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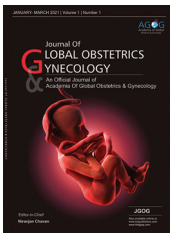
Case Report



Prenatal Diagnosis of Apert Syndrome: A Case Report

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ABSTRACT

Apert syndrome is a form of acrocephalosyndactyly, type 1, a congenital disorder characterized by malformations of the face, skull, hands, and feet. A key feature of Apert syndrome is the premature closure of the bones of the skull (craniosynostosis). The facial bones can be affected by craniosynostosis and lead to characteristic facial abnormalities. This syndrome is associated with syndactyly of fingers and toes. The severity of syndactyly varies and it involves hands more than feet, three digits on each hand and foot are fused together. Severe cases may have fusion in all fingers. It is a genetic disorder, usually without family history of the syndrome, but it can also be inherited from a parent. A diagnosis of this syndrome is most often made at birth or during infancy. The abnormal sonographic findings in Apert syndrome fetuses should be confirmed by the detection of a mutation in the FGFR2 gene. Specific therapies for Apert syndrome are symptomatic and supportive. Surgery may be recommended to help correct craniofacial malformations and other skeletal deformities. We will present a case of Apert syndrome who was diagnosed prenatally by ultrasound.

Key words: Apert syndrome, Prenatal diagnosis, Ultrasound

INTRODUCTION

The syndrome is named for the French physician, Eugene Apert, who described the syndrome acrocephalosyndactylia in 1906.[1] It is classified as a branchial arch syndrome, affecting the first branchial (or pharyngeal) arch, and the precursor of the maxilla and mandible. Apert syndrome is a birth abnormality caused by a mutation of the FGFR2 gene. In up to 95% of patients, it results from a new mutation in the FGFR2 gene. It appears to affect males and females equally and affects an estimated 1 in 65,000–88,000 newborns.[2] Apert syndrome has some specific craniofacial deformities include acrocephaly (cone-shaped calvarium), prominent forehead (frontal bossing), proptosis, hypertelorism, and flattened nose with a low bridge.[3] Other signs and symptoms of this syndrome include hearing loss, eyebrow hair loss, severe acne, oily skin, heavy sweating, fused spinal bones, growth and developmental delays, recurrent ear infections, cleft palate, mild-to-moderate intellectual disabilities, cardiac structural defects, and genitourinary and gastrointestinal anomalies. An ultrasound is a non-invasive procedure that can detect differences in skull shape, facial anomalies, and syndactyly. The diagnosis is confirmed with classic clinical characteristics include midface retrusion, multisuture craniosynostosis, and syndactyly and/or by the detection of a heterozygous pathogenic variant in FGFR2 and clinical features consistent with Apert syndrome.[4] Other genetic disorders which can be seen apart from craniosynostosis include Crouzon, Carpenter, Chotzen, and Pfeiffer syndromes.[3] A craniofacial team with appropriate specialties is needed for proper planning and coordination so that the affected individual may receive the best possible care.[4]

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Received: 10-10-2021
Accepted: 20-10-2021
DOI: 10.15713/ins.jgog.29

CASE PRESENTATION

A 27-year-old Iranian woman, Gravida 2, parity 1, came to our center at the gestational age of 24 weeks for an anomaly scan. She had a history of term delivery 7 years ago and her daughter was healthy. Her husband was 36 years old. She had no history of

medical disease, surgery, or medication usage. Nuchal translucency ultrasound and combined first screening tests were normal in this pregnancy. In anomaly scan, the fetal clenched hands were reported and due to that, amniocentesis was recommended. The fetal karyotype was normal male, but comparative genomic hybridization (CGH) array was not performed. In the sonography performed in 24 weeks in our center, she underwent a detailed anomaly scan due to the abnormal shape of the skull. On ultrasound, the following items were discovered: Bicoronal sutures fusion (craniosynostosis) and skull deformation (mild turricephaly) [Figure 1], frontal bossing [Figure 2], hypertelorism [Figure 3], bilateral hand syndactyly [Figure 4], and right foot syndactyly [Figure 5]. The long bones of the lower and upper limbs [Figures 6-8], spine [Figure 9], chest, and palate [Figure 10] were normal. No other abnormalities were detected on ultrasound. All of the above findings were in favor of diagnosing the Apert syndrome and confirmed with reamniocentesis and CGH array.

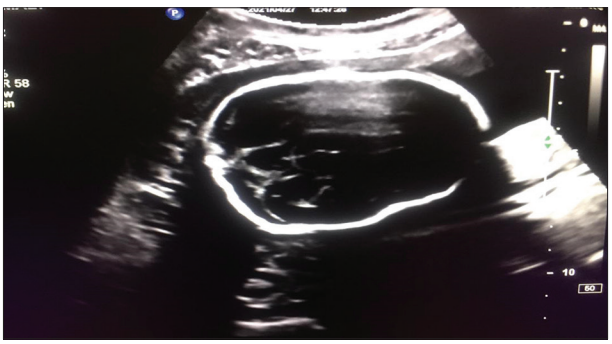

Figure 1: Axial view shows bicoronal sutures fusion (craniosynostosis) and skull deformation (mild turricephaly)

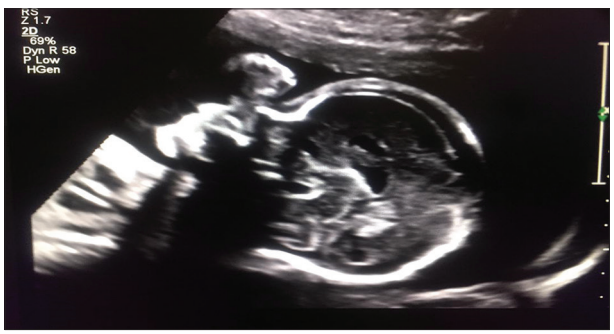

Figure 2: Frontal bossing in sagittal view

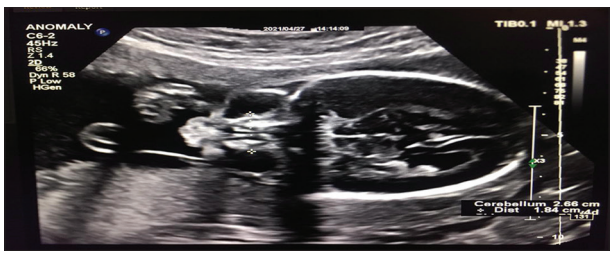

Figure 3: Hypertelorism

DISCUSSION

Apert syndrome is a rare congenital disorder characterized by craniosynostosis, midfacial malformation, and symmetrical syndactyly. Craniosynostosis is the main cause of many facial features of Apert syndrome. Premature fusion of the skull bones prevents the normal head growth. Abnormal head growth leads to a sunken appearance in the middle of the face and midface hypoplasia, a beaked nose, a wrinkled forehead, and cleft palate. Furthermore, an underdeveloped upper jaw can lead to dental problems. The prodromal characteristics of typical turribrachycephaly head shape are early craniosynostosis of coronal sutures, sagittal, and metopic sutures which result as a wide defect extending from glabella to posterior fontanelle.[5] Other brain abnormalities include hydrocephalous, absent corpus callosum, heterotopia of the gray matter, and Arnold-Chiari malformation.[6] These anatomical abnormalities may have a negative impact on the ability to perform essential functions.[7] The FGFR2 gene produces a protein called fibroblast growth factor receptor 2. This protein has many important roles in

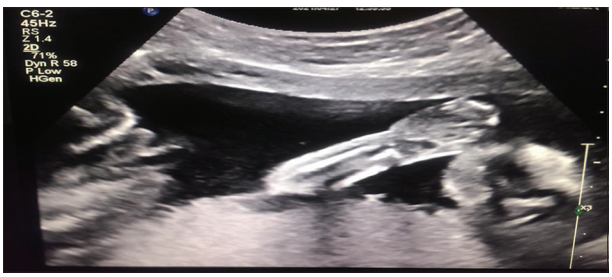

Figure 4: Hand syndactyly

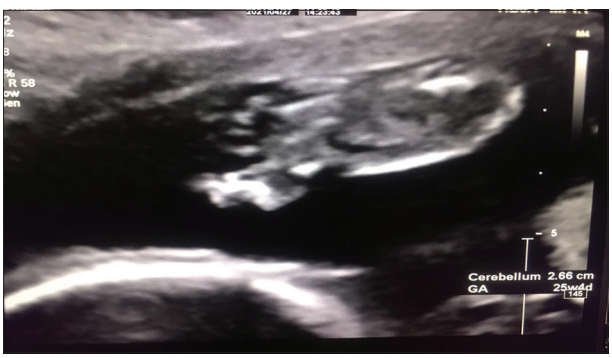

Figure 5: Right foot syndactyly

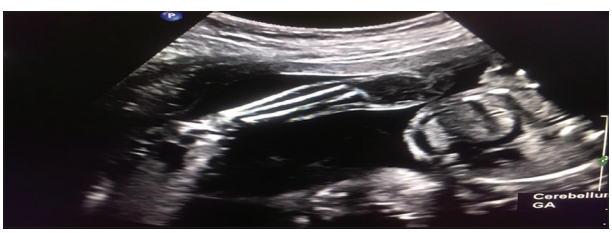

Figure 6: Normal radius and ulna

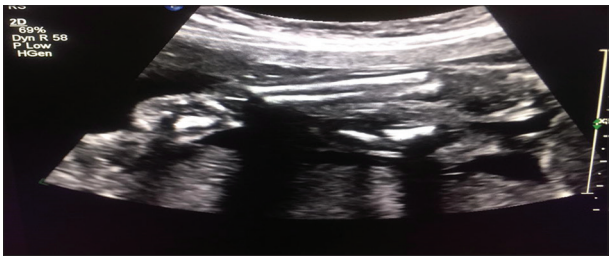

Figure 7: Normal tibia and fibula

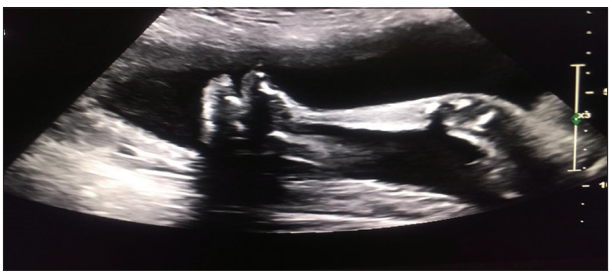

Figure 8: Normal axis between foot and long bones.

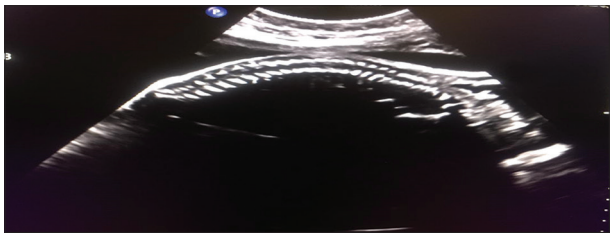

Figure 9: Normal spine

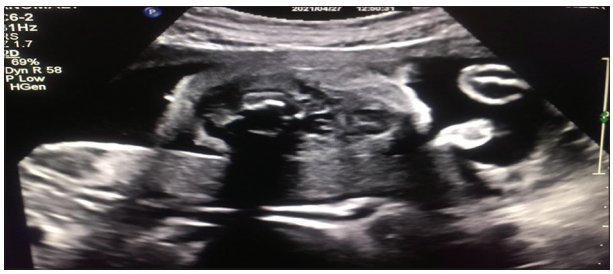

Figure 10: Normal palate.

signaling bone cell development and mutation in FGFR2 gene can lead to early fusion of the facial, skull, feet, and hands bones. Mutations to the FGFR2 gene can also cause other disorders, including Pfeiffer, Crouzon, and Jackson-Weiss syndrome. Most mutations are *de novo*. Rarely, it is inherited in an autosomal dominant fashion. It has been reported that sporadic cases may be associated with increased age of the father.[8] Mortality and morbidity in children with this syndrome are due to upper and lower airway compromise causing early death, obstructive sleep apnea, and cor pulmonale. Another cause of mortality is elevated intracranial pressure due to craniosynostosis.[9] Management of Apert syndrome requires multidisciplinary approach.[10] In severe cases, respiratory, cerebral, and ocular emergent problems should be taken into account, particularly at birth.[6] These children usually require surgery for release of the skull bones to allow normal brain development. The older a child is before this surgery is performed, the lower the chance for reaching normal intellectual ability. Hand, foot, eye, and orthopedic therapies must be performed.

REFERENCES

1. DeGiovanni CV, Jong C, Woolons A. What syndrome is this? Apert syndrome. Pediatr Dermatol 2007;24:186-8.
2. Cohen MM Jr., Kreiborg S. New indirect method for estimating the birth prevalence of the Apert's syndrome. Int J Oral Maxillofac Surg 1992;21:107-9.
3. Koca TT. Apert syndromre: A case report and review of the literature. North Clin Istanbul 2016;3:135-9.
4. Wenger TL, Hing AV, Evans KN. Apert syndrome. 2019 May 30. In: Adam MP, Ardinger HH, Pagon RA, Wallace SE, Bean LJ, Gripp KW, editors. GeneReviews®. Seattle, WA: University of Washington, Seattle; 1993-2022; 2019.
5. Khan S, Chatra L, Shenai P, Venna KM. Apert syndrome: A case report. Int J Clin Pediatr Dent 2012;5:203-6.
6. Fearon JA, Podner C. Apert syndrome: Evaluation of a treatment algorithm. Plast Reconstr Surg 2013;131:132-42.
7. Fadda MT, Ierado G, Ladniak B, Di Giorgio G, Caporlingua A, Raponi I, *et al.* Treatment timing and multidisciplinary approach in Apert syndrome. Ann Stomatol 2015;2:58-63.
8. Glaser RL, Broman KW, Schulman RL. The paternal-age effect in Apert syndrome is due, in part, to the increased frequency of mutations in sperm. Am J Hum Genet 2003;73:939-47.
9. Kosam A, Nahrel R. Apert syndrome: A case report. Int J Med Res Rev 2014;2:63-6.
10. Kaplan LC. Clinical assessment and multispecialty management of craniosynostosis. Childs Nerv Syst 2000;16:645-58.

How to cite this article: Rahimi-Sharbaf F, Saleh M, Marsusi V, Saleh M, Radi V. Prenatal Diagnosis of Apert Syndrome: A Case Report. J Glob Obstet Gynecol 2021;1(3):130-132.

Source of support: Nil, **Conflicts of Interest:** Nil.