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Case Report

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Apert syndrome: a case report

İbrahim Alanbay, Hakan Çoksüer, Emre Karaşahin, Mutlu Ercan, Uğur Keskin, Seyit Temel Ceyhan, İskender Başer

Department of Obstetrics and Gynecology, Gülhane Military Medical Faculty, Ankara, Turkey

Abstract

Objective: To present a case of Apert syndrome diagnosed by prenatal ultrasonography.

Case: In prenatal ultrasound examination, a 29-year-old G2P1 patient has been found to have a fetus with craniosynostosis, hypertelorism, frontal bossing, nasal bridge depression, syndactyly in the hands and feet, moderate ventriculomegaly. These findings lead to the diagnosis of Apert syndrome and the pregnancy was terminated with the will of the family. Postmortem examination confirmed the diagnosis.

Conclusion: Apert syndrome should be considered in the differential diagnosis when certain ultrasonographic findings such as abnormal craniofacial look or extremity abnormalities are encountered during prenatal examination.

Key words: 2-D ultrasonography and 4-D ultrasonography, Apert syndrome.

Apert sendromu: Olgu sunumu

Amaç: Prenatal ultrasonografide Apert sendromu tanısı konulan olgunun sunulması.

Olgu: 29 yaşında, G2P1 olguda, 23. haftada yapılan sonografide kraniyosinostozis, hipertelorizm, frontal bossing, burun kökü basıklığı, el ve ayaklarda sindaktili, orta derecede ventrikülomegali saptanmıştır. Bu bulgular ile Apert sendromu ön tanısıyla, ailenin de isteği ile terminasyona karar verilmiş olup, postmortem incelemede bulgular teyit edilmiştir.

Sonuç: Prenatal tanı için birinci basamakta bazı bulgular (anormal kraniyofasiyal görünüm, ekstremite anomalileri) görüldüğünde Apert sendromu da akılda tutularak detaylı sonografik incelemelere geçilmelidir.

Anahtar sözcükler: 2D ultrasonografi ve 4D ultrasonografi, Apert sendromu.

Introduction

Apert syndrome is a rare congenital malformation syndrome and characterized by progressive cutaneous and bone syndactyly, midfacial hypoplasia and triad of craniosynostosis. It was first defined by Whearon in 1894 and was revised by Apert widely in 1906.[1] Prevalence of this syndrome is reported as 15.5/1,000,000 (1/65,000) in newborns and it is 4.5% of all craniosynostosis cases.[2-4] The mutation coding fibroblast growth factor receptor 2 (FGFR2) in genes exists in 97% of all known cases.[2-4]. Visceral malformations and mental retardation accompany at various frequencies as well as skeletal anomalies.[5] Our purpose in this case study is to present 2D and 4D ultrasonographic findings of Apert syndrome together with the literature due to a case that was diagnosed by Apert syndrome in prenatal ultrasonography.

Case Report

Our case was 29-year-old with G2P1 and was referred to our clinic by pre-diagnosis of Apert syndrome in the sonography performed on 23rd week. Craniosynostosis, hypertelorism, frontal bossing, depressed nasal bridge (**Fig. 1**), syndactyly in hands and feet (**Fig. 2**), and medium ventriculomegaly (**Fig. 3**) were observed in the ultrasonography performed. 2D and 4D images of these

Correspondence: Hakan Çoksüer, MD. Gülhane Askeri Tıp Akademisi Kadın Hastalıkları ve Doğum Anabilim Dalı, Ankara, Turkey.
e-mail: coksuer@gmail.com

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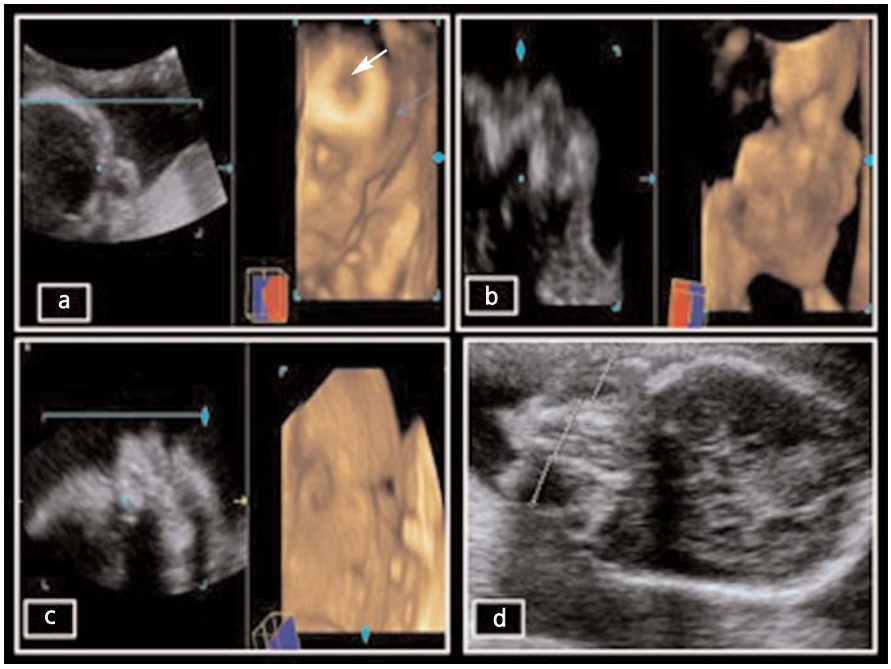

Fig. 1. (**a-d**) 2D and 4D craniofacial images of the fetus. Coronal craniosynostosis (arrow), frontal bossing (arrowhead) and depressed nasal bridge can be seen in the images, and the significant difference can be clearly observed when compared to 2D images. [Color figure can be viewed in the online issue, which is available at www.perinataljournal.com]

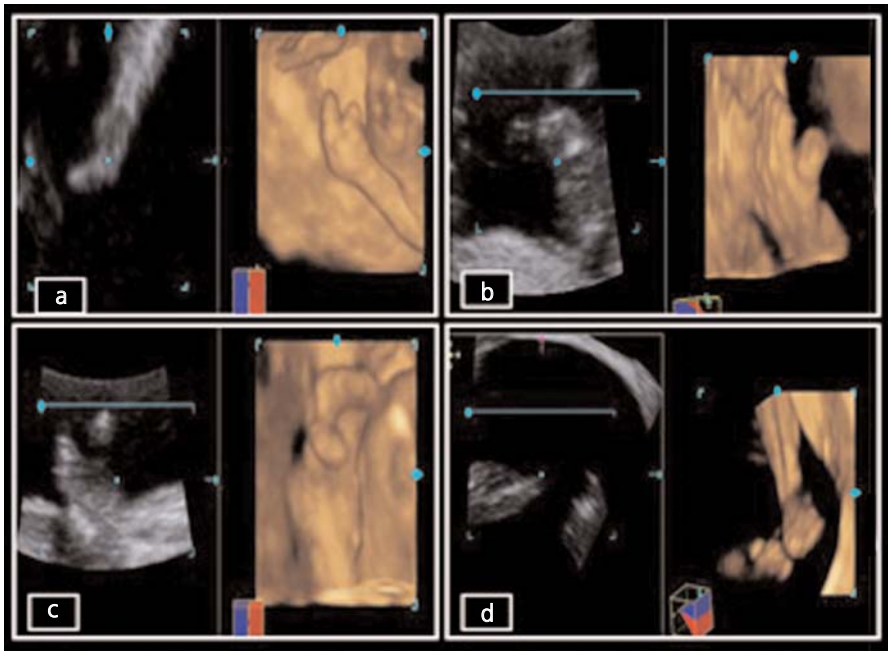

Fig. 2. 2D and 4D images of extremity anomalies. (**a-c**) Upper extremity images. 'Mitten hand' can be seen on hands. (**d**) Lower extremity (feet) images. [Color figure can be viewed in the online issue, which is available at www.perinataljournal.com]

findings were obtained. According to these findings, termination was decided together with the consent of the family, and the findings were confirmed in post-mortem examination of the fetus.

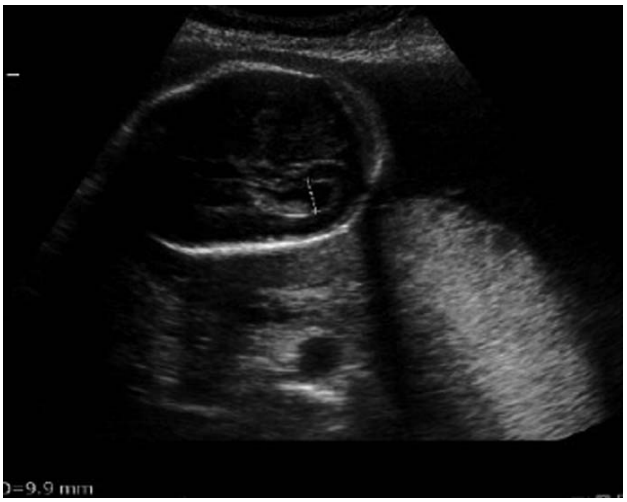

Fig. 3. Medium ventriculomegaly image.

Discussion

Apert syndrome is classically characterized by coronal craniosynostosis, midfacial hypoplasia and symmetric bone syndactyly in hands and feet and its prevalence was reported as 15 cases in one million live births. It constitutes 4.5% of craniosynostotic syndromes. The mutation coding FGFR2 in genes exists in 97% of all known cases.[2-7] Although the mutations in FGFR2 are autosomal dominant, most of the cases (98%) are sporadic due to de novo mutation in sperm and they appear depending on new mutations.[6,8] Mutations in FGFR2 increase together with paternal age as due to possible increase in frequency of these mutations and therefore, advanced paternal age is significant in the etiology of Apert syndrome.[8] Mutation in this gene is also seen in other craniosynostosis and skeletal dysplasia cases.[9] As a result of the mutation in this gene, regulation, proliferation and differentiation in cell migration degenerate and consequently, premature osteogenesis and skeletal anomalies occur. Cranial deformities and syndactyly in hands and feet appeared due to premature fusion in cranial sutures are anomalies observed in all cases with Apert syndrome.[6,7,9] Coronal synostosis is observed in all Apert cases and it is detected at 19th week at the earliest. Premature fusion in coronal sutures distinguishes Apert syndrome from other craniosynostosis cases. Deformities such as lambdoid and sagittal craniosynostosis frequently cause head deformities like frontal bossing.[9,10]

Various abnormalities reported in the literature such as brain, craniofacial, cardiac, genitourinary (10%), gastrointestinal (1.5%), obstetric and skeletal anomalies. Craniofacial anomalies are significant frontal bossing, flat occiput, short flat nose, micrognathia and cleft palate. Midface hypoplasia is classic in Apert cases and it is observed as significant depressed nasal bridge. Other craniofacial anomalies are reported as choanal stenosis, lens ectopia and proptosis. Hypertelorism, proptosis and strabismus are frequently observed due to contracted bone orbitae. Non-progressive ventriculomegaly (48.5%), complete or partial corpus callosum agenesia (ACC), holoprosencephaly, partial deficiency of septum pellucidum, posterior fossa anomaly, increased nuchal thickness were reported as brain-central nervous system lesions.[7,9,10] Corpus callosum agenesia and ventriculomegaly are the findings frequently defined in Apert syndrome cases. Renier reported complete ACC rate as 5% and partial ACC rate as 45% in the series of 60 cases.[11] It is recommended to consider Apert syndrome additionally in cases that ventriculomegaly or corpus callosum agenesis are detected prenatally.

Major cardiac anomalies are reported as cardiovascular anomalies and hypoplastic left heart while genitourinary anomalies are reported as polycystic kidney and hydronephrosis. Obstetric anomalies are polyhydramniosis.[4-7] Syndactyly in hands and feet are bilateral.[7,9,10] Syndactyly is known as 'mitten hands' and it distinguishes this syndrome from other craniosynostosis cases. It is seen in 97% of cases.

Findings seen in our case were abnormal head malformation, craniosynostosis, frontal bossing, flat nose, ventriculomegaly, hypertelorism and syndactyly in hands and feet; and our case was diagnosed as Apert syndrome due to these findings. While Apert syndrome can be diagnosed early by many methods (ultrasonography, molecular test) in risky patients, the diagnosis is hard due to reporting various non-specific sonographic findings in sporadic cases; therefore, serious sonographic examination is required to confirm diagnosis.[6,7,10] The diagnosis was obtained by performing detailed examining on many non-specific findings found in our case during routine prenatal scanning. Prenatal sonographic diagnosis of Apert syndrome is

established by detecting abnormal cranial deformity, midfacial hypoplasia and the triad of syndactyly in bilateral hands and feet. Ocular hypertelorism and exorbitism are significant characteristics accompanying other important Apert syndrome characteristics or craniosynostosis and they alert during ultrasonography. The aim in scanning families with high risk is to detect changes of 'mitten hand' in extremities at 16th-17th weeks at the earliest and changes of craniosynostosis at 20th week via ultrasonographic follow-up.[12,13] Nevertheless, cranial and orbital deformities and hypertelorism are not frequently apparent towards the end of second trimester and they become more apparent at third trimester.[14] In our case, craniosynostosis could only be detected in the ultrasonography at 23rd week. Since intracranial anomalies appear before cranial changes in Apert syndrome, they can be diagnosed even before complete development of corpus callosum. As these findings can be detected at a wide spectrum, it is recommended to evaluate accompanying abnormalities by karyotype analysis with amniocentesis.[15] Although it is not possible to evaluate corpus callosum agenesia completely before 19th-20th week, ultrasonographic evaluation of septum pellucidum at routine second trimester check will provide significant contribution for early evaluation of corpus callosum agenesia shown in most of prenatal cases.[6,10] Though detailed evaluation of fetal hands is not involved into standard obstetric evaluation, it would be beneficial to perform in cases with high risk such as ventriculomegaly or corpus callosum agenesia. Ventriculomegaly was detected in our case. Evaluation of fingers can be performed at second trimester even it is hard to do, and diagnosis can be established by guiding in target scanning in many cases which are detected craniosynostosis syndrome such as Apert or Pfeiffer and other anomalies.[16] It is essential to distinguish Apert syndrome which carry poor prognosis from Pfeiffer syndrome or similar other craniosynostosis cases which have better prognosis. Evaluation of extremities is particularly essential for performing this distinction. Clear evaluation of craniofacial structures may not be completely possible by 2D ultrasonography. It is particularly essential to evaluate craniosynostosis. In our case, these structures were shown clearly in 4D ultrasonography compared to normal ultrasonographical imaging. When images are examined, it will be seen that full anatomic view is obtained. There is no publication about 4D images of Apert syndrome in the literature. However, there are publications about 3D imaging used in the diagnosis of Apert syndrome. When these publications are examined, it will be seen that craniofacial anomalies and anomalies of other extremities are imaged clearly in a way that cannot be compared to normal ultrasonography. In these publications, it is reported that 3D imaging methods would be a good way to distinguish Apert syndrome from other cases.[13,17] Even though ultrasonographic characteristics are sufficient to diagnose, they can be confirmed by molecular tests. It is known that there is mutation in FGFR2 gene in 98-99% of cases and this finding is confirmed by detection of these mutations.[18] Although molecular diagnosis is diagnostic in suspected cases, detection of suspected prenatal findings can be delayed until third trimester in cases that do not have children who are affected previously. Therefore, it becomes prominent to detect ultrasonographic findings early. In our case, ultrasonographical findings were sufficient to establish diagnosis. Molecular diagnosis is still not performed in our country.

Conclusion

Apert syndrome includes many specific ultrasonographical findings. First step of diagnosing cases in prenatal period is to do detailed sonographical examinations by keeping Apert syndrome in mind when some findings (abnormal craniofacial view, extremity anomalies) are observed. The 4D ultrasonography provides essential advantages in the diagnosis of syndromes with specific findings such as especially face anomalies and extremity anomalies.

Conflicts of Interest: No conflicts declared.

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