Mosaic Pentasomy X/Tetrasomy X Syndrome and Premature Ovarian Failure

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A 16 year-old girl with pentasomy X mosaicism (47,XXX(1) 48,XXXX(12)/ 49,XXXXX) presented with primary amenorrhea. She had epicanthal folds, long philtrum, high-arched palate, facial asymmetry, short webbed neck, low posterior hairline, mild scoliosis, cubitus valgus, mental retardation and clinodactily. She was diagnosed with osteoporosis and premature ovarian failure.

Key words: *Osteopenia, Pentasomy X syndrome, Premature ovarian failure, Tetrasomy X syndrome.*

Pentasomy X syndrome is a very rare chromosomal disorder, first reported by Kesaree and Woolley in 1963 [1]. It is estimated to 1/85,000 [2], with less than 30 cases reported in the literature [3]. Since most cases are 10 years of age or younger**,** gonadal function has not been well described. In a few cases, delayed puberty and dysfunctional ovaries have been reported [4-6].

CASE REPORT

A 16-year-old girl with mosaic pentasomy X syndrome presented to the pediatric endocrinology clinic with the complaint of primary amenorrhea. She was diagnosed with mosaic pentasomy X syndrome in the neonatal period because seizures and hypotonia prompted a chromosome evaluation. The karyotype revealed mosaic pentasomy, 47,XXX(1) 48,XXXX [12]/49,XXXXX [7]. Past medical history included patent ductus arteriosus repair at age 7 days and cholecystectomy for gallstones (nonpigmented) at age 13. She had normal fasting lipid profile and normal oral glucose tolerance test. The gallstone work-up revealed no apparent etiology. In early childhood, she was noted to have developmental delay. She sat without support at 9 months, walked at 18 months and had a significant speech delay. She was toilet trained by 2.5 years of age. The Woodcock-Johnson III tests of cognitive abilities at age 14 years showed mild to moderate cognitive impairment. The estimated IQ was 65-70. Her first sign of puberty reportedly was breast development at age 12, reaching Tanner stage IV between the ages of 14 and 15; however, she had not achieved menarche. She was in 9th grade in special education, and was taking a mood stabilizer for behavioral issues.

Physical examination revealed epicanthal folds, long philtrum, high-arched palate, facial asymmetry, short webbed neck, low posterior hairline, mild scoliosis, cubitus valgus, limited supination of the forearms suggesting radioulnar synostosis, and clinodactyly. She was 168.2 cm tall, weighed 62.5 kg (both at the 75th percentile), had Tanner IV pubic hair and breast development. Laboratory testing revealed a very high follicle stimulating hormone (FSH) level of 104.7 mIU/mL (normal range: 3-22 mIU/mL), a luteinizing hormone (LH) level of 63.1 mIU/mL (normal range: 2-11 mIU/mL) and an estradiol level of 23 pg/mL (normal range: 24-400 pg/mL). Fragile X molecular analysis was negative. Anti-ovarian antibody to test for autoimmune ovarian failure was negative. Bone mineral densitometry (axial and appendicular scan) showed osteoporosis, with a *Z*-score of -1.5 between L1 and

L4 and a *Z*-score of -1.5 for total bone mineral density. Subsequently, she was started on hormone replacement with an oral contraceptive.

DISCUSSION

Pentasomy X syndrome is a rare chromosomal disorder characterized by five copies of the X chromosome resulting in 49 total chromosomes. The most accepted explanation for this occurrence is two nondisjunctions of the X-chromosomes during meiosis. The first nondisjunctions occurs during meiosis I and second in meiosis II resulting in four maternally inherited X chromosomes and the fifth X-chromosome is provided by the father [7-9].

The phenotype of the pentasomy X syndrome is similar to those of Turner and Down syndromes including bilateral transverse palmar creases [8], craniofacial anomalies, cognitive impairment (average IQ of 50, range: 20 to 75), short stature, skeletal and articular abnormalities [6] (talipes equinovarus, radioulnar synostosis, clinodactyly of the fingers and toes, and general laxity of joints leading to frequent dislocations**)** and congenital heart defects [10] (patent ductus arteriosus and ventricular septal defect). These girls typically have speech problems, difficulty communicating and a shy personality [3].

Tetrasomy X syndrome is slightly more commonly seen (40 cases) than pentasomy X syndrome. The findings in general are similar but only milder than pentasomy X syndrome, including milder facial abnormalities, taller stature and higher IQ with an average of 60 [3].

Pentasomy X/tetrasomy X mosaicism is even less frequently reported in the literature than pentasomy X [9]. The mosaicism in petasomy X syndrome is the result of a presumed post-fertilization loss of one X chromosome**.** In our patient, although the karyotype analysis showed higher percentage of 48XXXX than 49 XXXXX cell line in peripheral blood, based on the mechanism involved in this chromosomal abnormality, one can conclude that the initial abnormality was pentasomy X. Furthermore, mosaicism is known to vary in percentage in different tissues in the body. It has been reported that patients with 48XXXX/49XXXXX mosaicism have similar findings to those with pentasomy X [5,9]. Fertility in pentasomy X is suspected to be compromised, but insufficient data are available to validate this as most patients reported are younger than 11 years of age. The girl with pentasomy X mosaicism reported by Gordon and Paulsen [5] had premature menopause at age 17. The other three girls, two of whom were age 10 years and one of whom was 15 years, were all prepubertal, but one of the 10 year-old girls had high gonadotropin levels similar to our patient [4], suggesting premature ovarian failure. In the other two cases [3,6], gonadotropin levels were not reported. In tetrasomy X syndrome, 50% of the adult females had normal fertility, menarche and menopause and 50% had menstrual irregularities [3].

To conclude, patients with pentasomy X syndrome, should undergo early screening for ovarian failure during early adolescence. Hormone replacement should be considered at the normal age of puberty to prevent severe osteoporosis.

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REFERENCES

1. Kesaree N, Woolley PV Jr. A phenotypic female with 49 chromosomes, presumably XXXXX. A case report. J Pediatr. 1963;63:1099-1103.
2. Broeck A, Gfatter R, Braun F, Fritz B. Pentasomy X and hyper IgE syndrome: co-existence of two distinct genetic disorders. Eur J Pediatr. 1999;158:723-6.
3. Linden MG, Bender BG, Robinson A. Sex chromosome tetrasomy and pentasomy. Pediatrics. 1995;96:672-82.
4. Archidiacono N, Rocchi M, Valente M, Filippi G. X pentasomy: a case and review. Hum Genet. 1979;52: 69-77.
5. Gordon DL, Paulsen CA. Premature menopause in XO/XX/XXX/XXXXX mosaicism. Am J Obstet Gynecol. 1967;97:85-90.
6. Dryer RF, Patil SR, Zellweger HU, Simpson JM, Hanson JW, Aschenbrenner C, *et al*. Pentasomy X with multiple dislocations. Am J Med Genet. 1979;4:313-21.
7. Martini G, Carillo G, Catizone F, Notarangelo A, Mingarelli R, Dallapiccola B. On the parental origin of the X's in a prenatally diagnosed 49,XXXXX syndrome. Prenat Diag. 1993;8:763-6.
8. Cho YG, Kim DS, Lee HS, Cho SC, Choi SI. A case of 49,XXXXX in which the extra X chromosomes were maternal in origin. J Clin Pathol. 2004;57:1004-6.

9. Silengo MC, Davi GF, Franceschini P. The 49 XXXXX syndrome. Report of a case with 48 XXXX/49XXXXX mosaicism. Acta Pediatr Scand. 1979;68:769-71.

10. Kassai R, Hamada I, Furuta H, Cho K, Abe K, Deng HX, *et al*. Penta X syndrome: a case report with review of the literature. Am J Med Genet. 1991;40:51-6.

Pericardial Tamponade in a Newborn Following Umbilical Catheter Insertion

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We present a case of cardiac tamponade following umbilical venous catheterization in a neonate, an uncommon, yet potentially fatal complication. Timely diagnosis by echocardiography and urgent pericardiocentesis proved lifesaving.

Key words: *Cardiac tamponade; Neonate; Pericardial effusion; Umbilical venous catheter.*

Umbilical vein catheter insertion is a routine procedure in neonatal units looking after sick babies. There are reports of newborns who died or became severely ill as a result of cardiac tamponade after umbilical catheterization. In neonates with central venous catheters the incidence of cardiac tamponade is 0.5-2% [1] and mortality varies from 45-67% [2]. We describe the clinical-surgical evolution and successful resuscitation of a case of cardiac tamponade following insertion of umbilical venous catheter.

CASE REPORT

38-week-old newborn, weighing 3.35kg was admitted to the neonatology unit with congenital pneumonia, pulmonary hypertension and shock, requiring ventilation. A silastic umbilical venous catheter (Vygon) was inserted on day one of life. Radiography post procedure showed the tip of the catheter at the level of the atrium. ECHO evaluation done for pulmonary hypertension showed a small hypoechoic region at the cardiac apex suggesting accumulation of fluid in pericardial space and catheter tip at the right atrium. Removal of the catheter was planned but the procedure was inadvertently delayed.

Two hours after the catheter placement, the neonate developed acute asystole and hypoperfusion not responding to positive pressure ventilation and external cardiac massage. One previous experience with cardiac tamponade following PICC insertion and successful resuscitation made us think of cardiac tamponade [3]. Urgent pericardiocentesis was done with a presumed diagnosis of cardiac tamponade. An emergency echocardiogram done few minutes later showed pericardial effusion and further tapping was done under sonographic guidance. Around 20 mL of clear fluid was drained. Fluid analysis showed very high glucose levels (1240 mg/dL) suggesting presence of infused dextrose in the pericardial space. The umbilical catheter was removed. Repeat ECHO showed no reaccumulation of fluid. The baby had no cardiac emergency thereafter and was discharged on day 9 of life. The baby has normal growth and development on his 9 month follow up.