

Prenatal diagnosis of Jacobsen syndrome with cystic hygroma

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ABSTRACT

Jacobsen syndrome (JBS) is a rare, contiguous genetic deletion syndrome caused by partial deletion of chromosome 11q. It is difficult to diagnose JBS by ultrasonography during the prenatal period because it has atypical clinical findings. Although nuchal thickening is associated with JBS, cystic hygroma has not been previously reported in conjunction with this syndrome. We describe the first prenatal diagnosis of JBS with cystic hygroma, which was clinically diagnosed at 13 weeks gestation in a Japanese woman, although it had not been detectable at the 11th week of gestation. In addition, a single ventricle fetal heart defect was suspected. Amniocentesis was performed, and G-banded karyotype evaluation revealed 46,XX,del(11)(q23), which is consistent with JBS. Cystic hygroma and congenital heart malformation have been reported to be associated with chromosomal anomalies. The present case indicates that a fetal cystic hygroma without increased nuchal thickness might be associated with JBS.

Key words: 11q deletion, Cystic hygroma, G-banded chromosome analysis, Jacobsen syndrome, Prenatal diagnosis

Jacobsen syndrome (JBS, MIM #147791), a rare, contiguous genetic deletion syndrome involving terminal chromosome 11q, is characterized by prenatal and postnatal physical growth restriction, psychomotor restriction, characteristic facial dysmorphism, cardiac malformation, immunodeficiency, and thrombocytopenia. Its prevalence has been estimated at 1/100,000 live births, with a female/male ratio of 2:1 [1]. A prenatal diagnosis of JBS is especially rare. The deletion is reported to arise *de novo* in 85% of cases, whereas in the other 15%, it results from parental translocation or some other chromosomal structural rearrangement. Cystic hygroma has been described to be associated with chromosomal structural anomalies, monogenic disorders, and pregnancy loss [2]. However, it has not been previously reported in subjects with JBS, although nuchal thickening is associated with this syndrome [3]. We suspect that this cardiac malformation or the deletion of terminal chromosome 11q led to cystic hygroma. We describe a unique case of prenatally diagnosed JBS with cystic hygroma.

CASE REPORT

A 27-year-old Japanese woman was clinically diagnosed as carrying a fetus with cystic hygroma during a routine pregnancy checkup at 13 weeks gestation (Fig. 1a and b). Increased nuchal thickness was not detectable at 11 weeks gestation. A previous pregnancy had resulted in spontaneous abortion at 6 weeks gestation. Her medical and family history was unremarkable. She was referred to a perinatal medical center to be investigated thoroughly, where her course was followed.

Ultrasonography (USG) revealed a suspected single ventricle fetal heart defect, although fetal growth restriction, oligohydramnios, or other structural anomalies were not detected. A fetal chromosomal anomaly was suspected. After genetic counseling, amniocentesis was performed at 16-week, 2-day gestation at our hospital. The fetal G-banded karyotype revealed 46,XX,del(11)(q23), which is consistent with JBS. A copy number variation analysis of 11q23 was not further investigated. Following further genetic counseling and discussion with the parents, the pregnancy was terminated legally at 19 weeks gestation. The female fetus was malformed with low-set ears, which corresponded to the phenotype of JBS, and had edema around the neck (Fig. 1c and d). After the termination, parents consented to genetic counseling but refused investigation of their karyotypes.

DISCUSSION

JBS is a rare contiguous genetic syndrome caused by partial long arm deletion of chromosome 11. Such a prenatal diagnosis is rare. In general, the prognosis of a patient with JBS depends on severe heart malformations and bleeding during the neonatal period, and the survival rate of the fetus in the presence of a fetal cystic hygroma is 10% [4,5]. In our case, a single ventricle fetal heart defect was suspected, so the prognosis was most likely poor.

A prenatal diagnosis of 11q deletion is possible by amniocentesis or chorionic villous sampling. Prediction of JBS during the prenatal period is difficult because it has phenotypic



Figure 1: Ultrasonographic images and fetal postmortem photographs. (a) Axial image of the fetal cystic hygroma (arrow). (b) Longitudinal image of the cystic hygroma (arrow). (c) Postmortem photograph shows low-set ears. (d) Postmortem photograph shows edema around the neck

variations. Cystic hygroma and increased nuchal thickness have been reported to be associated with chromosomal anomalies, single-gene disorders, and fetal cardiac pathology [6].

PubMed database search did not reveal any reports of the association of JBS and cystic hygroma. In addition, JBS has not been reported in association with a vascular/lymphatic malformation. In our case, cystic hygroma was confirmed by USG at 13 weeks gestation, although increased nuchal thickness was not detected at 11 weeks. In addition, USG revealed the possibility of a single ventricular defect in the fetus. We, therefore, suspected that the cardiac malformation or deletion of the terminal chromosome 11q led to the cystic hygroma. However, it is difficult to confirm whether the cardiac malformation or JBS itself was the main causative factor of cystic hygroma. We could not confirm whether JBS had arisen *de novo* or had been inherited because the parents refused chromosomal analyses for themselves. Therefore, the risk of recurrence in another pregnancy was uncertain. Nevertheless, the fetal G-banded chromosomal analysis by amniocentesis or chorionic villous sampling might be useful for future pregnancies.

Liu *et al.* reported detecting interstitial deletion of 11q using array comparative genomic hybridization, although conventional G-banded chromosome analysis revealed an apparently normal karyotype [7]. Therefore, array comparative genomic

hybridization during fetal chromosomal analysis may be useful for detecting genome-wide gains and losses with higher resolution surrounding 11q23 due to the uncertain risk of recurrence in our case.

CONCLUSION

Our case indicates that a fetal cystic hygroma without increased nuchal thickness might be associated with JBS.

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