Clinical Brief

Triple X Syndrome with Rare Phenotypic Presentation

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ABSTRACT

Triple X syndrome is a rare numerical chromosomal anomaly, occurring as a result of non dysjunction in meiosis I. Most cases have neurodevelopmental defects and functional problems. We report two cases diagnosed in our centre. The first was a fetus with cleft lip and palate, 47, XXX was identified by Fetal Blood Sampling. The second was a child with multisystem anomaly including cleft lip and palate, whose karyotype also revealed 47, XXX. Though isolated cases of associated abnormalities have been reported there have not been consistent phenotypic changes reported with this condition. **[Indian J Pediatr 2008; 75 (6) : 629-631]** *E mail - fcrfchennai@yahoo.com*

Key words : *Triple X syndrome; XXX syndrome; Triple X with cleft lip and palate*

Triple X is a sex chromosomal abnormality that involves the presence of three sex chromosomes resulting in 47, XXX karyotype. The numerical abnormality occurs as a result of nondysjunction in meiosis I. 90% of these cases are of maternal origin and 10% paternal in origin. Association has been reported with advanced maternal age and gestational diabetes. It usually is of sporadic origin.

Most of these cases do not manifest as structural anomaly. Low IQ, learning difficulties, behavioral problems and psychological problems has been reported. They attain puberty at normal age and fertility is normal.

Antenatal detection poses problems in genetic counseling as postnatal manifestations may be varied.

CASE REPORTS

CASE 1

Mrs. G aged 30 years, non consanguineously married primigravida referred at 26 -27wks of gestation for second opinion following hydramnios reported in the scan. A repeat scan at our centre revealed unilateral – right sided cleft lip and palate with prominent sandal gap in both feet. There were no antenatal risk factors and family history was not contributory. Fetal blood sampling was performed to rule out chromosomal anomalies. The blood sampling revealed 47, XXX by regular karyotype and confirmed by FISH (Fig. 1 a,b)

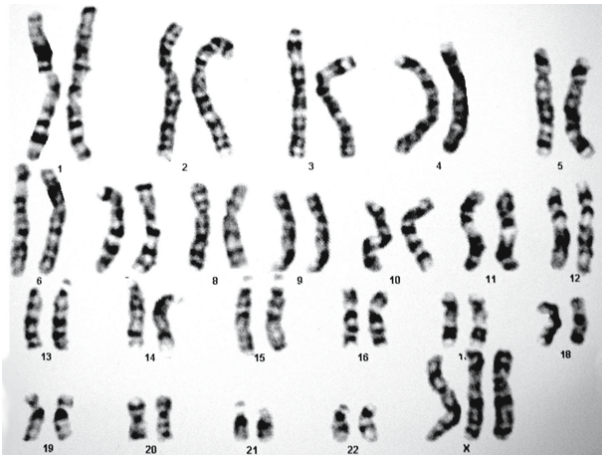


Fig. 1a. 47,XXX Karyotype

Later on the parents were counseled, postnatal implications of cleft lip and palate and the need for surgery were explained. The known facts known about triple X syndrome were also explained.

The couple however decided to terminate the pregnancy and fetus was given for autopsy. (Fig. 2). Autopsy confirmed scan findings and the female fetus also had other features such as hirsutism, bilateral postaxial polydactyly, syndactyly, bronchogenic cyst.

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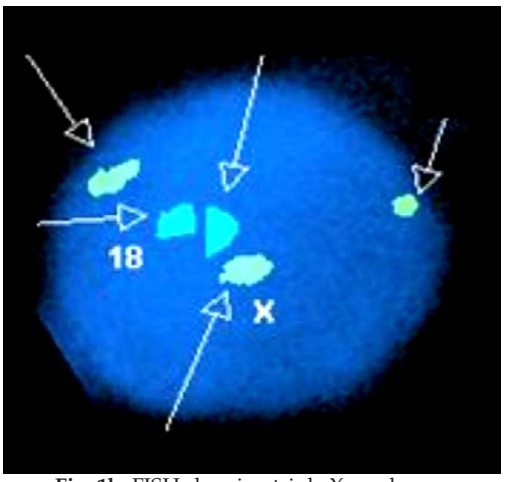


Fig. 1b. FISH showing triple X syndrome



Fig. 2. Fetus with cleft lip and wide sandal gap on autopsy

Fetogram revealed abnormal cervical vertebrae and absent sacral tapering.

CASE 2

A seven-year-old girl with multiple congenital anomalies was brought to the genetic clinic for diagnosis. Her parents were of third degree consanguineous marriage. The mother was 30 years at conception and had uneventful antenatal period and antenatal scans were reported normal.

Child was delivered at term by LSCS in view of breech presentation with a birth weight of 2.6 Kg. Multiple congenital anomalies were identified. Various corrective surgeries were performed on her over a period of time. She had curved bushy eyebrows with small palpebral fissures. Her ear lobule was very small and she had broad nasal bridge (Fig. 3). There was bilateral cleft lip and palate (operated). There was residual camptodactyly in her right hand, even after surgical correction. (Fig. 4) She had been operated for a sacral meningomyelocele. There was contracture in her right hip and bilateral CTEV.

She had not yet attained bladder control. There was history of recurrent UTI and MCU revealed grade III VUR on left side. Renal DMSA scans revealed small scars in both poles of left kidney and good function of right kidney



Fig. 3. 7 year old child with Triple X syndrome with facial dysmorphism



Fig. 4. Post operative picture of the hands

CT Brain identified that parietal bone was not formed well but brain parenchyma was normal.

Milestones were delayed in her. She was on speech therapy. Her vision and hearing status were normal. She was attending normal school. Family history revealed that her maternal uncle had cleft lip and cleft palate.

A chromosomal study with a high resolution banding was done which showed 47, XXX. Hence, a pelvic scan done showed mullerian abnormalities in the form of non visualization of uterus and ovaries.

DISCUSSION

Triple X syndrome is a rare chromosomal aneuploidy affecting the X chromosome in female fetuses / girls. The reported incidence is 1 or less/1000 live births. Most cases have been picked up following a karyotype done as a part of work up of children with behavioural disorders [1]. These individuals are usually normal at birth. They grow normally and may even be tall statured. No structural

anomalies have been reported with Triple X syndrome. Most of these girls have normal reproductive functions, including menstruation and fertility.

A few cases have been reported with associated anomalies. Triple X has been reported in a 22 week old fetus with renal, genitourinary, anal and vertebral anomalies.[2] Jejunal atresia has been reported in a 33 week old fetus with polyhydramnios and dilated bowel loops.[3] A case of Congenital Adrenal Hyperplasia[4] and another with Schizencephaly[5] have been reported with this condition.

There were a few similarities in both our cases. Both had cleft lip and palate, vertebral anomalies and abnormalities of digits. The second child also had mullerian and genitourinary abnormalities. Cleft lip and palate have not been reported in cases with Triple X syndrome as far as our literature survey has revealed.

Hence, these phenotypic problems could be due to single gene abnormalities situated on the X chromosome. X - linked mutation (CPX - X linked Cleft Palate) has been identified in a British Columbian family with clefting disorder.[6] Members of the family had an X – linked condition presenting as cleft palate and absent or bifid uvula and or ankyloglossia. The mutation (CPX) has been localized between PGK1 and DXYS1 in the Xq13 – q21.31 region. More studies in affected individuals may throw some light in this direction.

Problems arise in counseling when the fetus has been identified to have triple X syndrome, particularly when diagnosed incidentally, without structural anomaly, as the outcome could be highly variable. Postnatally these children need supportive therapy apart from the corrective surgeries as indicated for the specific problems.

The recurrence risk of this condition would be as in other non –disjunction types of chromosomal anomalies. The baseline risk is low, but would also vary with factors such as advanced maternal age.

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