Prenatal Diagnosis of Congenital Diaphragmatic Hernia in a Fetus with 46,XY/46,X,-Y,+der(Y)t(Y;1)(q12;q12) Mosaicism: A Case Report

INTRODUCTION

Congenital diaphragmatic hernia (CDH), a defect of the diaphragm which allows abdominal organs to herniate into the thoracic cavity, is serious and complex condition with high perinatal mortality. CDH results from failure of the pleuroperitoneal membrane to fuse in the first trimester and impacts on developing fetal lung (1). The incidence of CDH is approximately one in 2,200 to 5,000 pregnancies (2). The perinatal mortality is up to 70% and directly related to the severity of lung hypoplasia and other major combined anomalies (2, 3). Additional structural anomalies such as congenital heart defects, neural tube defects, hydronephrosis, renal agenesis, and anencephaly are present in 25% to 57% of all cases of CDH (4-6). The defect has also been reported in association with multiple syndromes such as Pallister-Killian syndrome, Fryns syndrome, Di George syndrome and Apert syndrome. Among the chromosomal abnormalities associated with CDH, trisomy 21, 18, and 13 are most common. Association with complex chromosomal aberrations such as mosaicism has also been reported. However, CDH presented in a fetus with Y-autosome translocation is extremely rare. Herein, we reported a case of fetus with 46,XY/46,X,-Y,+der(Y)t(Y;1)(q12;q12) mosaicism who presented with CDH diagnosed by ultrasonography at 19 weeks’ gestation.

CASE REPORT

A 25-yr-old nulliparous woman with unremarkable past medical history and no significant prenatal risk factor was referred to our department at 19 weeks’ gestation. Her previous medical history revealed that she had menarche at 16 yr of age and regular menstrual cycle before conceiving. She had a routine antenatal care. Maternal serum triple marker test was negative, showing 1.191 MoM (48.63 ng/mL) of -FP, 0.368 MoM (14.37 IU/mL) of hCG, and 0.789 MoM (1.47 ng/mL) of uE3.

On ultrasonography a single fetus was present and fetal bio- metric was consistent with the patient’s dates. Transabdominal ultrasonography showed a fluid-filled stomach in the left thoracic cavity with the heart displaced to the right in the axial scan (Fig. 1). Sagittal scan showed a defect in the left posterolateral diaphragm with herniation of stomach (Fig. 2). There was no associated anomaly in central nervous system, heart, both kidneys and extremities in ultrasonography. Neither polyhydramnios nor oligohydramnios was found. In order to rule out chromosomal abnormalities, we performed a cordocentesis at 20 weeks’ gestation. Chromosome analysis was performed using the GTG band method (G-banding by the Trypsin-Giemsa technique). Fetal karyotype is 46,XY/46,X,-Y,+der(Y)t(Y;1)(q12;q12) (Fig. 3).

The couple was informed of the diagnosis and decided to...
have a termination of pregnancy at 21 weeks’ gestation. A male fetus weighing 180 g was delivered vaginally. An autopsy after delivery demonstrated an isolated CDH of Bochdalek (Fig. 4). Her non-consanguineous husband was 29-yr old. Paternal karyotyping was done to assess whether the Y-autosomal translocation is transmitted from father, which subsequently revealed normal karyotype, 46, XY. Maternal karyotype was also normal.

**DISCUSSION**

Many authors have reported that CDH was frequently combined with additional anomalies or chromosomal defects (6, 9). Associated anomalies including congenital heart defects, hydrenephrosis, renal agenesis, intestinal atresia, extralobar sequestrations, hydrocephalus, anencephaly and spina bifida are seen in 26 to 57% of all cases of CDH, but this figure rise to 95% in stillbirths. CDH has also been described as a part of syndrome such as Frey’s syndrome, Beckwith-Wiede-

[Fig. 1. A fluid-filled stomach in the left chest displacing the heart to the right in the axial scan (H, heart; S, stomach).]

[Fig. 2. Sagittal scan shows a defect (arrow head) in the posterolateral diaphragm with herniation of a stomach (H, heart; S, stomach).]

[Fig. 3. Fetal karyotype reveals 46,XY/46,X,-Y,+ der(Y) t (Y;1) (q12; q12).]

[Fig. 4. A photography of the autopsy specimen demonstrates a heart (arrow head) and a herniation of a stomach (arrow) in the left thoracic cavity.]
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been reported, which include de novo reciprocal translocation 1:15 with tetralogy of Fallot, deletions of 15q24-ter with other malformations, balanced translocation 46,XY,Y(5;15) (p15.3;q24) and deletion 15q25.1q26.2 with growth retardation (19-22).

Complete or mosaic trisomy for all of chromosome 1q has been rarely seen in a recognized pregnancy. There are only three reported cases of partial mosaic trisomy 1 by translocation between the long arm of chromosome 1 and Y, which is similar to our case. Usually, Y-autosome translocation occurs in the Y chromosome breakpoint, which is in the distal euchromatic part (Yq11.23) and in the heterochromatic part (Yq12). Watson et al. (23) reported a monzygotic twin pregnancy at 30 weeks’ gestation in which one of the twins was normal and the other had a 46,XY/46,X,-Y,+der(Y)t(Y;1)(q12;q21) with multiple anomalies such as severe hydrocephalus, micrognathia, microstomia, left eye hypoplasia with complete coloboma, hypoplastic cerebellum and macrocephaly. Kaufman et al. (24) described a fetus whose ultrasound at 19 weeks showed an absent calvarium, large omphalocele, possible proboscis, and a suggestion of a VSD and whose karyotype was 46,XY/46,X,-Y,+der(Y)t(Y;1)(q12;q12) (24). Zeng et al. (25) presented a twin following in vitro fertilization at 31 weeks’ gestation. The karyotype of twin A was normal, while the other’s karyotype was 46,XY/46,X,-Y,+der(Y)t(Y;1)(q12;q12) with left diaphragmatic hernia, hypoplastic lungs, a partial cleft palate, camptodactyly, syndactyly, ventriculomegaly, and hypoplastic cerebellum.

Other chromosomal aberrations associated with CDH include tetrasomy 12p, mosaicism, 9p syndrome, deletion 8, an unbalanced translocation 5q;9p resulting trisomy for 5q and monosomy 9p, supernumerary derivatives (22) chromosome abnormality and de Lange syndrome (chromosome 3, q25-2a band region duplication) (26, 27).

Despite the advances in fetal intervention and development of extracorporeal membrane oxygenation, the pregnancy outcome of CDH with chromosomal aberrations has been known as poor. Herein, we present this case of isolated CDH with partial mosaic trisomy 1 diagnosed prenatally and conclude that fetal karyotype must be performed to find any chromosomal aberrations in CDH without additional malformations by prenatal ultrasound, even if the risk for a chromosomal anomaly in isolated CDH seems small.

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