

Case Report

Apert Syndrome: Late presentation and treatment challenges

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ABSTRACT

Apert syndrome is a rare autosomal dominant disorder characterized by craniosynostosis, craniofacial anomalies, and severe symmetrical syndactyly of the hands and feet. Anomalies of the viscera, skeleton and cardiovascular system have also been reported. . Untreated craniosynostosis leads to inhibition of brain growth and an increase in intracranial and intraorbital pressure. Most cases are sporadic, resulting from new mutations with a paternal age effect. The prognosis of Apert Syndrome depends on the severity of brain

malformation and early surgical interventions. We describe a Sudanese infant with Apert syndrome who presented for the first time at the age of three months and had limited options for intervention.

Key words:

Apert Syndrome; Craniosynostosis; Syndactyly; Infant; Sudan.

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How to cite this article:

Kheir AEM, Hamed AA, Maki WM, Hasan LHM.

Apert Syndrome: Late presentation and treatment challenges. Sudan J Paediatr 2014; 14(2):71 - 75.

INTRODUCTION

Apert syndrome is named after the French physician who described the syndrome acrocephalosyndactylia in 1906. Apert syndrome is a developmental malformation characterized by craniosynostosis, a cone-shaped calvarium (acrocephaly), hypertelorism, midface hypoplasia, pseudo cleft-palate, a parrot beak-shaped nose, pharyngeal attenuation, and syndactyly of the hands and feet. Abnormalities of the upper and lower respiratory tracts include cleft soft palate, bifid uvula, choanal stenosis, and anomalies of the tracheal cartilage [1]. Other findings include a reduction in the size of the maxilla which may result in tooth crowding and an anterior open-bite of the maxilla. Mouth breathing, observed in most cases of Apert's syndrome, is related to alteration in facial growth [2]. Previous studies report affected individuals with anomalies of the viscera, elbows and shoulders, skeleton and central nervous system, which often results in impaired mental function [3, 4]. The inheritance of Apert's syndrome is autosomal dominant with the locus of FGFR2 mutation causing the disease on chromosome 10q (10q25–26). Suture progenitor cells with fibroblast growth factor receptors (FGFR2) that have undergone a mutation cannot transduce signals from extracellular fibroblast growth factors (FGFs). Therefore, these cells do not receive the signal to produce the necessary fibrous material essential for a normal calvarial suture [5-7]. In the United States the prevalence is estimated at 1 in 65,000 (approximately 15.5 in 1,000,000) live births. Apert syndrome accounts for 4.5% of all cases of craniosynostosis [8]. Most cases are sporadic, resulting from new mutations with a paternal age effect. The incidence of FGFR2 mutations increases with paternal age [9, 10]. We report a Sudanese infant with Apert syndrome who presented for the first time at the age of three months with very limited options for any intervention. To our knowledge this is the first case report of Apert syndrome from Sudan [11].

CASE REPORT

A 3-month-old female infant presented with an abnormal head shape since birth. Pregnancy was uneventful but there was no antenatal care and no antenatal ultrasound scans. She was born by normal spontaneous vaginal delivery at home. The mother noticed that the baby had an abnormal head shape but was reassured by the midwife. No vaccination has been given to her so far. This was the first baby for a young couple who are first degree relatives with no family history of a similar condition.

Clinical examination revealed a sick baby who was dysmorphic. The baby had a clover leaf skull deformity with midfacial hypoplasia, all the skull sutures were closed (craniosynostosis) with ridging all over the skull. There were also visible veins. She had a very high arched palate and bilateral proptosis (Figure 1). The rest of the clinical examination revealed a normal cardiovascular system examination, polydactyly and syndactyly of both hands and feet (Figure 2).



Figure 1 - Clover leaf skull deformity, bilateral proptosis and midfacial hypoplasia



Figure 2 - polydactyly and syndactyly of the hands and feet

The diagnosis of Apert syndrome was made on clinical grounds and ophthalmological assessment revealed bilateral optic atrophy with complete blindness, whereas hearing assessment was normal as well as echocardiography. A three- dimensional CT brain scan with reconstruction showed craniosynostosis and brachycephaly with multiple skull defects (Figure 3A). The CT also showed generalized brain atrophy with multiple extra axial cystic lesions (Figure 3B). All these findings were in favor of Apert syndrome. Plain X ray of the hands and feet showed osseous syndactyly.

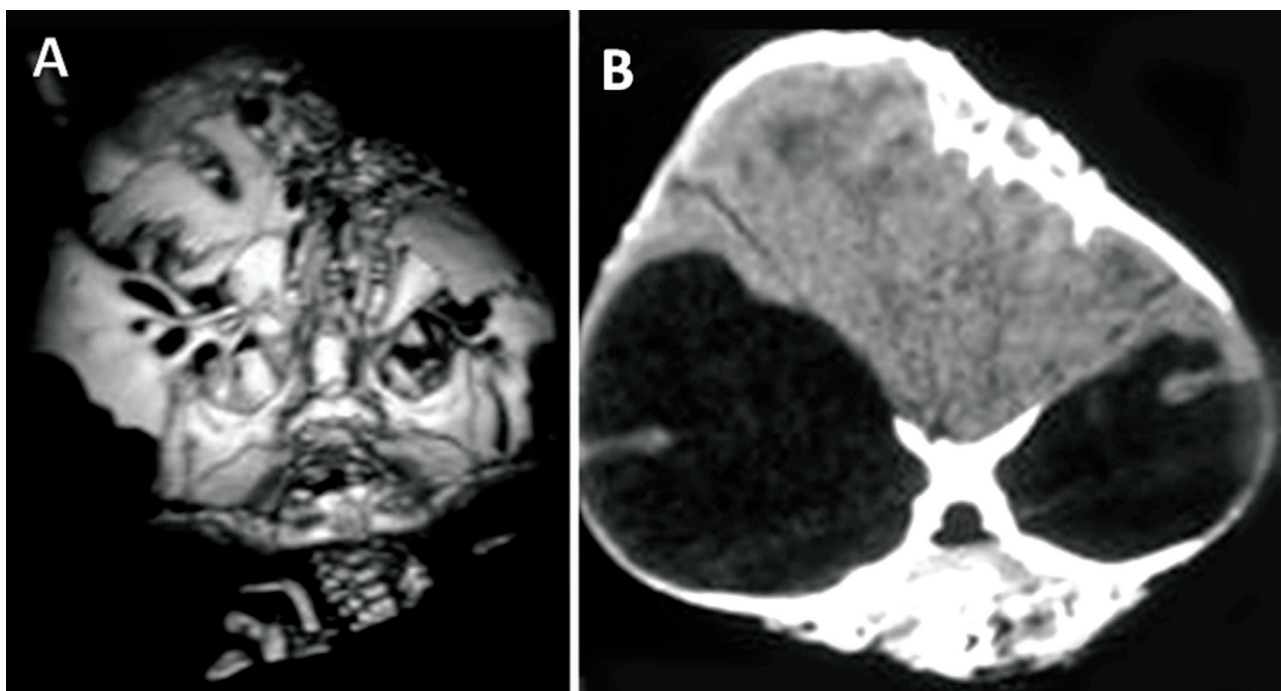


Figure 3 – A) Three- dimensional CT brain scan with reconstruction showing grossly abnormal skull with craniosynostosis. B) The CT also showed generalized brain atrophy with multiple extra axial cystic lesions.

The parents were counseled regarding the need for multidisciplinary approach in the management of their child. Neurosurgical consultation felt strongly that no intervention could be done at this stage in their present setup because of the brain atrophy and the grossly

abnormal skull shape and this was conveyed clearly to the parents whose main concern was the abnormal skull shape; and they left the hospital against medical advice without any intervention being done.

DISCUSSION

Apert, in 1906, described the triad of craniosynostosis, severe syndactyly of the hands and feet, and dysmorphic facial features, characterizing the syndrome. Later, a rare autosomal dominant heritage was linked to the syndrome, with mutations in the fibroblast growth factor receptor (FGFR2) gene at locus 10q26 [12]. The clinical and radiological features of Apert syndrome are well established and in agreement with the case described in the present study. The typical hand anomalies of Apert syndrome distinguish it from other forms of craniosynostosis. The hands in Apert's syndrome have three types; type I (spade), type II (mitten) and type III (rose bud) [13]. The present case has type II, mitten variety.

With craniosynostosis, coronal sutures most commonly are involved, resulting in acrocephaly, brachycephaly, turribrachycephaly, flat occiput, and high prominent forehead. Our case had a cloverleaf skull deformity which is extremely rare and presents only in 4% of infants with Apert syndrome. A case of Apert syndrome, confirmed by molecular genetic analysis, was observed in a newborn infant who did not have craniosynostosis at birth [14]. Because this disturbance in osteogenesis may vary in timing and extent, the diagnosis of Apert syndrome should be considered even in the absence of this hallmark finding [14].

About one quarter of cases with Apert syndrome have cardiovascular system abnormalities including VSD, ASD, coarctation of the aorta and patent ductus arteriosus [13]. Our case had a normal cardiovascular system examination. Some affected individuals have

anomalies of the viscera, elbows and shoulders and skeleton [4]. Abnormalities of the upper and lower respiratory tracts were also reported [1, 2]. However, our patient did not show any symptoms related to these anomalies during clinical examination.

Most cases of Apert syndrome are sporadic, resulting from new mutations with a paternal age effect. The present case is probably sporadic as there was no family history and parent's age was below 30 years.

The prognosis of Apert syndrome depends on the severity of brain malformation and early surgical interventions. However our patient presented late with brain atrophy and major skull deformities and nothing could be offered at that stage. Advances in craniofacial surgery have enabled patients of Apert's syndrome to attain intellectual and physical competence and thus lead a normal life [15].

In conclusion, Apert syndrome is a rare autosomal dominant disorder characterized by craniosynostosis, craniofacial anomalies and severe symmetrical syndactyly of the hands and feet. Management should include a multidisciplinary approach provided by pediatricians, neurosurgeons, plastic surgeons, ophthalmologists and geneticists for the effective planning and treatment of such patients.

ACKNOWLEDGEMENTS

The authors would like to thank the family of the baby mentioned in this report for consent of reporting this case and using the photographs. Thanks are also extended to the staff of the Pediatric Ward at Soba University Hospital, Khartoum, Sudan.

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