was no evidence of familial recurrence. Michaud *et al.*[4] reported familial cases and, in addition to genetic causes, cite teratogens such as thalidomide, alcohol, vascular compromise by amniotic bands or other causes and maternal diabetes as possible etiological factors. Mastroiacovo *et al.*[3] reported an incidence of amelia, and possibly other limb reductions, but no non-limb malformations in 0.4 per 100 000 live births.

In our case, the macroscopic aspect of the right arm revealed two segments but there was only one bone, the humerus. According to the classification of limb defects proposed by the meeting of the International Clearinghouse for Birth Defects Monitoring Systems[1], our fetus showed a right upper limb deficiency of the mesial transverse type.

Our case again shows the value of morphological ultrasound examinations at 10 weeks' gestation.

In our case the diagnosis was made using 2D, B-mode ultrasound. Three-dimensional ultrasound revealed the humerus, which was not seen by 2D ultrasound, but its use did not influence clinical management.

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Identification of unexpected parental Robertsonian (13q;14q) translocations following prenatal sonographic detection of holoprosencephaly

In a recent issue of the Journal, Blaas *et al.*[1] reported perinatal findings of 30 cases of holoprosencephaly (HPE). Trisomy 13 was found in five out of 11 cases with chromosomal abnormalities. Interestingly, one case (Case 4) belonged to unbalanced translocation trisomy 13. The karyotype, 47,XY, + 13,t(13;14), as described in the report, was in fact 46,XY, + 13,der(13;14)(q10;q10) according to An International System for Human Cytogenetic Nomenclature (1995)[2].

We have identified parental Robertsonian (13q;14q) translocations following prenatal sonographic detection of HPE in two fetuses. Case 1 was a 32-year-old, gravida 2, para 0 woman referred for genetic counseling at 17 weeks' gestation because of relative oligohydramnios, cystic hygromas, intrauterine growth restriction (IUGR), hydrops fetalis and alobar HPE. Chorionic villus sampling revealed a karyotype of 46,XX, + 13,der(13;14)(q10;q10). The karyotype contained two normal chromosomes 13, one normal chromosome 14, and the derivative chromosome, der(13;14), consisting of the long arm of chromosome 13 and the long arm of chromosome 14. The resulting net imbalance was loss of the short arm of 14 and trisomy for the long arm of chromosome 13. Cytogenetic analysis of the mother's blood showed a balanced Robertsonian translocation, 45,XX,der(13;14)(q10;q10). The father's karyotype was normal. The pregnancy was terminated subsequently. At birth, the proband manifested additional findings of cyclopia and polydactyly. Case 2 was a 39-year-old, gravida 5, para 1 woman referred for amniocentesis at 20 weeks' gestation due to advanced maternal age. Cytogenetic analysis revealed a karyotype of 46,XX, + 13,der(13;14)(q10;q10). The father had a normal karyotype, whereas the mother was found to be a Robertsonian translocation carrier with a karyotype of 45,XX,der(13;14)(q10;q10). Level II ultrasonography at 24 weeks' gestation showed polydactyly, cebocephaly, hypotelorism, IUGR and alobar HPE. The pregnancy was terminated. The proband manifested all prenatally observed abnormalities.

The association of HPE with trisomy 13 has been well documented in the literature. Both cases in this report were secondary to unbalanced translocation trisomy 13 rather than free trisomy 13. However, the phenotypic features of unbalanced translocation trisomy 13 are basically the same as those of free trisomy 13. In this Letter, we emphasize the importance of identification of parental Robertsonian translocation in addition to the phenotype–genotype correlation. Carriers with balanced Robertsonian translocations are known to be associated with repeated spontaneous miscarriage, male infertility and having abnormal offspring with aneuploidy, especially Down syndrome and Patau syndrome, and uniparental disomy (UPD) involving chromosomes 14 and 15[3]. The prevalence of the rob(13q;14q) carrier is 0.075% or about 1 in 1300 persons[3]. Parents with a Robertsonian (13q;14q) translocation carry a 0.3–1.4% risk of having aneuploid offspring and a 0.6–0.9% risk of UPD 14 in the offspring[3,4]. The risks, though small, cannot be neglected. Since HPE is associated with as many as 70% of trisomy 13 cases[5], fetuses with translocation trisomy 13 may predominantly present HPE on prenatal ultrasound. Prenatal sonographic detection of HPE should therefore prompt cytogenetic investigations, which may lead to the identification of an unexpected parental Robertsonian translocation involving chromosome 13. The information acquired through perinatal studies is helpful for both genetic counseling and investigations in following pregnancies.

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Glutaric aciduria (type I): prenatal ultrasonographic findings

Glutaric aciduria type I (GA I) is an autosomal, recessively inherited metabolic disease which manifests as increased excretion of glutaric acid and its metabolites due to a defect of the enzyme glutaryl-CoA dehydrogenase (GCDH). Its clinical course is characterized by sudden onset of an extrapyramidal movement disorder, neurological deterioration, progressive dystonia and macrocephaly. Early diagnosis and intervention is important and may minimize brain damage. If untreated, most affected children will die during the first decade of life[1–3]. Prenatal diagnosis of GA I has previously been performed by the determination of GCDH activity in fetal tissue obtained by amniocentesis or chorionic villus sampling (CVS). There are reports, however, of patients with an affected child who have low excretion of glutarate or high residual GCDH activity which may hinder prenatal diagnosis in these families[4–6]. With the advance of molecular biology, prenatal molecular diagnosis of GA I from CVS has been reported by Busquets *et al.*[7]. Neuroimaging of cases affected by GA I has mainly involved postnatal magnetic resonance imaging (MRI) or computed tomography (CT). We present a case of GA I diagnosed prenatally by molecular analysis of CVS samples and describe the prenatal ultrasonographic findings.

Case report

A 32-year-old gravida 2, para 1 was referred at 10 completed weeks of gestation due to a history of having a previous boy affected by GA I. He was diagnosed at 10 months of age with macrocephaly, progressive dystonia and neurological deterioration. Biochemical studies of his urine revealed marked elevation of glutaric acid and glutamine concentrations. The MRI findings of his head were consistent with those of GA I reported by others: widening of the subarachnoid space, frontal subdural effusion, hydrocephalus, cyst-like structure over sylvian fissure and periventricular hyperintensity over both frontal and occipital horns on T2. Molecular study disclosed a homozygous IVS10 –2A > C GCDH mutation, which has not been reported in a Caucasian population. In her current pregnancy, following counseling about the risks involved with CVS and the feasibility of a molecular diagnosis of GA I, the woman underwent CVS at 11 weeks of gestation. Molecular analysis revealed an affected homozygous female fetus. After thorough discussion between the couple and a pediatric endocrinologist, they opted to continue the pregnancy. At 16 completed weeks, cytogenetic amniocentesis was performed which confirmed the diagnosis of a homozygous GA I-affected female with normal karyotype. Detailed ultrasound examination at 20 weeks of gestation was unremarkable. However, a repeat scan at 30 weeks showed dilatation of the quadrigeminal cistern (QC, 14 × 18 mm) and the suspicion of macrocephaly (head circumference: 293 mm, 95th percentile: 298.7 mm). A three-dimensional (3D) ultrasound examination was also performed at 30 weeks and confirmed the location of the dilated QC (Figure 1). Progressive dilatation of the QC (up to 21 × 27 mm), macrocephaly (above 95th percentile), frontotemporal atrophy and enlarged sylvian fissure were found in the follow-up scans (Figure 2). Due to a previous Cesarean section and the possible deterioration

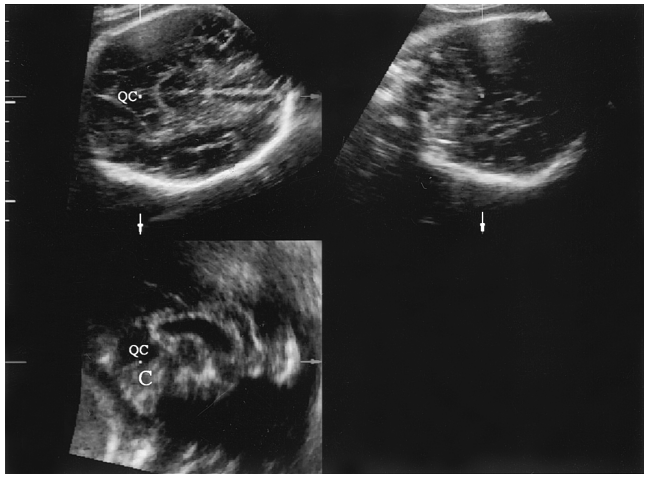

Figure 1 The spatial relationship of the quadrigeminal cistern (QC) to the cerebellum (C) is shown in three-dimensional ultrasonographic images of the fetal head at 30 weeks of gestation. Transverse section at the biparietal diameter plane, coronal section and sagittal section are shown in the left upper, right upper and lower panels, respectively.

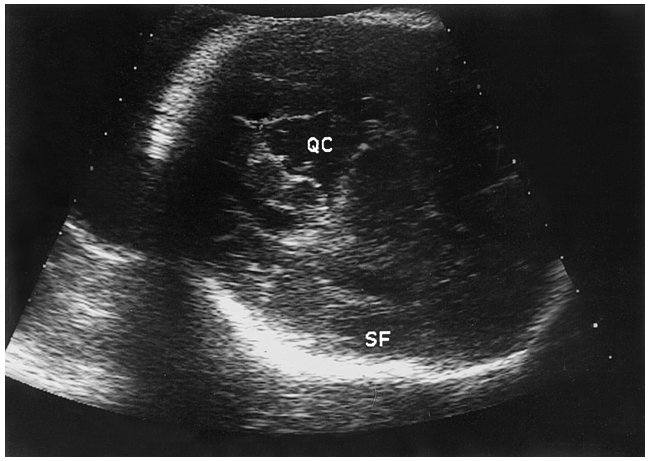

Figure 2 Prominent spaces of the quadrigeminal cistern (QC) and sylvian fissure (SF) of the fetal head are shown in the follow-up scan.