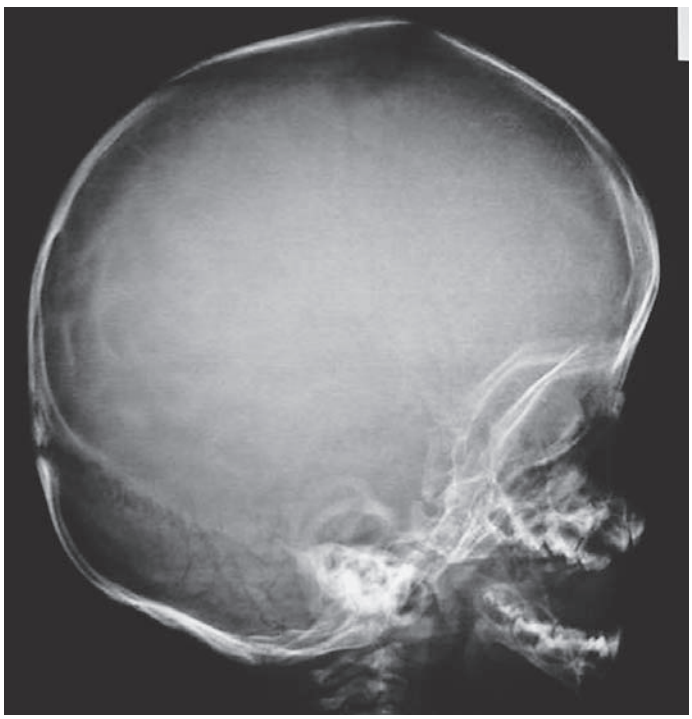

Figure 3. *Lateral skull radiograph: 1) Silver beaten appearance of skull 2) Frontal bossing*
Slika 3. *Lateralni rendgenogram lubanje: (1) srebrnasti izgled lubanje; (2) izbočeno čelo*

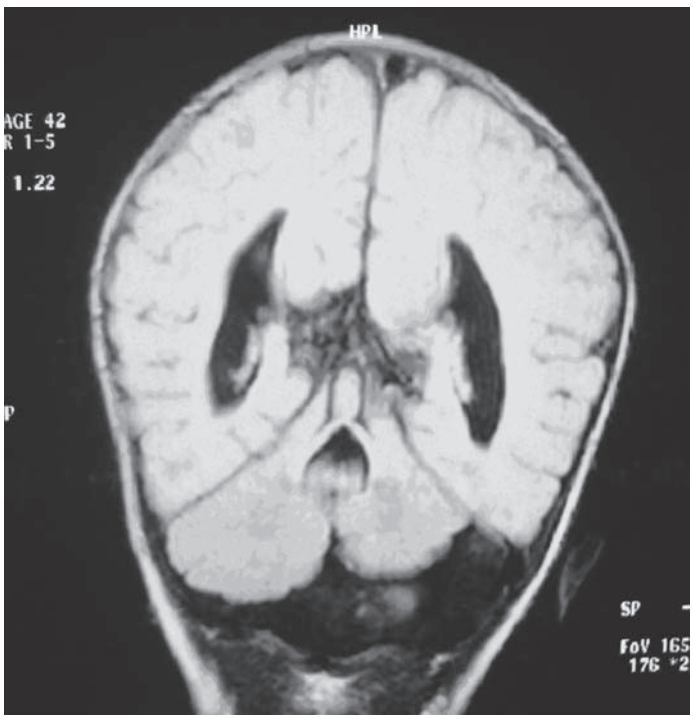

Figure 4. *Cranial MR showing: left cerebellar hypoplasia and agenesis of the corpus callosum*
Slika 4. *MR kranijuma pokazuje lijevostranu cerebelarnu hipoplaziju i agenezu korpusa kalozuma*

depressed nasal bridge, anteverted nostrils and hallux duplication). Most patients with ACS present with relative macrocephalic appearance, which is caused by craniofacial anomalies as in our case. Although this macrocephalic appearance is congenital, it might be appear later (6).

Acrocallosal syndrome is a multisystem disorder. Ocular (strabismus, retinal pigment anomaly, optic atrophy, nystagmus), cardiovascular (VSD, ASD, dysplastic pulmonary valves), genital, skeletal, nipple and visceral anomalies, inguinal, umbilical and epigastric hernia are other anomalies that can be seen in ACS (8). The main skeletal deformities of ACS are pre- or post-axial polydactyly, syndactyly, clinodactyly, long tapered fingers, hallux valgus and hallux duplication (3).

Digital malformations and craniofacial abnormalities may be part of a number of syndromes. Greig's cephalopolysyndactyly syndrome is the main disorder that must be considered in differential diagnosis of ACS, and the others are orofacial-digital syndromes Type I, Type II, Smith-Lemli-Opitz syndrome and Rubinstein-Taybi syndrome. The main descriptive features of these syndromes are listed in Table 1.

Table 1. *Main clinical features of syndromes*
Tablica 1. *Glavna klinička obilježja sindroma*

Syndrome Sindrom	Main Clinical Features Glavna klinička obilježja
Acrocallosal Syndrome Akrokalozni sindrom	Hypoplastic or absent corpus callosum, postaxial polydactyly of hands and feet, hallux duplication, macrocephaly Hipoplastični ili odsutan korpus kalozum, postaksijalna polidaktilija šaka i stopala, duplikacija haluksa, makrocefalija
Smith-Lemli-Opitz Syndrome Smith-Lemli-Opitzov sindrom	Anteverted nostrils, ptosis of eyelids, syndactyly of second and third toes, hypospadias, cryptorchidism in male, microcephaly Antevertirane nosnice, ptoza očnih kapaka, sindaktilija drugog i trećeg nožnog prsta, hipospadija, kriptorhidizam kod muške djece, mikrocefalija
Greig's Cephalopolysyndactyly Syndrome Greigov sindrom cefalopolisindaktilije	Preaxial and postaxial polydactyly, syndactyly, frontal bossing Predaksijalna i postaksijalna polidaktilija, sindaktilija, izbočeno čelo
Oro-facial-digital Syndromes Type I Orofacijalno-digitalni sindrom tip I.	Oral frenula and clefts, hypoplasia of alae nasi, digital asymmetry, microcephaly Oralni frenuli i rascjepi, hipoplazija nosnica, asimetrija prstiju, mikrocefalija
Oro-facial-digital Syndromes Type II Orofacijalno-digitalni sindrom tip II.	Cleft tongue, conductive deafness, partial reduplication of hallux, microcephaly Rascjep jezika, provodna gluhoća, djelomična reduplikacija haluksa, mikrocefalija
Rubinstein-Taybi Syndrome Rubinstein-Taybijev sindrom	Broad thumbs and toes, slanted palpebral fissures, hypoplastic maxilla Široki ručni i nožni palci, koso postavljeni očni rasporci, hipoplastična maksila

Severe hypotonia in the first months of life is a typical finding and about one-third of patients with ACS develop seizures (4, 9). In our patient, hypotonia was present but he had no history of seizures. Prognosis depends on the degree of hypotonia and early onset of seizures rather than the degree of craniofacial and limb malformations (4).

Several central nervous system anomalies have been reported in ACS. Corpus callosum anomalies and intracerebral cysts are the most frequent ones. Cerebral atrophy, hypoplasia of the pons or medulla oblongata, hypoplastic cerebellar hemispheres, small cerebellum, agenesis or hypoplasia of the cerebellar vermis and cortical dysplasia have been rarely reported in ACS (4). In the present case, there was unilateral cerebellar hypoplasia in addition to agenesis of the corpus callosum. To the best of our knowledge, this is the first ACS case with cerebellar hypoplasia reported.

In conclusion, ACS is a genetic disorder with a wide spectrum of clinical manifestations involving most of the systems. The patients usually present with hypotonia, macrocephalic appearance and dysmorphic features, and ACS should be considered in differential diagnosis of these patients.

Autori izjavljuju da nisu bili u sukobu interesa.
Authors declare no confilct of interest.

REFERENCES

1. Gulati S, Menon S, Kabra M, Kalra V. Schinzel Acrocallosal syndrome. Indian J Pediatr. 2003; 70:173-6.
2. Schinzel A. Postaxial polydactyly, hallux duplication, absence of the corpus callosum, macrencephaly and severe mental retardation: A new syndrome? Helv Paediatr Acta. 1979;34:141-6.
3. Shilpa BJ, Ashok L, Sattur PA. Acrocallosal syndrome. J Indian Soc Pedod Prev Dent. 2006;24: 45-9.
4. Koenig R, Bach A, Woelki U, Grzeschik KH, Fuchs S. Spectrum of the acrocallosal syndrome. Am J Med Genet. 2002;108:7-11.
5. Fernandez C, Soulier M, Coulibaly B et al. Acrocallosal syndrome in fetus: focus on additional brain abnormalities. Acta Neuropathol. 2008;115:151-6.
6. Courtens W, Vamos E, Christophe C, Schinzel A. Acrocallosal syndrome in an Algerian boy born to consanguineous parents: review of the literature and further delineation of the syndrome. Am J Med Genet. 1997;69:17-22.
7. Hodgson BD, Davies L, Gonzalez CD. Acrocallosal syndrome: a case report and literature survey. J Dent Child (Chic). 2009;76:170-7.
8. Turolla L, Clementi M, Tenconi R. How wide is the clinical spectrum of the acrocallosal syndrome? Report of a mild case. J Med Genet. 1990; 27:516-8.
9. Thyen U, Aksu F, Bartsch O, Herb E. Acrocallosal syndrome: association with cystic malformation of the brain and neurodevelopmental aspects. Neuropediatrics. 1992;23:292-6.
10. Johnston JJ, Olivos-Glander I, Turner J et al Clinical and molecular delineation of the Greig cephalopolysyndactyly contiguous gene deletion syndrome and its distinction from acrocallosal syndrome. Am J Med Genet A. 2003; 15;123A:236-42.
11. Baraitser M, Winter, RM, Brett EM. Greig cephalopolysyndactyly: report of 13 affected individuals in three families. Clin Genet. 1983;24:257-65.
12. Jones KL. Smith's Recognizable Patterns of Human Malformation. 6th edition. Philadelphia, PA: Elsevier Saunders; 2006.

S a ž e t a k

AKROKALOZNI SINDROM S JEDNOSTRANOM CEREBELARNOM HIPOPLAZIJOM

A. Ekici, C. Yarar, A. Yakut, KB. Carman, S. Saylisoy

Akrokalozni sindrom je rijetka malformacija karakterizirana s kraniofacijalnim anomalijama, polidaktilijom, agenezijom ili hipoplaplazijom korpusa kalozuma i psihomotorne retardacije. Ovdje ćemo prikazati slučaj čije su malformacijske značajke makrocefalija, dvostruki hallux, agenezija korpusa kalozuma i jednostrana cerebelarna hipoplazija.

Deskriptori: AKROKALOZNI SINDROM; AGENEZIJA KORPUSA KALOZUMA; MAKROCEFALIJA; HALLUX - abnormalnosti; MALI MOZAK - abnormalnosti

Primljeno/Received: 4. 7. 2011.
Prihvaćeno/Accepted: 29. 9. 2011.