Three-Dimensional Ultrasonographic Findings of the Rare Chromosomal Abnormality 48, XXY/+18 : A Case Report

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Abstract

The 48, XXY/+18 is a very rare aneuploidy syndrome which combines the aberration in both autosome and sex chromosome. The authors report a case diagnosed prenatally by lymphocyte culture from fetal blood samples following cordocentesis, 2-dimensional (2DUS) and 3-dimensional ultrasonography (3DUS). At 33 $^{1/7}$ weeks gestation in an ultrasound examination by indication large for date; single umbilical artery with absence of the left umbilical artery, polyhydramnios and fetal growth restriction were demonstrated. The fetus presented with microcephaly, prominent occiput, low-set ears, micrognathia, hypertelorism, small mouth, bilateral club hands with overlapping fingers, rocker-bottom feet. Karyotyping from the cordocentesis led to the diagnosis of 48, XXY/+18, which was confirmed by the chromosomal analysis of the umbilical cord blood after the baby was born. This is the first reported case of the very rare aneuploidy syndrome in the literature.

Key word : Chromosomal Abnormality, Three-Dimensional Ultrasonography, 48, XXY/+18, Prenatal Diagnosis

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Chromosomal abnormalities are one of the major problems that contribute significantly to morbidity and mortality during fetal and neonatal life. They occur in approximately 1 in 120 livebirths[1]. Aneuploidy is the most common type of chromosome aberration which results from the non-disjunction process

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which occurs during meiosis or mitosis of the cell division. The most common recognized human aneuploidy syndromes are autosomal trisomies 21, 18, 13 and sex chromosome aneuploidies 45, XO; 47, XXY; 47, XYY, and 47, XXX

The authors report a very rare case of aneuploidy syndrome, 48, XXY/+18 which combines the aberration in both autosome and sex chromosome in terms of ultrasonographic findings by 3-dimensional ultrasound. In our review this is the first case of a very rare aneuploidy syndrome that has been reported.

CASE REPORT

A 21-year-old Thai woman, gravida 1, para 0 with last menstrual period on April 16, 2000, and an expected date of confinement on January 23, 2001 was seen at 33 1/7 weeks gestation with a large for gestational age fetus. The 2-dimensional and 3-dimensional ultrasonography were performed by the Medison-Kretztechnik Voluson 530D (MT) ultrasound mechine and revealed that the fetus had micrognathia, bilateral club hands and clenched hands, rocker-bottom feet as shown in Fig. 1-5, single umbilical artery with absence of the left umbilical artery and polyhydramnios. The fetus showed growth restriction by increased femur length to abdominal circumference ratio to 25.28 per cent and the head circumference to abdominal circumference ratio was 1.17 which is greater than the normal value for this gestational age. The fetal blood sampling for chromosome study was discussed with the pregnant woman and cordocentesis was accepted. The fetal lymphocyte cell cultures revealed 48, XXY/+18 in 15 of analysed metaphase 15 cells as shown in Fig. 6. The patient was delivered vaginally at 38 2/7 weeks gestation. The male infant weighed 2,200 grams with the Apgar scores of 9 and 4 at 1 and 5 minutes. The umbilical cord blood was sent for confirming the karyotype. The lymphocyte cell cultures revealed the same karyotype in 18 of analysed metaphase 18 cells. On physical examination microcephaly with prominent occiput, hypertelorism, bilateral cataract, micropthalmia with blepharophimosis, low- set ears with microtia and primitive pinnae, micrognathia, small mouth, bilateral club hands, bilateral clenched hands, bilateral Simian crease of both hands, rocker-bottom feet, micropenis with undescended testes bilaterally, and two vessels cord were noted as shown in the Fig 1-5. The infant died on day 18 after birth.

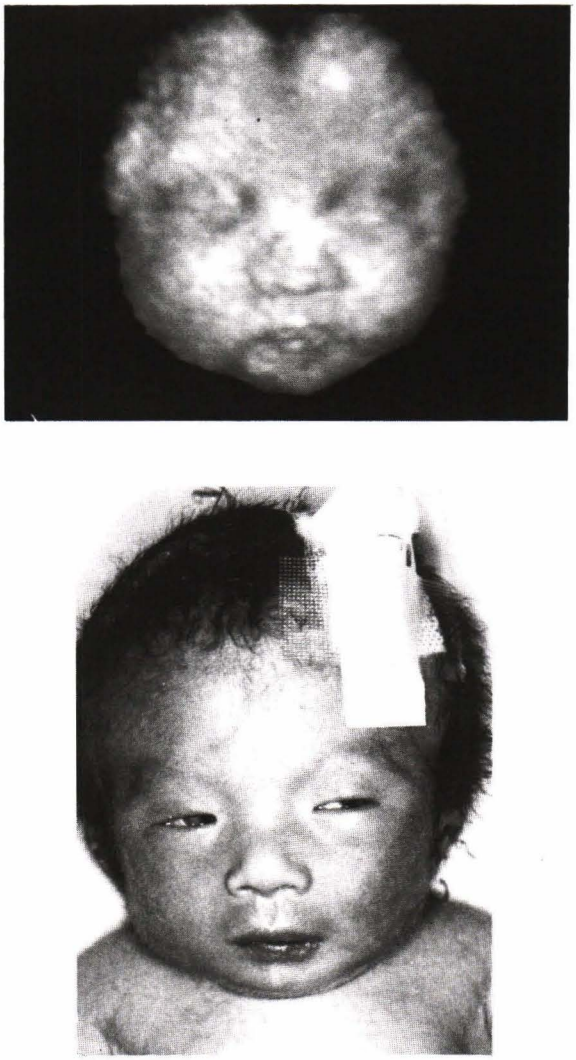
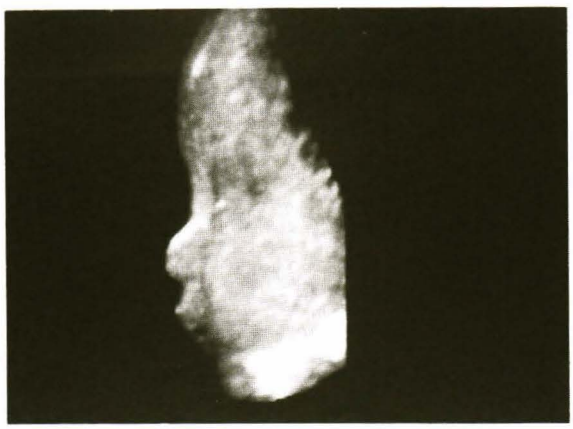
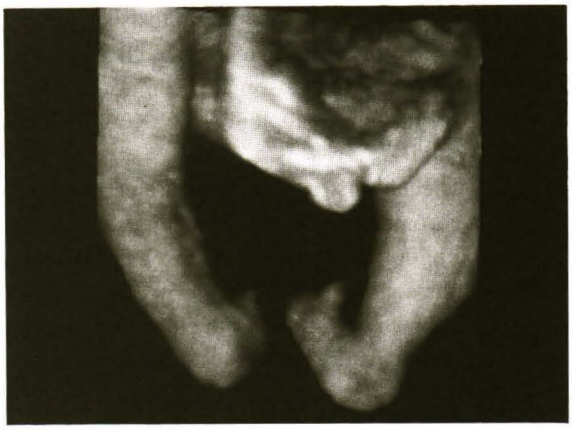


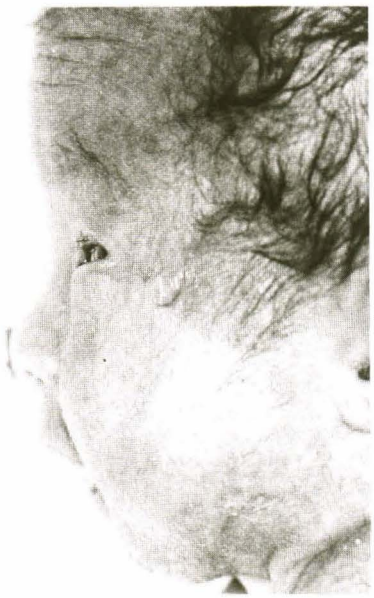
Fig. 1. 3DUS (surface rendering) demonstrating facial dysmorphic features compared with the newborn.

DISCUSSION

48, XXY/+18 is a very rare primary trisomy by which the additional chromosome is one of those normally present in the complement (2n + 1 whole chromosome). The predominant mechanism is the non-disjunction during meiosis which produces aneuploid gametes. The resulting zygote then has the identical chromosome constitution in all cells[1]. In our reviews, this is the first case of a very rare aneuploidy syndrome.







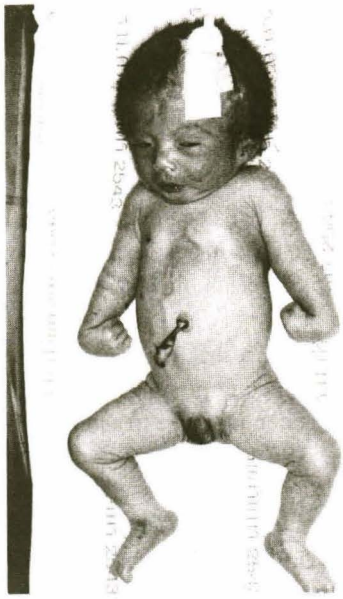
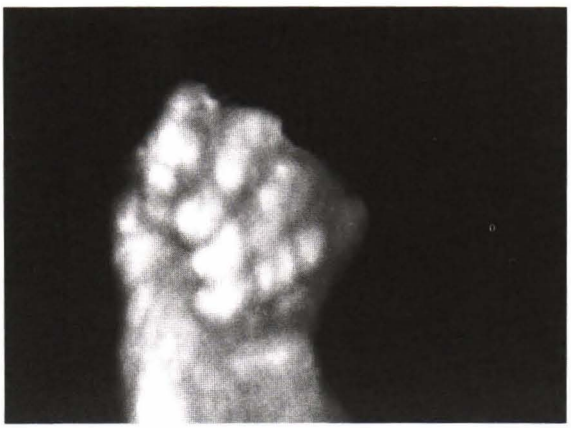


Fig. 2. 3DUS (surface rendering) demonstrating facial dysmorphic features at lateral side compared with the newborn.

Fig. 3. 3DUS (surface rendering) demonstrating bilateral club hands compared with the newborn.

The congenital anomalies found in this case were mainly the characteristics of trisomy 18 which are microcephaly with prominent occiput, hypertelorism, bilateral cataract, micropthalmia with blepharophimosis, low set ears with microtia and primitive pinnae, micrognathia, small mouth, bilateral club hands, bilateral clenched hands, bilateral Simian crease of both hands, rocker-bottom feet, and growth restriction. The Klinefelter characteristics in this case were only micropenis and undescended testes bilaterally. The other characteristics include seminiferous tubule dysgenesis, androgen deficiency and gynecomastia which usually present in adult life were very difficult to identify in this case because the baby died on day 18 of life.

The occurrence of this aneuploidy syndrome, 48, XXY/+18 is extremely rare. Upon literature review, the authors found that this is the first case that has been reported. The other aneuploidy syndrome involving chromosome 18 and sex chromosome which have



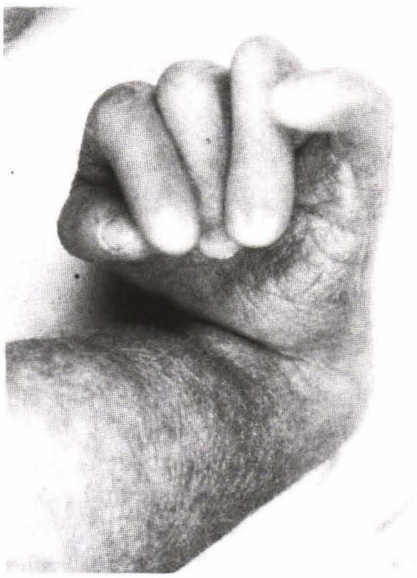
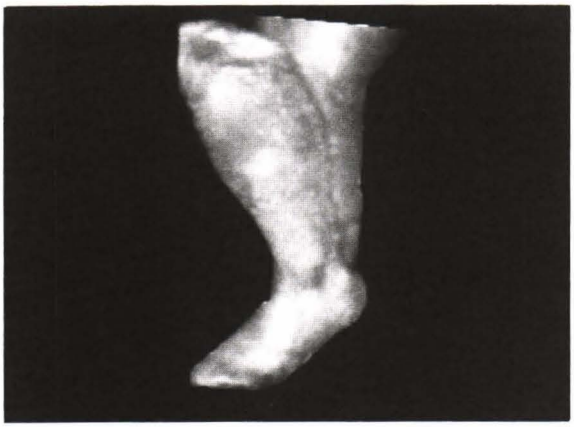


Fig. 4. 3DUS (surface rendering) demonstrating clenched hand, overlapping of the third finger by the index and the fourth finger by the fifth compared with the newborn.



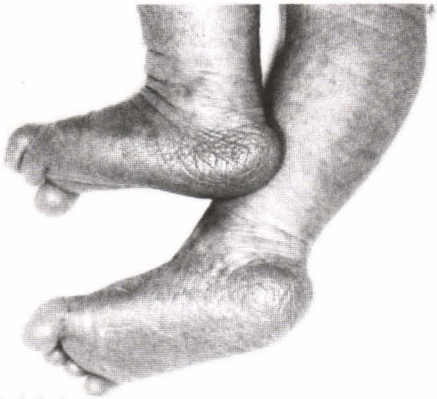


Fig. 5. 3DUS (surface rendering) demonstrating rocker-bottom feet compared with the newborn.

been reported more often were 48, XXX/+18[2-6]. All cases had the manifestations of trisomy 18 similar to the present findings.

Many reports have published the accuracy of ultrasonographic detection of fetuses with chromosomal abnormalities. Benacerraf et al 1988[7] found that 100 per cent of fetuses with trisomy13 and 80 per cent of trisomy18 detected cytogenetically were identified sonographically. However, by 2DUS the assessment of detailed structure of the fetus is somewhat limited and difficult as the result of fetal movement, an improperly positioned fetus, acoustic shadow from fetal skeletal, oligohydramnios and maternal obesity. In addition, unattainable planes on conventional 2DUS in the complex anatomy preclude the correct interpretation of the fetal anomalies. Recently, several clinical reports have published the accuracy and advantage of the newly developed technique of 3DUS over the 2DUS in prenatal diagnosis of fetal anomalies[8,9]. Merz et al 1995[8] summarized that 3DUS provides diagnosis gain in 64.2 per cent of cases. Using the combination of orthogonal image plus a 3DUS surface rendering or transparent view increases the diagnosis gain to 71.5 per cent. They concluded that the

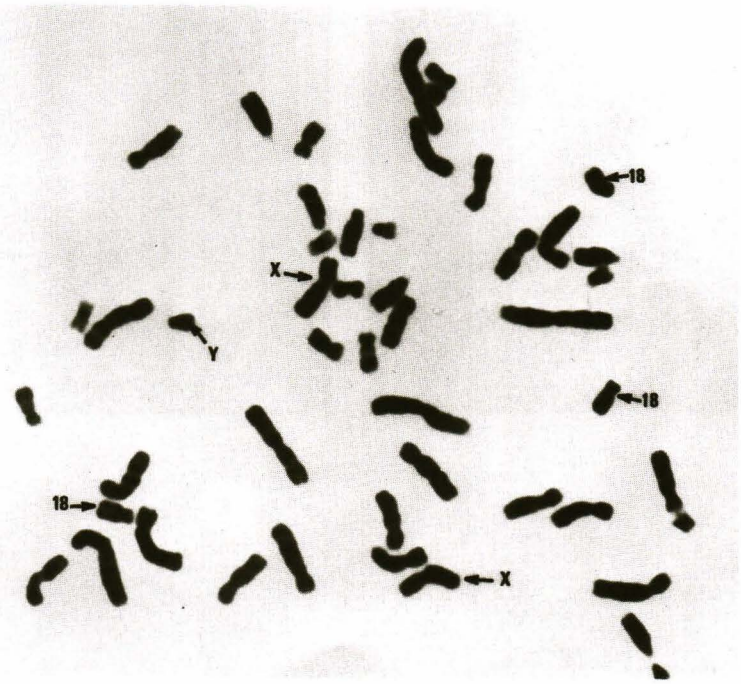


Fig. 5. G-banding analysis of lymphocyte-derived metaphase chromosome demonstrating 48, XXY/+18.

higher percentage resulting from the additional 3DUS surface reconstruction, the ability to view and evaluate the fetus from various angles, the ability to determine the exact size of fetal defect, the depiction of skeletal anatomy in the transparent mode, and the improved delineation of complex malformations. In this case, by surface rendering mode, the authors could image the fetal face which clearly demonstrates the characteristics of trisomy 18 that is not possible to view by 2DUS. Evaluation of the abnormalities of fetal fingers is an essential part of detecting fetal anomalies. 3DUS also facilitates the depiction of fetal digits which enhancing the more precise image of the club hands and overlapping fingers in this case.

In conclusion, prenatal ultrasonography has become an important procedure in the detection of fetal chromosomal abnormalities. The authors believe that 3-dimensional ultrasonography can enhance the diagnostic potential and can improve the prenatal detection rates of structural anomalies of fetuses with chromosomal abnormalities. The conjunction use of conventional 2DUS and 3DUS can greatly increase the accuracy in fetal diagnosis of congenital malformation.

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REFERENCES

1. Shephard B, Kupke KG. Specific genetic disorders presenting in the newborn. In : Taeusch HW, Ballard RA, editors. Avery's diseases of the newborn. 7th ed. Philadelphia: WB. Saunders; 1998: 209-28.
2. Chen CP, Chern SR, Yeh LF, Chen WL, Chen LF, Wang W. Prenatal diagnosis and genetic analysis of double trisomy 48, XXX/+18. Prenat Diagn 2000; 20: 750-3.
3. Rosenfeld W, Verma RS, Jhaveri RC, Salazar D, Dosik H. Double trisomy 48, XXX/+18 in a newborn. Am J Med Genet 1981; 8: 67-71.
4. Imai I, Shimao S, Suzuuki Y, Okada T. A case of 48, XXX/+18 double trisomy. Acta Paediatr Jpn 1987; 29: 178-81.
5. Jaruratanasirikul S, Jinorose U. An infant with double trisomy (48, XXX/+18). Am J Med Genet 1994; 49: 207-10.
6. Sonoda T, Ohdo S, Madokoro H, Akimoto K, Ohba K. Clinical and postmortem findings of two cases with karyotype: 48, XXX/+18. Acta Paediatr Jpn 1987; 29: 173-7.
7. Benacerraf BR, Miller WA, Frigoletto FD Jr. Sonographic detection of fetuses with trisomies 13 and 18: Accuracy and limitations. Am J Obstet Gynecol 1988; 158: 404-9.
8. Merz E, Bahlmann PF, Weber G. Volume scanning in the evaluation of fetal malformations: A new dimension in prenatal diagnosis. Ultrasound Obstet Gynecol 1995; 5: 222-7.
9. Chan L, Uerpairojkit B, Reece EA. Diagnosis of congenital malformations using two-dimensional and three-dimensional ultrasonography. Obstetrics and Gynecology Clinics 1997; 24: 49-69.

สิ่งตรวจพบจากการตรวจด้วยคลื่นเสียงความถี่สูง 3 มิติของทารกในครรภ์ที่มีความผิดปกติของโครโมโซมชนิด 48, XXY/+18 : รายงานผู้ป่วย 1 ราย

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48, XXY/+18 เป็นความผิดปกติในจำนวนของโครโมโซมที่พบได้น้อยมาก ซึ่งความผิดปกตินี้เกิดขึ้นทั้งจากออโตโซมและโครโมโซมเพศ ผู้เขียนได้รายงานทารกในครรภ์ที่มีความผิดปกติชนิดนี้จำนวน 1 ราย ซึ่งได้รับการวินิจฉัยก่อนคลอดโดยการเก็บตัวอย่างเลือดทารกในครรภ์ส่งตรวจโครโมโซม การตรวจวินิจฉัยด้วยคลื่นเสียงความเสี่ยงสูง 2 มิติ และ 3 มิติ เมื่ออายุครรภ์ 33 $^{1/7}$ สัปดาห์ เนื่องจากมารดามีปัญหาขนาดมดลูกโตกว่าอายุครรภ์ จากการตรวจทารกในครรภ์อย่างละเอียดด้วยคลื่นเสียงความถี่สูงพบความผิดปกติดังนี้ คือ เส้นเลือดสายสะดือมี 2 เส้น น้ำคร่ำมีปริมาณมากผิดปกติ ทารกมีภาวะเจริญ-เติบโตช้าในครรภ์ ศีรษะมีขนาดเล็ก กระโหลกท้ายทอยนูน หูต่ำ ตาห่าง คางเล็กสั้น ปากเล็ก ข้อมืองอร่วมกับมีนิ้วมือกำผิดปกติทั้งสองข้าง และบริเวณส้นเท้ามีลักษณะนูนโค้งผิดปกติ ผลโครโมโซมเพศจากเลือดสายสะดือก่อนและหลังคลอดยืนยันว่ามีความผิดปกติของโครโมโซมชนิด 48, XXY/+18 ซึ่งเป็นความผิดปกติของโครโมโซมที่พบยากและเป็นรายงานแรก

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