Prenatal Diagnosis Of Osteogenesis Imperfecta: A Case Report

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Abstract

Background: Osteogenesis imperfecta is a heterogeneous group of genetic disorders characterized by severe bone fragility, abnormal ossification and multiple fractures. We report here a terminated case of osteogenesis imperfecta diagnosed with obstetric ultrasonography during sixteenth week of pregnancy.

Case: A 19 year-old gravida 2, para 1 patient was referred to our institution following a secreening ultrasound which demonstrated skeletal anomalies of the fetus. Sonographic evaluation revealed that all long bones were short and angulated with multiple fractures, the chest was narrow and bell-shaped, the echogenity of the skull was decreased and visualization of the intracranial structures were increased. Termination of the pregnancy was decided due to the ultrasonographic findings predicting lethality. The diagnosis of Osteogenezis Imperfecta type II was confirmed by postmortem radiography and autopsy examination.

Conclusion: Today with the advances in obstetric ultrasonography, the early prenatal diagnosis of lethal skeletal dysplasias is possible. In existence of ultrasonographic findings predicting lethality, the choice of termination should be offered to parents after giving a detailed information about the fetal prognosis even if the true ultrasonographic diagnosis is not available.

Keywords: Osteogenesis imperfecta, prenatal diagnosis.

Osteogenezis Imperfektanın Prenatal Tanısı: Olgu Sunumu

Amaç: Osteogenezis imperfekta kollagen maturasyonunda defekt nedeniyle kemik kırılganlığında artış, anormal kemikleşme ve çok sayıda kırıklarla karakterize heterojen bir genetik hastalıktır. Bu çalışmada gebeliğin 16. haftasında yapılan obstetrik ultrasonografi ile tanısı konularak sonlandırılan bir Osteogenezis imperfecta olgusu sunulmuştur.

Olgu: 19 yaşında gravida 2, parite1 olan olgu gebeliğin 16. haftasında yapılan ultrasonografisinde fetal iskelet anomalisi saptanması üzerine kliniğimize refere edildi. Olgunun yapılan prenatal 2. düzey ultrasonografisinde tüm ekstremitelerde uzun kemiklerin kısa bükülmüş ve çok sayıda kırık içerdiği, göğüs kafesinin kısa dar olduğu, ayrıca kafatasının düşük ekodansitede olup kafa içi yapıların olağandan daha net görüldüğü saptandı. Letaliteyi gösteren ultrasonografi bulguları nedeniyle gebeliğin terminasyonuna karar verildi. Postnatal radyografi ve otopsi bulgularıyla Osteogenezis imperfekta tip II tanısı kondu.

Sonuç: Günümüzde obstetrik ultrasonografideki gelişmelerle ölümcül iskelet displazilerinin erken prenatal tanısı mümkün olabilmektedir. Spesifik ultrasonografik tanı konulamasa bile letaliteyi öngören ultrasonografik belirteçlerin varlığında aileye fetal prognoz hakkında bilgi verilerek terminasyon seçeneği sunulmalıdır.

Anahtar Sözcükler: Osteogenezis imperfekta, prenatal tanı.

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Background

An osteogenesis imperfecta type II case diagnosed with prenatal ultrasonography and aborted at 16th pregnancy week is presented. Because of the case it is aimed to draw attention to the ultrasonographic diagnosis criteria of fatal prognosed osteogenesis imperfecta Type II and reviewing the ultrasonographic markers preceding fatal prognosis.

Case

The case is 19 years old, G2P1, having a normal son; in the ultrasonography that was made for the first time in this pregnancy at 16th week upon determining a morphologic defect in fetus, the patient is referred to our clinic. In ultrasonographic evaluation cranium echogenity is decreased, intracranial structures were seen more evident than usual (Figure 1). Thorax diameter was decreased significantly and increased to the favor of heart. Spine was morphologically normal. Long bones in extremities were short and curled, their measurement was below 5 % percentile, and some parts of hand and foot bones could not be seen (Figure 2). With these findings a fatal skeletal displasia prognosed with mineralization defect was considered

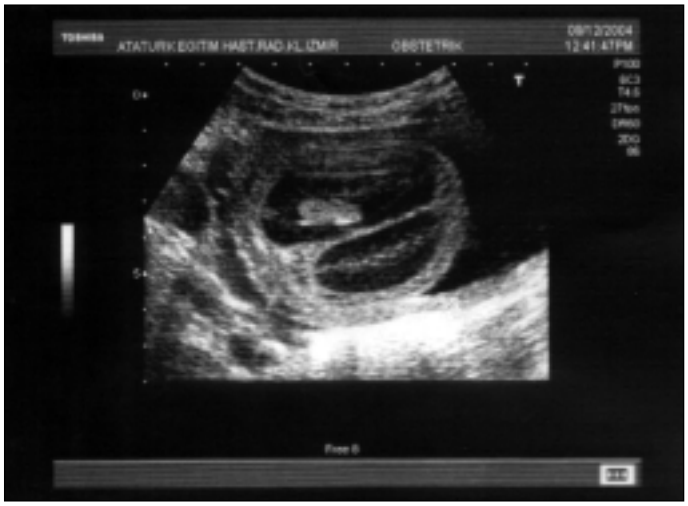

Figure 1. Ultrasonographic view of the cranium.

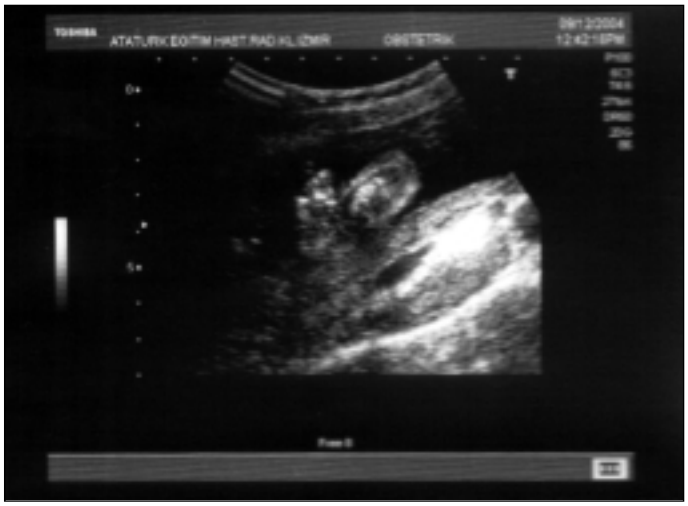

Figure 2. Ultrasonographic view of the limbs.

clinically and radiologically. After giving prenatal consultancy it is decided to end the pregnancy. With induction of misopristol dead male fetus was delivered.

It is seen that cranium bones were not developed, Thorax was significantly short and thin, long bones of extremities were fairly short and curled in the inspection after birth and postmortem radiography (Figure 3).

In autopsy examination caudo rectal length was 16, 5 cm, head to heel length was 20 cm (Figure 4). It was seen that cranial bones were not developed when the cranial cavity opened. There were multifractures in costae and small nodular struc-

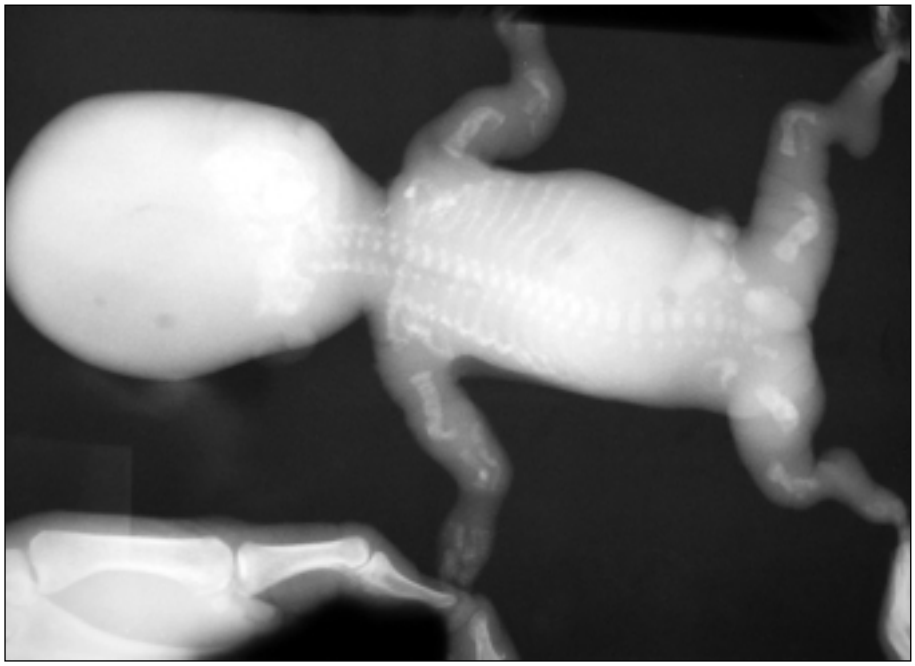

Figure 3. Postmortem radiographic view.

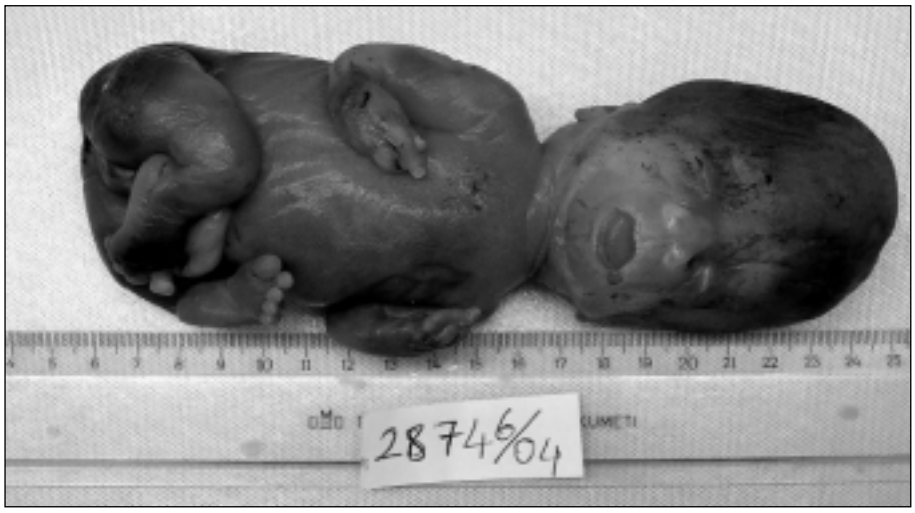

Figure 4. Morphological view.

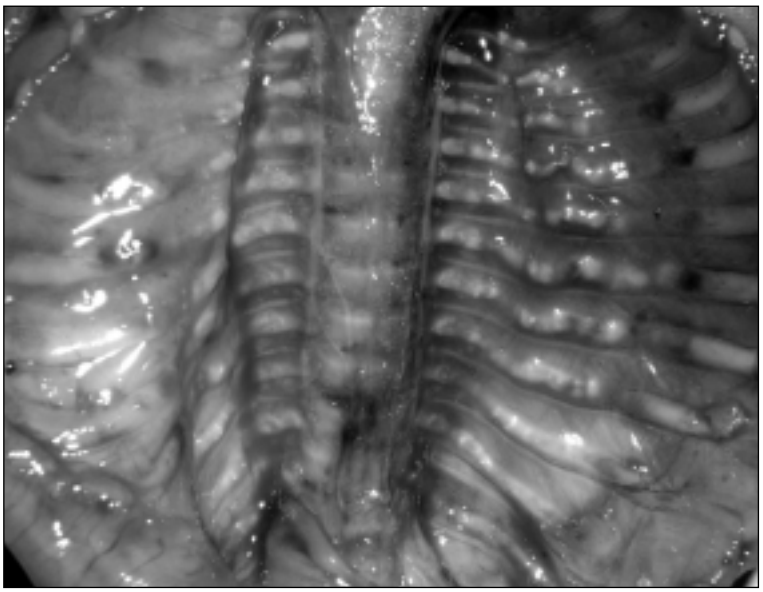

Figure 5. View of the costal fractures.

tures made of callus tissue in thorax cavity (Figure 5). Fibrocartilagenous young repairment tissue was observed in samples taken from costae. There was microfractures and callus tissue in samples from tibia. Furthermore bone spicules in metaphysis could not be seen clearly and it showed marked ossification defect (Figure 6). There were immature organ findings in samples from the other organs.

Discussion

Osteogenesis imperfecta type 1 is a heterogen genetic disease developing with collagen metabolism disorder and seen clinically in a broad spectrum. It is characterized with increase in bone fragility, abnormal osteogenesis and multifractures. Type II is the most severe form among four known

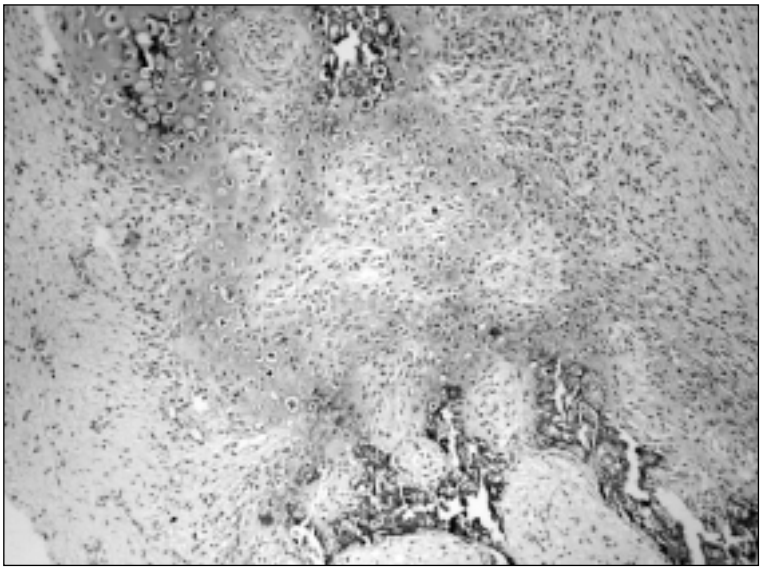

Figure 6. Ossification defects on microscopy.

clinical forms. Incidence is 0.4 in 10000 liveborns, approximately half of them are (0,19 : 10000) type II.[1]

Osteogenesis imperfecta type II is divided into 3 subgroups according to radiologic criteria. The most severe and frequently seen type is type II A. Severe micromelia, decreased thorax diameter and short thorax length, decreased mineralization and multifractures in bones are the mainly characteristics of the disease. There is normal bone echogenity in type II B and C and fractures are seen rarely. There is shortness in all bones in type II B while only an isolated shortness is found in femur in type II C.[2,3] Our case is consistent to Osteogenesis imperfecta type II A with phenotypic and radiologic characteristics.

Most of osteogenesis imperfecta type II cases occur with de novo otosomal dominant mutations. It is also reported rare otosomal recessive and germ line mosaism.[4,5]

Type 1 is developed as a result of a dominant mutation in one of COL1A1 or COL1A2 genes responsible from collagen production. Disease type 1 occurs in collagen containing organs and tissues (skin, ligament, tendon, demineralized bone, dentine) with clinical pathologic findings. In osteogenesis imperfecta, both intramembraneous production and enchondral bone production and repairment are effected from type 1 collagen production defect.[4] Failure in intramembranous bone production leads to diaphysial cortical bone production and calvarial ossification defect. In our case, it is shown that there is no ossification in sculp with ultrasonography, radiography and autopsy findings. Failure in enchondral osteogenesis leads defect in bone growing and also in healing of bone fracture.[4] It showed severe micromelia in our case, long bone measurements are determined below the 5% percentile. Ossification defect is showed histologically in slices taken from metaphysis.

Prenatal diagnose of osteogenesis imperfecta type II can be done with ultrasonographic examination and DNA analysis on chorion villus samples.[6] Most frequently described prenatal sonographic signs are being the long bones short thick untidy margin, short thorax, being the skull in low echogenity, seeing intracranial structures more evident. It can be diagnosed by ultrasonography from beginning of the second trimester.[3,7] It is reported cases that are diagnosed in first trimester.[8,9]

At high risk patient population severe displasia cases can be diagnosed early with transvaginal fetal biometry followings. But, fetal biometry following is not found effective in early diagnosing of mild form skeletal displasias.[7]

Since skeletal displasias are a quite heterogen disease group, their spesific and differential diagnose is hard. The spesific diagnose can be done with clinical findings, biochemistry analysis, radiography in postnatal period, and with radiography, autopsy and biochemistry analysis on fibroclast cultures of samples taken from fetus and autopsy in fatal cases.[10]

Tretter et al confirmed specific antenatal diagnose of 13 cases (48%), 26 cases were fatal in postnatal period in a series of 27 cases that they are determined fatal skeletal displasia.[11]

Parilla et al made a true specific antenatal diagnose to the 20 cases (65%) in a serie of 31 cases that they diagnosed skeletal displasia by ultrasonography. They project its fatality is 100 % with the findings such as severe shortness of long bones, bone curlings and fractures, being the FL/AC ratio smaller than 0.16, cloverleaf shaped skull, hypoplastic thorax, short ribs. They did not determine false positive sign showing it is fatal.[10]

Hers et al investigated that definite ultrasonographic findings are whether indicative or not in cases of suspected skeletal displasia. They projected 23 of 26 cases who they diagnosed skeletal displasia were fatal, specific diagnose of 11 of them were confirmed postnatally. They found positive predictive value 92 % in determining the fatal prognosis when evaluated with narrow thorax, being femur percentile smaller than 1 and decreased bone echogenity.[12]

In our case osteogenesis imperfecta Type II is pre-diagnosed with short narrow thorax, lack of ossification in cranium, severe micromelia and fractures and pregnancy is ended because of the presence of findings determining fatal prognosis.

Its prenatal diagnose is important because of its fatality and osteogenesis imperfecta type II mostly occurs with de novo mutations. Severe shortness of long bones, multifractures in long bones and angling, short and narrow thorax, decreased bone echogenity, cloverloaf shaped sculp are the most important ultrasonographic markers of fatal prognosis.

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