Prenatal Diagnosis of Osteogenesis Imperfecta

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Skeletal dysplasias are a group of diseases with a wide spectrum related to bone and cartilage. Some forms are lethal whereas some forms have milder clinical progression. Prenatal diagnosis of skeletal dysplasias may be possible especially when there is an index case in the family. Ultrasonography plays the central role in prenatal diagnosis and most common sonographic features are angulation of long bones, bending of femur or bowing signin the long bones. We present a case whose follow up for fetal short extremities ended with termination of pregnancy. The differential diagnosis is hard and depend especially on the fetal x-ray. Final diagnosis was lethal type osteogenesis imperfecta.

Key Words: Prenatal Diagnosis, Skeletal dysplasias, Osteogenesis imperfecta

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Introduction

Osteogenesis Imperfecta (OI) is a heterogenous group of disorders affecting the long bones, caharacterized by multiple fractures. This disorder is caused by a defect in Type I collagen synthesis. Although some forms may be autosomal recessive, inheritance is mostly autosomal dominant. OI has 4 subtypes according to Sillence's classification.[1] Type I and II are lethal forms and can be diagnosed antenatal by sonographic visualization of intrauterine fractures. Type III has a slower progression leading to severe handicap. Type IV is the mildest form with a very high tendency to fractures. Certain subtypes may be diagnosed even in the prenatal stage due to fractures and shortening of the long bones, and in increased bone transparency.

Here, a case with an antenatal diagnosis of lethal Osteogenesis Imperfecta is presented.

Case Report

A 23 year old primigravid patient admitted to our centre at 27 weeks of gestation. She had no complications other than threatened abortus at 8-10th week of gestation which was treated by progesterone supplementation. There was no consanguinity, short stature or a family history of any skeletal disorder.

The ultrasonography at 16th week revealed that biparietal diameter and abdominal circumference were appropriate with the gestational age but femur and humerus lengths corresponded to 12 weeks of gestation. Ultrasonographic measurements were repeated at 20th weeks, fetal long bone measurements were below 3rd percentile for the corresponding gestational age. No any other malformations were observed on prenatal ultrasonography. At 25th week, sonography also showed multiple fractures on bony structures including ribs.

Free Protein S deficiency and increased activated Protein C Resistance were detected on laboratory. The sonographic evaluation at 27th week of gestation revealed short extremities with multiple fractures and ossification defects on bony structures. A diagnosis of Osteogenesis Imperfecta was made and pregnancy was terminated at 27th week. In postpartum X-Ray evaluation of the fetus, multiple fractures, bowing and shortness at the long bones are observed (Figure 1).

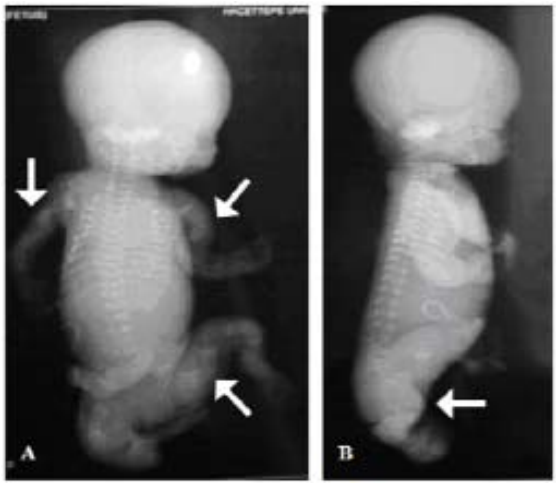

Figure 1 and Figure 2: Aantero-posterior and lateral plain x-ray graphies of the fetus

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Her second pregnancy resulted with an early first trimester spontaneous abortion at 6 weeks of gestational age. She has been on folic acid medication and vitamin B complex combined with low dose acetyl salicylic acid and supported with restricted methionin diet. The results of investigation performed on bad pregnancy outcome and early pregnancy loss revealed that she had heterozygous mutation for both MTHFR 677T and 1298, also homozygous mutation of lasminogen Activator Inhibitor-1 (PAI-1) (5G) gene. At her third pregnancy, low molecular weight heparin (2000 IU/SC/day) is added to her medication protocol. Routine antenatal care protocol is followed. Third pregnancy of the patient resulted with a live birth, without detectable minor or major congenital abnormalities.

Discussion

Prenatal diagnosis may be possible with ultrasonography and the most common features seen on sonography are angulations of the long bones, bending of femur or bowing sign.[2, 3] In presence of an index case, molecular genetic studies can also be performed for certain disorders. These may include DNA based studies after chorionic villus sampling between 10-14th weeks of gestation and protein based studies made between 12-15 week of gestation.[4] After 14th week careful sonographic follow-up may be successful in detecting skeletal dysplasias. However gold standard diagnostic procedure in differential diagnosis of skeletal dysplasias is fetal conventional radiography.[5]

Osteogenesis Imperfecta results from a defect in Type 1 collagen production.[5] Mutations at the COL1A1 and COL1A2 genes result in this disorders[5] Since DNA synthesis is activated when there are mutations at MTHFR gene, genetic problems may occur more commonly among patients having these mutations.

In differential diagnosis, entities to be considered from the most likely to the least for short extremities with angulation of long bones are Osteogenesis Imperfecta, Campomelic dysplasia, Thanatophoric dysplasia, Hypophosphatasia, Short rib-Polidactyly syndrome, Femoral hypoplasia, Achondroplasia and Metaphyseal dysplasia. All these skeletal dysplasia syndromes show different genetic penetrance, so differential diagnosis should help us for algorithm of follow up period for each group. The presented case was clinically and radiographically diagnosed as Osteogenesis Imperfecta Type II (Prenatal lethal type). The family was counselled accordingly.

Osteogenesis Imperfecta'nın Prenetal Tanısı

İskelet displazileri kemik ve kıkırdak dokusu ile ilgili geniş bir hastalık grubunu oluşturur. Bazı formların hafif klinik ilerleme göstermesine karşın bazı formları ölümcüldür. İskelet displazilerinin prenatal tanısı, özellikle ailede indeks bir vaka olması durumunda, dikkatli bir takip süreci ile mümkün olabilir. Prenatal tanı ultrason takibi ile mümkün olup, en sık görülen bulgular, uzun kemiklerin açılanması, femurun eğimlenmesi ve bükülme (yaylanma) işaretidir. Burada fetal kısa ekstremiteler için yapılan takibi gebelik sonlandırması ile sonuçlanmış bir vaka sunmaktayız. Ayırıcı tanı zor bir süreç olup , özellikle fetusun düz x-ray grafilerine dayanmaktadır. Son tanı prenatal letal tip osteogenesis imperfekta olarak belirtilmiştir.

Anahtar Kelimeler: Prenatal tanı, İskelet displazileri, Osteogenesis imperfekta.

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