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CASE REPORT

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Trisomy 8 Mosaicism

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INTRODUCTION

Trisomy 8 mosaicism (T8M) is a well-described syndrome first reported by Grouchy in 1971. More than 75 cases have been reported with a frequency of 1:25,000 to 50,000 births. Trisomy 8 is more commonly seen as mosaic in 85% of cases attributable to a tendency for abnormal cell lines to disappear from the peripheral lymphocytes with increasing age of the patient. Full trisomy 8, arising from errors in maternal meiosis, is non-viable and leads to spontaneous abortions.

The diagnosis of T8M is often delayed because of its widely variable phenotypic and cytogenetic expression. Age of diagnosis has been delayed up to 28 years of age. The male to female ratio is 5:1. This report describes a case of a female infant diagnosed with T8M (mos 47, XX + del (8)(p11.2)[19 cells]/46,XX[1 cell]) by chromosome studies after presenting with several congenital anomalies at birth.

CASE REPORT

The proband was born to 28-year old, healthy and unrelated parents of Mexican descent. Four other siblings were normal. Pregnancy was unremarkable. The newborn was full term, appropriate for gestational age with a birth weight of 3,201 g. At birth, the patient was noted to have a unilateral, dysplastic low-set ear, a broad bulbous nose, clinodactyly, cardiac murmur and deep palmar and plantar furrows. The dermatoglyphic features are pathognomonic for trisomy 8 mosaicism syndrome. Several imaging studies demonstrated cardiomegaly associated with a large ventriculoseptal defect (VSD) and patent ductus arteriosus (PDA), pulmonary edema, "handle-bar" configuration of the clavicles, thoracolumbar scoliosis, butterfly vertebrae of T6, bilateral hydronephrosis and bilateral grade IV-V vesiculoureteral reflux (VUR). Chromosomal studies from peripheral blood and dermal fibroblast demonstrated trisomy 8 mosaicism. The chromosomal studies of the parents were normal.

The clinical course was complicated since birth with respiratory distress that persisted until one month of life requiring VSD repair and PDA ligation. She had prolonged feeding difficulties secondary to gastroesophageal reflux that was improved with gastrostomy. At two months, the patient developed *E. coli* urosepsis that required re-admission for parenteral antibiotics.

DISCUSSION

The mechanism leading to T8M is unclear. Chromosome 8 is

the largest autosome that is found to be trisomic and compatible with life. Most common autosomal trisomies arise from errors in maternal meiosis whereas mosaicism of trisomy 8 results from a mitotic non-dysjunction, ie. a postzygotic error making recurrence risk in future pregnancies negligible. Full trisomy 8 is not viable and has been observed in spontaneous pregnancy losses. Mean maternal and paternal ages at birth of affected individuals are higher than the mean parental ages in the general population.

Since abnormal cell line tends to disappear from lymphocytes with age, it is more reliably diagnosed with a skin biopsy. Prenatal diagnosis through chorionic villus sampling, amniocentesis, or fetal blood sampling is indeterminate. The percentage of abnormal mosaic cells determined through chorionic villus sampling does not indicate the likelihood of true fetal mosaicism neither does it correlate with phenotypic severity if fetal mosaicism is present.

Due to the extremely variable phenotypic and cytogenetic expression, Trisomy 8 mosaicism has gone undiagnosed in certain patients. Wisnieska and Mazurek (2002) reported a case a 15 year old male who had a chronic history of recurrent respiratory infections, mild psychomotor retardation and hypotonicity along with poor coordination and delayed speech. He also manifested skeletal defects, hypospadias, contractures of toes and fingers, wandering hypoplastic patella and typical deep creases on both soles. He was initially diagnosed with Marfan syndrome.

Life expectancy of patients with T8M is normal but such patients require complex, multi-specialty care as they are likely to develop cognitive, orthopedic, and ophthalmologic complications. Most suffer from mild to moderate mental retardation, campyloactyly and other contractures and cataracts. Other clinical features include soft tissue abnormalities, low-set and/or malformed ears, broad bulbous nose, palate deformity, hydronephrosis, cryptorchidism and the characteristic dermatoglyphics. Spinal deformities which may be found in 65% include scoliosis and hemivertebrae. The commonly associated cardiac and renal anomalies also pose further challenges and place affected individuals to cardiac failure and infection just as our patient experienced within the first weeks of life. Patients also have a higher susceptibility to developing preleukemia and may have an association with myelodysplastic syndrome complicated with Bechet's dis-

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ease.

CONCLUSION

Early diagnosis of T8M depends on thorough physical examination and a high index of suspicion. The skeletal thoracic deformities are present in almost every patient with Trisomy 8 mosaicism. The presence of skeletal abnormalities especially joint contractures and mental retardation warrants cytogenetic analysis. Patients with T8M require long-term, multi-specialty care that needs meticulous anticipation.

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Figure 1
Chest X-Ray: Butterfly vertebrae T6, widened distal ends clavicle



Figure 2
Hallmark of T8M: Thickened, bulging skin with deep plantar furrows (Pli capitonné)

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