Acrocephalosyndactyly, Apert type, in a newborn: Cerebral sonography

C. Poggiani ^{c,*}, C. Zambelloni ^a, A. Auriemma ^{b,c}, A. Colombo ^b

^a Pediatric Department, Neonatal Intensive Care Unit, Istituti Ospitalieri di Cremona, Italy

^b Neonatal Intensive Care Unit, Ospedali Riuniti di Bergamo, Italy

^c Advanced School of Ultrasonography in Pediatrics and Neonatology, Ospedali Riuniti di Bergamo, Italy

KEYWORDS

Apert syndrome;
Acrocephalosyndactyly;
Ultrasound;
Intracranial
morphology.

Abstract We describe the clinical and cerebral ultrasonographic features of a rare case of type 1 acrocephalosyndactyly (Apert syndrome). The patient was a newborn male whose twin had died *in utero*. Most cases of Apert syndrome are sporadic, although autosomal dominant inheritance has also been reported. Diagnosis is based on physical examination together with imaging data. Since Apert syndrome can give rise to numerous CNS abnormalities, affected newborns should undergo echoencephalography for more complete characterization of their malformations.

Sommario Vengono descritti il caso clinico e le caratteristiche ecografiche cerebrali di un gemello (in gravidanza con gemello premorto) affetto da acrocefalosindattilia, Tipo Apert, quadro malformativo complesso e raro con implicazioni genetiche, appartenente al gruppo delle disostosi cranio-facciali. La diagnosi si basa principalmente sull'esame clinico e sulle indagini per imaging. Poiché la sindrome di Apert è accompagnata da diverse anomalie del Sistema Nervoso Centrale, è necessario e utile prevedere una indagine ecografica transfontanellare in epoca neonatale.

© 2007 Elsevier Masson. All rights reserved.

Introduction

The first case of Apert syndrome was reported exactly 100 years ago in the Bulletin of the Medical Society of Paris. The author was the French physician afterwhom the syndrome is named [1]. Apert syndrome, which is also known as type 1 acrocephalosyndactyly (ACS1 — OMIM 101200), is a rare

genetic disorder characterized by multiple malformations. It affects 15.5 out of every 1,000,000 live births [2]. Although many cases are sporadic, others appear to result from the inheritance of an autosomal dominant trait linked to advanced paternal age. The molecular bases of the syndrome are still obscure.

Clinically speaking, the syndrome is characterized by brachycephaly or turriccephaly, hypoplasia of the facial mass, exophthalmos, hypertelorism, canthal dystopia, hypoplasia of the upper airway cavities and ethmoid, cleft palate, cutaneous and/or bony syndactyly of the hands and feet. The cerebral anomalies described in the literature include agenesis of the corpus callosum (CC), progressive

* Corresponding author. Via Giorgio e Guido Paglia, 22 — 24121 Bergamo, Italy.

E-mail addresses: c.poggiani.aioc@e-cremona.it, carloppogg@yahoo.com (C. Poggiani).

and nonprogressive hydrocephalus, and hippocampal abnormalities. Most of the patients are mentally retarded [2,3].

In this report, we describe the sonographic features of the cerebral structures in a newborn with Apert syndrome. The syndrome can be diagnosed prenatally, especially if 3D sonography is used, but there are very few descriptions of findings obtained with transfontanellar sonography [4].

Case 1

A male infant was transferred to our unit shortly after normal vaginal delivery in another hospital. The gestational age was 40 weeks, and the birth weight was 4300 g. The mother was 32 years old, and the father was 29. A previous pregnancy had ended in abortion, and the present pregnancy had been complicated by the death *in utero* of the patient's twin. The 1- and 5-min APGAR scores were 9 and 8. Multiple malformations were evident at birth, including turricephaly, frontal bossing, wide anterior fontanel, flattened face, hypertelorism with down-slanting palpebral fissures, bulging eyes, micrognathia (Fig. 1), high arched palate, cleft palate, cutaneous syndactyly of the hands and feet with deformity of the great toes (Fig. 2), and hypotonic extremities. On transfontanellar sonography all components of the ventricular system were present. The midline structures were characterized by extreme craniocaudal elongation, and the lateral ventricles appeared mildly enlarged and square-shaped on anterior coronal scans. The anterior and middle portions of the CC appeared normal whereas the posterior CC was underdeveloped with sulci arranged in a radial pattern (Figs. 3 and 4). A small cyst was noted at the level of the right anterior plexus. The 2D US study was supplemented with color Doppler studies of the major cerebral arteries (anterior cerebral, middle cerebral, internal carotid) to identify any signs of increased intracranial pressure. Qualitative and quantitative analysis of the flow curve revealed antero-grade systodiastolic flow and a normal Resistance Index (0.70) for the anterior cerebral artery.

Skeletal films revealed craniofacial dysostosis characterized by a tower-shaped skull, synostosis of multiple

Fig. 1 Typical Apert syndrome facies: high, broad, flat forehead; hypertelorism; depressed nasal bridge; down-slanting palpebral fissures; bulging eyes; open mouth; low-set ears.

Fig. 2 Complete syndactyly involving all five digits of the right foot; the great toe is also enlarged.

sutures, signs of intracranial hypertension, and hypoplasia of the facial mass. The metacarpal bones of the feet were shortened, and the first metatarsal was larger than normal and bifid. When present, the first ray consisted exclusively in a large, stubby bone element. The bones of the hands did not appear to be fused, but the phalanges were markedly shortened. Computed tomography of the brain with 3D-VR reconstruction confirmed the presence of brachy/turricephaly caused by premature fusion of the coronary sutures and partial lambdoid synostosis. The sagittal and metopic sutures appeared to be widened (Fig. 5). The orbital cavities were smaller than normal, and the roofs and lateral walls were elevated due to anterior displacement and "frontalization" of the greater wing of the sphenoid. The result was bilateral proptosis, hypertelorism, and partial stenosis of both optic canals. Cerebral MRI without contrast enhancement was performed along with MRI angiographic studies of the venous structures. These examinations confirmed the presence of cranioencephalic dysmorphism with decreased anteroposterior and interparietal diameters. They also revealed: mild cerebellar hypoplasia with signs of lamina quadrigemina hypertrophy; elongation of both optic nerves and of the hypophyseal peduncle caused by deformity of the base of the skull (reduction of the angle formed by the ethmoid-sphenoid plane and the posterior surface of the *clivus*), hypoplasia of the CC and absence of the splenium in the posterior portion, dysmorphism of the dural sinuses and signs of hypertrophy and

Fig. 3 Cranial sonography. An anterior coronal scan reveals elongation of the encephalic structures and squaring of the frontal horns of the lateral ventricles, which also appear to be mildly enlarged.

verticalization of the straight sinus, and finally, finger-shaped impressions on the inner surface of the cranial vault that were particularly evident at the parieto-occipital level (bilaterally). There were no focal signal alterations at the

Fig. 4 Midline sagittal scan shows partial agenesis of the CC reflected by a narrowed "C" shape and radial arrangement of the cerebral sulci.

Fig. 5 Cranial CT with 3D-VR reconstruction. The skull deformity is a result of premature closure of the coronal and lambdoid sutures (partial in the latter case). The sagittal and metopic sutures are enlarged.

level of the brain parenchyma. The electroencephalogram revealed nonspecific anomalies of organization.

The infant was referred to a center for pediatric and reconstructive plastic surgery. At the age of 6 months, he underwent craniotomy followed by remodelling of the cranial bones and the orbits to prevent intracranial hypertension. Surgical correction of the syndactyly and the cleft palate are scheduled to be performed at the age of 12 months.

The patient is now 11 months old. His motor development has been normal. He smiles and displays interest in the events that take place around him. He has now been fully accepted by the family in spite of their initial shock at his deformities, which had not been diagnosed prenatally.

Discussion

Prenatal sonographic diagnosis of Apert syndrome has become increasingly common in recent years thanks to the introduction of 3D scanners. Most cases are diagnosed during the third trimester of pregnancy although cranial anomalies associated with this syndrome have been detected as early as the 19th week of gestation. The most common findings are the peculiar shape of the head caused by premature closure of one or both of the coronal sutures (resulting in brachycephaly or plagiocephaly, respectively); major anomalies of the brain (hydrocephalus, agenesis or dysgenesis of the CC); and syndactyly [5–8].

Filkins et al. [8] maintain that the characteristic “miten-like” hand can be detected as early as the 14th week of gestation, especially in cases associated with the P253R mutation, which are characterized by evident marked syndactyly. As for cerebral anomalies, prenatal findings consistent with (or even suggestive of) agenesis of the CC should be followed by a search for other anomalies, including those that merely involve shape alterations, e.g., squaring of the lateral ventricles, which is caused in part by the cranial deformity and in part by the anomalous development of the CC; marked elongation of the structures that can be visualized on median sagittal scans; reduction of the distances between the cranial bones in a coronal plane leading to “compression” of the cerebral structures. In the case presented here, 2D transfontanellar sonography and Color Doppler studies revealed no evidence of ventriculomegaly or increased intracranial pressure at birth, and the surgeon was thus able to choose an ideal time for the complex process of craniotomy and bone remodelling.

In our opinion, the sonographic anomalies described in this report can be detected before or after birth with a simple 2D examination (as our illustrations show). However, MRI and 3D CT studies of the brain should be performed as soon as possible after birth to obtain more detailed information and establish a reference point for

comparison with studies performed later in the infant’s life.

References

- [1] Apert ME. De l’acrocephalosyndactylie. *Bull Mem Soc Med Hop Paris* 1906;23:1310–30.
- [2] Taybi H, Lachman RS. Apert syndrome. In: Taybi H, Lachman RS, editors. *Radiology of syndromes, metabolic disorders, and skeletal dysplasias*. 4th ed. St. Louis, Missouri: Mosby-Year Book; 1996. p. 25–7.
- [3] Maggio C, Pitarresi N, Cataldo F. Acrocephalia and syndactyly in a newborn. *Ital J Pediatr* 2005;31:23–5.
- [4] Tilley DH, Bluth EI, Goldsmith JP, Kenney III AJ. Echoencephalographic findings of Apert syndrome. *J La State Med Soc* 2001; 153:547–51.
- [5] Esser T, Rogalla P, Bamberg C, Kalache KD. Application of the three-dimensional maximum mode in prenatal diagnosis of Apert syndrome. *Am J Obstet Gynecol* 2005;193: 1743–5.
- [6] Miller C, Losken HW, Towbin R, et al. Ultrasound diagnosis of craniosynostosis. *Cleft Palate Craniofac J* 2002;39:73–80.
- [7] Benacerraf BR, Spiro R, Mitchell A. Using three-dimensional ultrasound to detect craniosynostosis in a fetus with Pfeiffer syndrome. *Ultrasound Obstet Gynecol* 2000;16:391–4.
- [8] Filkins K, Russo JF, Camous M, et al. Prenatal ultrasonographic and molecular diagnosis of Apert syndrome. *Prenat Diagn* 1997; 17:1081–4.