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Nuchal thickening in Jacobsen syndrome

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ABSTRACT

A routine detailed ultrasound examination performed at 20 weeks' gestation demonstrated the presence of nuchal thickening as an apparently isolated finding. The concentration of maternal α-fetoprotein was normal and the risk of Down's syndrome was 1 in 6800. Amniocentesis was performed and chromosome analysis showed the karyotype 46,XY, del(11)(q23) found in Jacobsen syndrome. Fetal autopsy performed following medical termination at 23 weeks confirmed the phenotype and internal abnormalities found in Jacobsen syndrome.

INTRODUCTION

Jacobsen syndrome[1] is a rare syndrome resulting from a terminal deletion of the long arm of chromosome 11, most commonly at 11q23[2] and requiring deletion of the 11q24.1 sub-band for the typical phenotype[3,4]. An association has previously been noted with a folate-sensitive fragility site in this region[5]. Most cases described previously have been identified postnatally as a result of chromosome analysis in patients with typical dysmorphic features including trigonocephaly or in mentally retarded individuals. Prenatal diagnosis has been described following detection of fetal abnormalities[6], but to our knowledge no case has previously been associated with increased nuchal translucency.

CASE REPORT

A 25-year-old woman, para 0 + 0, had a first-visit scan that confirmed a singleton pregnancy with crown–rump length (CRL) 71.8 mm and biparietal diameter (BPD) 23.4 mm, equivalent to 13 + 1 weeks' gestation. No abnormalities were detected, but it was not our routine practice to perform nuchal thickness measurement. The level of maternal α-fetoprotein measured at 16 weeks was normal (0.88 MoM) and Down's syndrome risk was calculated at 1 in 6800. A routine detailed ultrasound examination was performed at 20 weeks' gestation and showed an apparently isolated abnormality of nuchal thickening (Figures 1 and 2). No other structural abnormalities were identified.

The patient was counselled and offered amniocentesis. Amniocyte cultures showed a karyotype of 46,XY, del(11)(q23) consistent with Jacobsen syndrome. Following counselling and discussion with the parents, a medical termination of pregnancy was performed at 23 + 3 weeks. The postmortem examination showed dysmorphic features (Figures 3 and 4) including prominent epicanthal folds, wide straight mouth, low-set ears, relative micrognathia and high-arched palate. The neck was short and thick with increased nuchal fold and there was generalized mild edema. Widely spaced nipples were noted. There was no trigonocephaly. Cardiac abnormalities of a fenestrated foramen ovale, dominant right ventricle with relatively small left ventricle and supravalvular dilatation of the aorta were present with mildly hypoplastic lungs. Genitourinary

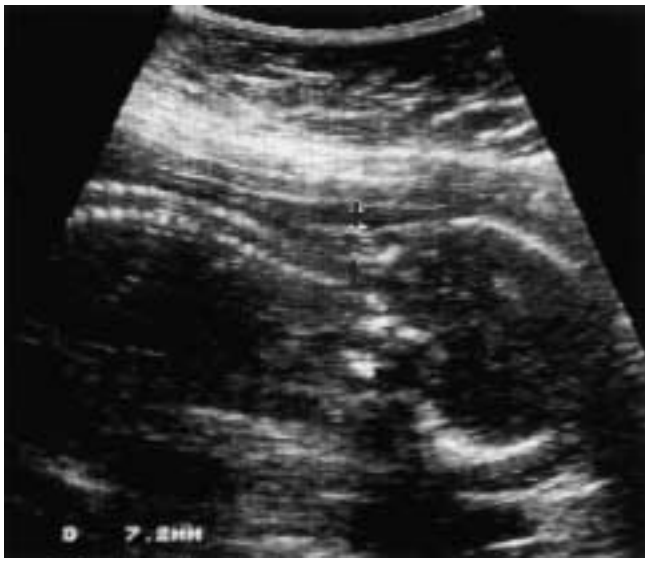

Figure 1 Longitudinal ultrasound image, showing nuchal thickening

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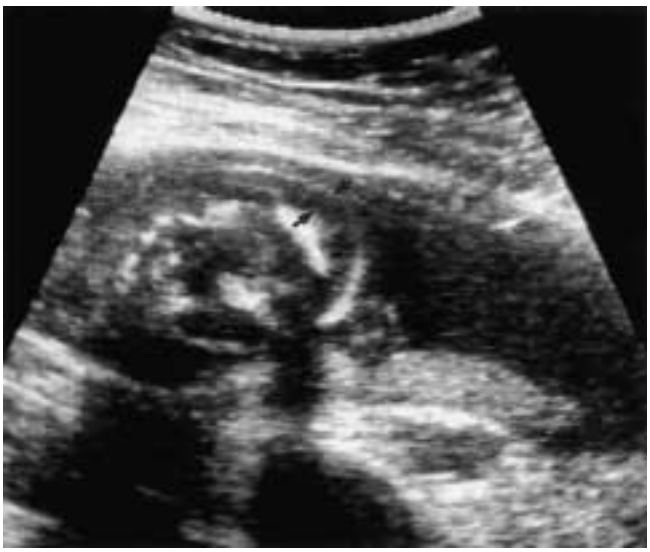

Figure 2 Transverse ultrasound image, showing increased nuchal thickening (arrowed)

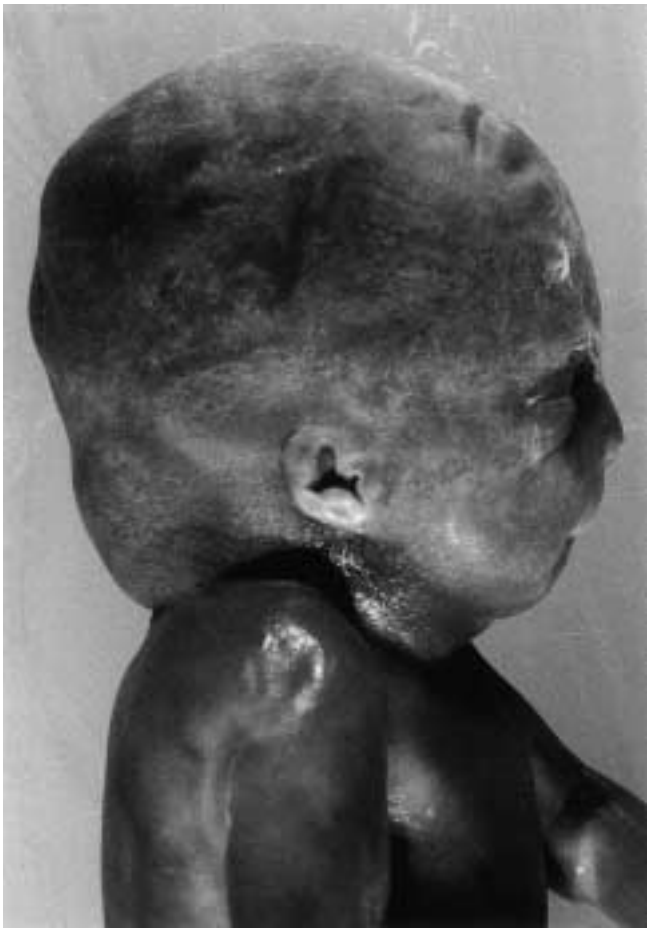

Figure 3 Postmortem photograph, showing micrognathia, low-set ears, short neck and increased nuchal thickness

abnormalities of moderate bilateral dilatation of the renal pelves and ureters with distended bladder and probable posterior urethral valves and high, small testes were seen. G banding studies performed on skin tissue confirmed the karyotype of 46,XY, del(11)(q23). Blood chromosomal analysis of the parents showed normal karyotypes, including folate-sensitive fragility studies of the break point on chromosome 11.

Figure 4 Postmortem photograph, showing dysmorphic features, including widely spaced nipples

DISCUSSION

Increased nuchal thickness and cystic hygromas have been described with many chromosomal abnormalities other than trisomy 21, including trisomies 18 and 13, aneuploidy, Turner syndrome, ring chromosome 6[7], ring chromosome 14[8] and Smith–Lemli–Opitz syndrome[9]. A recent report[10] showed an association of increased nuchal thickness at 10–14 weeks' gestation with cardiac abnormalities, possibly due to transient cardiac failure. There is already a well-recognized association in the second trimester between increased nuchal fluid and cardiac abnormalities[11], and we suspect this is the explanation in our case, where this finding led to the diagnosis of Jacobsen syndrome. This is a relatively rare syndrome with a wide range of reported clinical findings[12], the most common being trigonocephaly (a keel-shaped skull caused by premature fusion of the metopic suture). Hypertelorism, wide or low nasal bridge, low-set malformed ears, downslanted mouth corners, micrognathia and growth and variable psychomotor retardation are also reported. Various cardiac defects (including ventriculoseptal defect, hypoplastic aorta, tetralogy of Fallot, hypoplastic left heart, truncus arteriosus and aortic coarctation) are documented,

and digital anomalies, widely spaced nipples (both present in our case), cryptorchidism, urinary and adrenal[3,12] abnormalities and pyloric stenosis have also been described.

One previous case was diagnosed prenatally with bilateral renal pelvis dilatation at 20 weeks, with subsequent scanning at 29 weeks confirming this and showing trigonocephaly, hypotelorism, micrognathia, prominent anteverted nares, short femur and polyhydramnios. This case had an unbalanced translocation 46,XY, – 11, + der(11), *t*(5;11)(p14; q23.3) and the baby died in the neonatal period[6]. The outcome of these cases is variable, from early neonatal death[6,12,13] to mental retardation ranging from mild to severe[2], with other structural abnormalities.

Our couple requested a medical termination of pregnancy following discussion of the possible outcomes. Parental chromosomal studies including folate-deficient cultures looking for a heritable folate-sensitive break point[3,5] were all normal, and this case appears to have arisen *de novo*. The 11q23 band is known to contain a heritable folate-sensitive fragile site[3,5] that may predispose to deletion, as this region is the most common site of deletion, and occurs in approximately two-thirds of cases reported[2]. Genetic counselling has been given to the parents with a very low risk for future pregnancies, but for parental reassurance a detailed anomaly scan and possibly amniocentesis will be offered in future pregnancies.

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