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Case Reports

Amniocentesis can be useful during the third trimester of pregnancy for antenatal diagnosis of Pallister-Killian syndrome: a case report

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Summary

Pallister-Killian syndrome (PKS) is an extremely rare genetic disease characterized cytogenetically by tetrasomy 12p mosaicism. We recently encountered a case of maternal hydramnios associated with congenital diaphragm hernia according to the prenatal diagnosis. Prenatal diagnosis revealed a non-mosaic 47, XY, i(12)(p10) karyotype at amniocentesis of G-band and M-FISH analysis. We performed chromosomal analysis in both interphase and metaphase cells from a cord blood lymphocyte specimen. Mosaic tetrasomy of chromosome 12p was supported by G-banding or FISH analysis. When fetal observations are performed in detail using 2D/3D US, PKS may be diagnosed. In addition, it is effective to perform amniocentesis during the third trimester of pregnancy.

Key words: Pallister-Killian syndrome; Mosaic tetrasomy 12p; Amniocentesis; Timester.

Introduction

Pallister-Killian syndrome (PKS) is a rare genetic disorder characterized by mosaicism for tetrasomy of chromosome 12p [1, 2]. Gigenkrantz *et al*. reported the first prenatal diagnosis of PKS [3]. Including our report, there has, to date, been less than 70 prenatally diagnosed cases [4]. Routine cytogenetic postnatal diagnosis of PKS is difficult because of the specific tissue-limited mosaicism. The proportion of cells containing an isochromosome 12p has been reported to be 100% in amniocytes and bone marrow cells; however, a considerably lower percentage (0-2%) has been reported in lymphocytes [5, 6]. Moreover, it is difficult to decide prenatal diagnosis with ultrasound (US) findings so that the phenotypic variation of PKS is complicated [7]. The recent introduction of 3D US has made it easy to perform daily routine examinations, and 3D indicators have proved useful in the evaluation of fetal anomalies. However, almost all cases diagnosed prenatally as PKS result in spontaneous abortion or necessitate an artificial abortion [8]. Consequently, there have been few reports regarding 3D US findings of PKS during the third trimester. In this paper, we describe the use 3D US indicators of PKS in the third trimester of pregnancy.

Case Report

A 29-year-old woman (gravida 1, para 1) was admitted to our hospital at 31 weeks' gestation for suddenly developed severe hydramnios. She was diagnosed as having a congenital diaphragmatic hernia (CDH). Two-dimensional (2D) US revealed right-sided sifts of the aortic arch, heart, and right lung. In addition, the following cardiovascular defects were detected: pulmonary atresia with ventricular septal defect, right ventricular hypertrophy, and mitral regurgitation. We made the tentative diagnosis of tetralogy of Fallot (TOF). The 2D US showed enlargement of the cisterna magna. Moreover, the left lung could not be identified from the 2D US image. We suspected that the left lung was aplasic and that the right lung was hypoplasic. The 3D US indicators were flat nasal bridge, low-set ears, and overlapping upper limbs. At 31 weeks' gestation, amniocentesis and reduction of the amniotic fluid volume were performed. We removed approximately 4,000 ml of amniotic fluid. Moreover, continuous drip infusion of ritodrine was initiated to minimize the threat of preterm labor. At 35 weeks' gestation, approximately 3,900 ml of amniotic fluid was removed. A stable microbubble test performed at this time yielded a weak result. After vaginal delivery at 36 weeks, the male baby weighing 3,434 g was found to have not only US indicators but also neck webbing and sparse hair characteristic of temporal alopecia. His skin color was a durky red due to the general edematous condition. The first cry did not occur and he died 40 minutes after delivery. Although no postnatal autopsy was performed, postnatal magnetic resonance imaging (MRI) was performed approximately 32 hours after death, and the resulting images were used as autopsy images. According to the MRI findings, internal malfunctions comprised herniation of the stomach, spleen, and part of the liver and small intestine into the left pleural cavity due to a defect in the left diaphragm. As a consequence of the previously described anomalies, displacement of the heart had occurred, and thus cardiac anomalies could not be diagnosed.

Cytogenetic analysis and results

Amniocentesis

On the basis of the US findings of multiple fetal anomalies, prenatal karyotyping was recommended. Trans-abdominal

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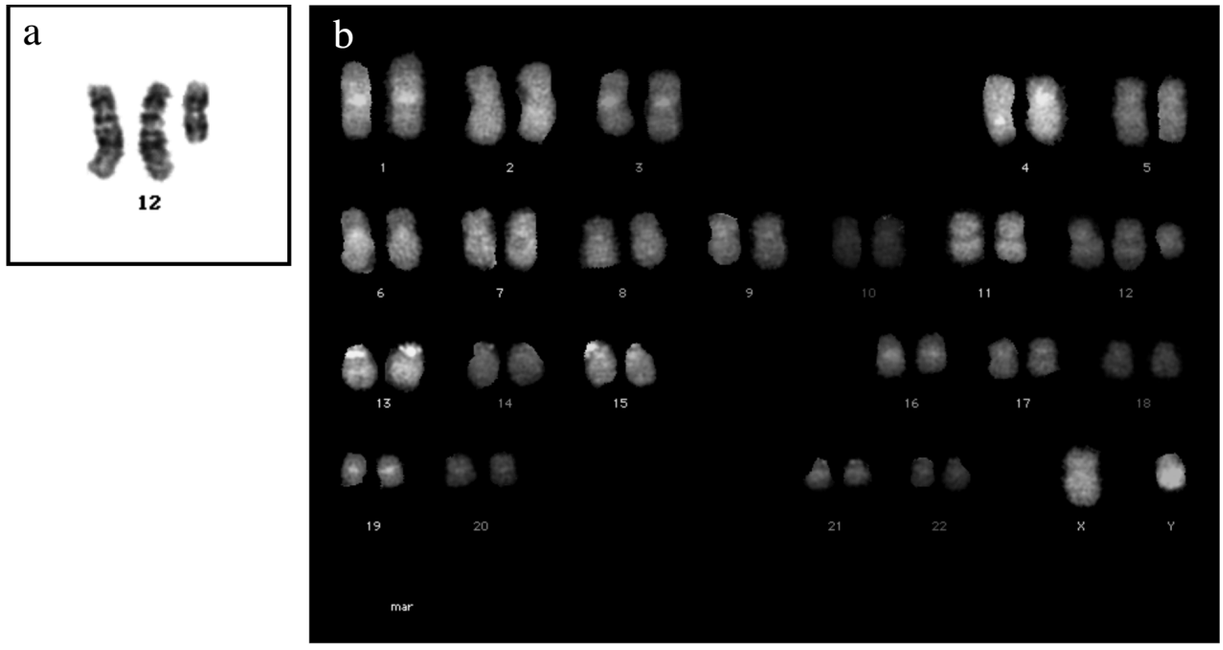

Figure 1. — G-band and M-FISH amniocentesis results. (a) Metaphase cell from amniotic fluid sample showing the i(12)(p10) marker chromosome, and (b) M-FISH shows that the marker chromosome consists of material derived from chromosome 12.

amniocentesis (at 31 weeks' of gestation) was performed to obtain an amniotic fluid sample for prenatal diagnosis. The chromosome abnormalities were examined using 10- to 12-day cultures of amniotic fluid cells. Chromosomes were stained with trypsin-Giemsa to produce the G-banded pattern (Figure 1a). Further, because the origin of the extra chromosome was unknown, multi-color fluorescence in situ hybridization (M-FISH) analysis was also performed, for which we used a whole chromosome painting probe (wcp12). The karyotype was accordingly determined to be 47, XY, +mar. ish i(12) (p10) (wcp12+) (Figure 1b).

Umbilical vein blood

A cord blood sample was obtained after birth. Cytogenetic analysis was performed using cord blood lymphocyte cultures, and metaphase chromosomes were banded using the GTG banding technique. The karyotype in 30 G-banded lymphocyte metaphase cultures was mos 47, XY, i(12) (p10) [1]/46, XY[29]. On the other hand, the results of FISH using a chromosome 12-specific probe (ETV6, cep12) were mos 47, XY, i(12) (p10) [9]. ish i (12) (ETV6+) [9]/46, XY[91] and mos 47, XY, i(12) (p10) [9]. ish i (12) (cep12+) [9]/46, XY[91].

Discussion

There have been several investigations of the prenatal diagnosis of PKS since the study of Gilgenkrantz *et al*. [3]. Similar to trisomy 21, the maternal age at conception is considered to be one of the risk factors for trisomy and tetrasomy 12p [9]. Kolarski *et al*. reported that one of the US markers for these conditions is intrauterine growth restriction [10]. Prior to the present study, there had been few similar reports, primarily because in approximately 80% of the cases diagnosed prenatally the women undergo therapeutic or spontaneous abortion. In the present case, we made the diagnosis of suspected PKS based on 3D US indicators (e.g., CDH, congenital heart disease (CHD), flat nasal bridge, low-set ears, and overlapping upper limbs) and performed amniocentesis. We were accordingly able to make a diagnosis prenatally and were thus in a position to inform the parents that the prognosis of their baby was severe. Moreover, it has been reported that PKS is associated with typical facial anomalies (e.g., a flat, very short nose with an upturned tip; a broad, elevated nose bridge; and thin lips, with the lower lip being protruded). However, it may be difficult to detect such facial anomalies in the early stage of pregnancy [10]. Therefore, the typical deformity pattern associated with PKS, as in this case, may be rare and, accordingly, the phenotypic variation of PKS may be complicated [7]. Diagnosis of CDH as the most common major anomaly in PKS is associated with a severe prognosis [8]; nevertheless, it has also been reported that newborn infants with PKS can be saved by early surgical correction for CDH [8]. Therefore, prenatal MRI enhances fetal anatomic evaluation and facilitates perinatal management and family counselling. MRI proves to be useful in confirming the utility of US indicators [11]. In the present case, we were able to prenatally determine a poor prognosis following the identification of CDH from 2D US indicators. The family decided against preserving the baby's life. Postnatally, such an analysis might help parents to accept their baby. In our case, it was easy to perform amniocen-

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tesis because of the necessity to remove amniotic fluid. In general, analysis of peripheral blood lymphocytes usually reveals a normal karyotype, whereas chromosome analysis from skin fibroblasts shows an isochromosome 12p mosaicism. Therefore, when the diagnosis is suspected PKS, even in the third trimester of pregnancy, it is beneficial to both the parents and the baby to perform prenatal amniocentesis.

Conclusion

We encountered a case involving the prenatal diagnosis of suspected PKS based on 2D/3D US indicators. As a consequence, amniocentesis was performed and the prenatal diagnosis could be confirmed. We were able the inform the parents that the prognosis of their baby might be very poor with the possibility of malfunction of fetal respiration due to CDH. Thus 3D US findings may prove to be useful for prenatal diagnosis of complicated cases in which typical dysmorphic features are absent.

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