

Trisomy - T(21;21) with Mosaicism in a Down Syndrome Girl Child Case Report

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ABSTRACT Mosaicism with a derivative of 21 translocation and normal cell line is one of rare cases of Down syndrome patients. In the present case dysmorphic features and developmental delay were compatible with clinical diagnosis of Down syndrome. Cytogenetic analysis demonstrated a mosaic pattern of normal cell line and a cell line with translocation 21;21[(46,xx/46,xx,T(21;21),+21)]. Presence of normal cell line as well as translocated 21 indicates the mitotic nondisjunction (NDJ) of an euploid zygote and mosaicism may be due to loss of the supernumerary chromosome of a trisomic zygote or some complex mechanism may be involved in chromosomal aberration. Present case shows the mosaicism in a girl child with features of Down syndrome and atypical karyotype.

INTRODUCTION

Trisomy-21 is the most common viable aneuploidy in humans causing Down syndrome with a frequency of about 1 in 700 live births (Van Buggenhout et al. 1999). Syndrome is characterized by mental retardation, reduced life expectancy and complex phenotype with characteristic facial and skeletal appearance. Approximately 95% of Down syndrome cases are due to free trisomy (Hamerton et al. 1975). Another 2% to 4% cases are caused by chromosomal translocation (Pangalos et al. 1994). The remaining 2% to 4% of Down syndrome patients show mosaicism for trisomy 21 and normal cell lines (Mikkelsen et al. 1997). Present report confirms the rare case of mosaicism of translocation 21 and normal cell line in a clinically diagnosed Down syndrome girl child.

CASE REPORT

The proposita is a clinically diagnosed Down syndrome patient. She is a third child, born to middle aged parents (mother 33 years, father 38 years). In prenatal period, there is history of more than normal foetal movements. Delivery was full term and normal. Birth weight was average

(2900gm) but birth cry was delayed. Convulsions were present in neonatal and postnatal period alongwith typical Down syndrome features. There were multiple associated problems like epilepsy, hypothyroidism and myopia. Dysmorphic features like brachycephaly, flat occipital region, slanting palpebral fissure, short nose from root to tip, protruded and creased tongue, lip with perpendicular furrow, epicanthal fold, brushfield spots, constantly open mouth, short stature, short stubby hand, skin scaliness with reddish rims and dry peeling were present.

The present case showed remarkably noticeable dysmorphic features as compared to other Down syndrome patients but surprisingly two key characters i.e. simian crease in hands and wide gap between 1st and 2nd toes were absent (Table 1). Dermatoglyphics showed ulnar loop pattern on thumb and 1st and 2nd finger. Whorls were present on ring finger and little finger of both right and left hands. Atd angle was more than 60° in both the hands (Table 2). First four toes of both feet showed fibial loop pattern while arch pattern was found on little toe. Hallucal area showed loop distal pattern in both right and left feet.

Cytogenetic and FISH Analysis

Chromosomal analysis was performed from 72 hrs cultured blood lymphocytes using GTG banding according to standard procedures (Seabright 1971). Fluorescent *in situ* hybridiza-

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Table 1: Dysmorphic features of 50 Down syndrome patients and present case.

Features	Down syndrome cases (%)	Present case
Brachycephaly	75	+
Upslanting palpebral fissure	78	+
Epicanthal fold	76	+
Brushfield spot	52	+
Small square ear	80	+
Simian crease at least one hand	72	-
Flat occipital region	70	+
Short stature	100	+
Mental retardation	100	+
Nose short from root to tip	70	+
Wide gap between 1st and 2nd toes	60	-

tion was done according to manufacturer's instructions, using LSI-21 probe (vysis (R) Downer Grove IL USA).

Out of 50 metaphase analysed, 10 contained normal female karyotype 46xx, 40 contained 46xx+T(21;21) (Fig. 1). Fluorescent in situ hybridisation confirmed the mosaicism. Cytogenetic analysis as well as FISH analysis

revealed mosaicism for trisomy-21 cell line and normal cell line. These chromosomal findings indicated an atypical presentation in a mosaic line Down's syndrome patient.

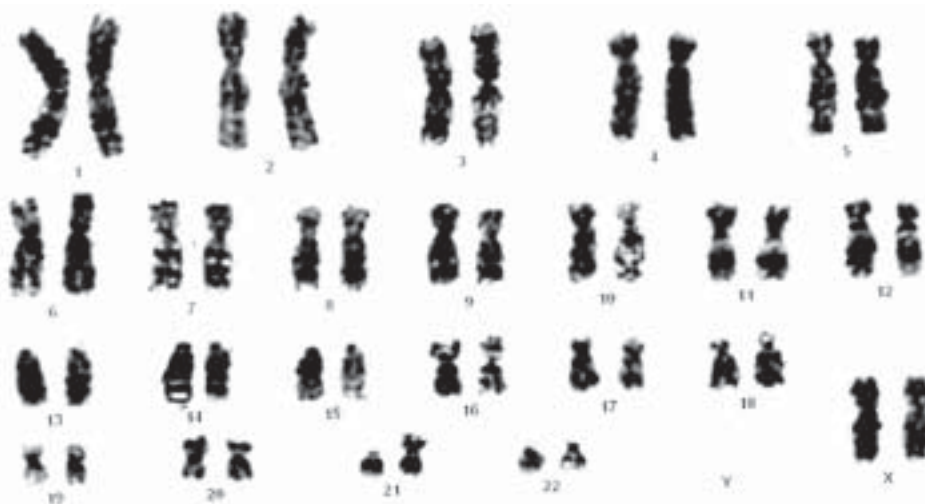
DISCUSSION

Mosaic Down syndrome involving different cell lines is a rare event and has only been reported in small number of cases (Clarke et al. 1989; Leal Garza et al. 1996). Mosaicism with one normal cell line or second with structural chromosomal aberration is generally assumed by postzygotic mechanism (Antonarakis et al. 1990).

The two most common acrocentric arrangements in Down syndrome are rob 14q;21q and (21q;21q) and these occur at approximately equal frequencies. In the present case (21q; 21q) is confirmed cytogenetically. To explain the karyotype of this patient, a minimum of two events may be theoretically possible. The first, must have occurred during paternal or maternal meiosis (either nondisjunction or formation of T (21;21).

Table 2: Dermatoglyphics of the present case.

Digits	Hand		Digits	Feet	
	Right	Left		Right	Left
1	Ulnar Loop	Ulnar Loop	1	Fibular Loop	Fibular Loop
2	Ulnar Loop	Ulnar Loop	2	Fibular Loop	Fibular Loop
3	Ulnar Loop	Ulnar Loop	3	Fibular Loop	Fibular Loop
4	Whorl	Whorl	4	Fibular Loop	Fibular Loop
5	Whorl	Whorl	5	Arch	Arch
Atd angle	62°	70°	Hallucal pattern	Loop distal	Loop distal

**Fig.1. Karyotype showing 21;21 translocation trisomy**

Subsequent errors must have occurred by other mechanism postzygotically resulting in a mosaic karyotype. To conclude we can say some complex meiotic and mitotic errors are responsible for mosaicism. However presence of remarkable dysmorphic features and distinct dermatoglyphics can be a help to identify mosaic Down syndrome cases for further analysis. The further investigation of mosaic karyotype will be of great significance to estimate the risk of recurrence as well as to establish new genotype- phenotype correlation.

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