Hypophosphatasia associated with increased nuchal translucency: a report of two affected pregnancies

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ABSTRACT

Perinatal hypophosphatasia is a lethal autosomal recessive skeletal abnormality with a birth prevalence of about 1 per 100 000. It is characterized by deficiency of the tissue-nonspecific isoenzyme of alkaline phosphatase causing abnormal bone mineralization. In the two affected fetuses from the same family ultrasound examination at 14 and 12 weeks, respectively, demonstrated increased nuchal translucency thickness, hypomineralization of the skull and spine, narrowing of the chest and shortening of the limbs.

INTRODUCTION

Subcutaneous accumulation of fluid at the back of the fetal neck at 10–14 weeks’ gestation, visualized by ultrasound examination as increased nuchal translucency thickness, is associated with chromosomal defects, structural abnormalities and a wide range of genetic syndromes, including many skeletal dysplasias1–4.

Hypophosphatasia is a rare autosomal recessive condition characterized by abnormal bone mineralization and low or absent activity of tissue nonspecific alkaline phosphatase5. In this paper we report on three consecutive pregnancies of a nonconsanguineous couple at risk of the perinatal form of the disease.

CASE REPORT

A 27-year-old Caucasian woman was referred to the Harris Birthright Centre for Fetal Medicine at 14 weeks of gestation in her first pregnancy because, at routine ultrasound examination at her local hospital, the fetus was found to have fixed flexed upper and lower limbs and increased nuchal translucency thickness. The crown–rump length (CRL) was 93 mm and the nuchal translucency was 4.1 mm. There was marked hypomineralization of the skull and spine, narrowing of the chest with short ribs, shortening of all the long bones and bilateral talipes. The findings were suggestive of a lethal skeletal dysplasia and the parents chose to have termination of the pregnancy, which was performed by induction of labor with prostaglandin. Pathological examination, including radiological studies, of the fetus led to the diagnosis of hypophosphatasia. Analysis of DNA from the fetus confirmed the radiological findings and showed the fetus to be a compound heterozygote for known disease causing mutations in the ALPL gene. These were at I195F and E337D on either allele.

In their second pregnancy the parents had an ultrasound examination in our center at 12 weeks of gestation. The fetus had a CRL of 53 mm and appeared normal with appropriate mineralization of the skull and the long bones. The nuchal translucency thickness was 1.4 mm. Follow-up ultrasound examinations at 16 and 20 weeks confirmed normal skeletal development. A healthy female infant was born at 41 weeks of gestation weighing 3912 g.

In the third pregnancy, ultrasound examination in our center at 12 weeks of gestation demonstrated hypomineralization of the skull (Figure 1b) and spine, narrowing of the chest and shortening and bowing of the limbs. The CRL was 63 mm and the nuchal translucency was increased (2.5 mm). The parents opted for termination of the pregnancy and a recurrence of hypophosphatasia in the fetus was confirmed from DNA extracted from the placenta.

DISCUSSION

The disease hypophosphatasia is clinically classified according to the age of onset of symptoms and subdivides into perinatal, infantile, childhood and adult forms5–7. The most severe type is perinatal hypophosphatasia, which has an autosomal recessive mode of inheritance and occurs in about...
Figure 1 Transverse section of the fetal head at 12 weeks of gestation in (a) a normal fetus and (b) one affected by hypophosphatasia.

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REFERENCES