A Case of Mosaic Down Syndrome

Saequa Habib

Abstract

Cytogenetic analysis in 44 clinically suspected cases of Down syndrome (DS) was carried out using conventional Giemsa-trypsin-banding technique. Among them 43 cases were cytogenetically proved as DS. Forty-two individuals (97.7%) exhibited pure trisomy 21. The remaining child was a seven years old boy, the second-born of non-consanguineous parents and had 46/47XY, +21 mosaicism. He also possessed most of the phenotypic characteristics of the classical trisomy 21.

Keywords: *Cytogenetic analysis, Down syndrome, syndrome.*

Introduction

Chromosome anomalies can be divided into numerical and structural, and may involve one or more autosomes, sex chromosomes or both simultaneously[1]. A third category consisting of different chromosome constitutions in two or more cell lines known as mixoploidy is also present[2]. All like cells originating from a single type of cell is called a cell line. The common mixoploidy is mosacism characterized by the presence of more than one cell lines with different karyotypes in a preson derived from a single zygote. It results from non-disjunction, chromosome lag or mitotic instability of a structurally altered chromosome[3].

Approximately 1% of Down syndrome (DS) patients are mosaics, having a mixture of cells with 46 and 47 chromosome. This patients have mild phenotypic changes and even have normal intelligentce[4].

Case History

A seven years old boy was referred for chromosomal analysis because of dysmorphic features suggestive of DS. He was the second child of an unrelated couple. The mother was 25 years of age at the time of the child's birth. The child was born following a normal gestation and delivery.

The boy had mild reduction in growth. He showed microceplaly, prominent epicanthic fold, upward slanting of palpebral fissures, small care, simian crease, clinodactyly and sandal gap. He also had a history of hypotonia during birth and delayed closure of fontanels. But protruding tongue and longitudinal line in sole were absent.

He had cardiac defect detected by echocardio graphy. His hearing and speech were also delayed.

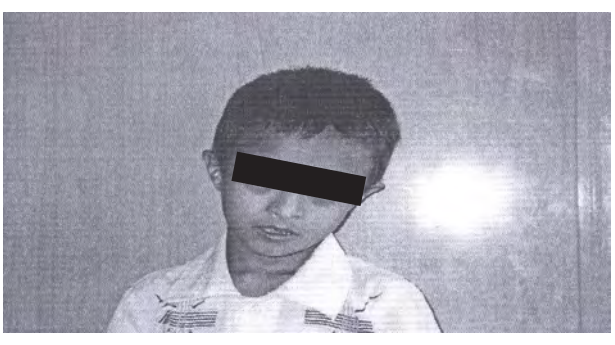

Figure 1. Photograph of the patient having mosaic Down syndrome.

Cognitive evaluation was done with several psychological tests and the results were within the average range.

Chromosomal analysis was carried out in the Department of Pathology of Bangabandhu Sheikh Mujib Medical University (BSMMU), Shahbag, Dhaka. A karyotype standard G- banding technique was done on PHA-stimulated lymphocyte culture 25 well- spread metaphases were analyzed of which 36% was trisomic cells chromosome analysis revealed 46, XY/ 47.XY, + 21(Fig. 2&3).

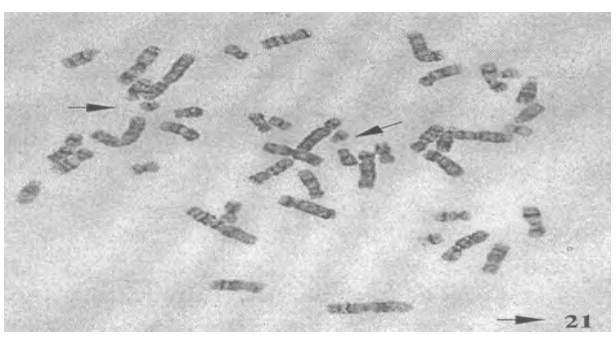

Figure 2. Photomicrograph of a metaphase spread of banded chromosomes showing 46,XY (Giemsa, X 100)

1. Dr. Saequa Habib, Assistant Professor, Dept. of Pathology, Bangabandhu Sheikh Mujib Medical University, Dhaka.

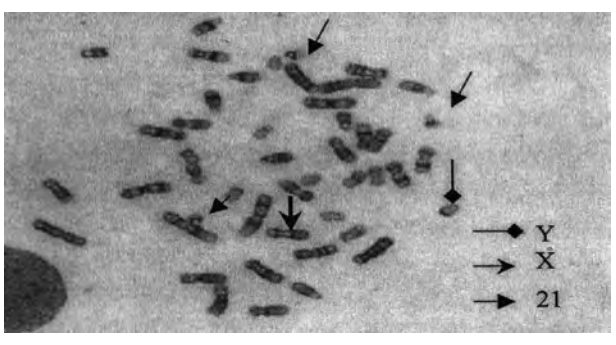

Figure 3. Photomicrograph of a metaphase spread of banded chromosomes showing 47,XY +21 (Giemsa, X 100)

Discussion

The case study describes a boy of seven years exhibited features typical of DS and has the karyotype 46,XY/47,XY,+21. This means the boy has more than one cell type of chromosome make up, known as mosaicism. Mosaicism can occur in two different ways. The initial zygote had three 21st chromosomes, which normally would result in simple trisomy 21, but during the course of cell division one or more cell lines lost one of 21st chromosomes. In another way, the initial zygote had two 21st chromosomes, but during the course of cell division one of the 21st chromosomes. It is possible to determine the origin of mosaicism in individual cases using special DNA markers[5.6].

The usual diagnosis of DS mosaicism is made through chromosomal analysis (karyotyping) of peripheral blood. Typically, 20 to 25 cells are examined some of the cells have trisomy 21 while some don't have. Mosaicesm can also occur across other cell lines such as skin and brain cells and these cells can be tested. Moreover the percentage of the trisomic cells may also different in different cell lines. Chromosomal analysis was also carried out from peripheral blood in the present case. For this purpose, peripheral blood lymphocytes were collected and cultured for three days. Then they were treated with colchicines and stained with Giemsa stain for G-banding after trypsin treatment. Then 25 well-spread metaphases were counted and analyzed and karyotyping was done according to ISCN 1995. Out of 25 metaphase spreads, 16 were normal (46 chromosome) and the 9 had extra #21 chromosome (47 chromosome). So the boy would be said to have mosaic DS and the level of mosaicism at 36%. But the percentage of mosaicism is not an accurate predictor of outcome. Because there is great variability in mosaic DS cases. The present case had the majority of phenotypic features of DS including cardiac defect although the percentage of the trisomic cells was not so high. But Avramopoulos et al reported a case of DS having 73% trisomic cells without showing such phenotypic features of DS[6].

The Department of Human Genetics at the Medical College of Virginia found that the development was delayed in 45 children with mosaicism comparing to their siblings. They also matched up 28 children with mosaicism with 28 children having typical DS for age and gender and found that the children with mosaicism had reached cretain milestones earlier than the children with typical DS. But the speech development was equally delayed in both the groups. The present case had also a history of delayed speech and hearing development.

One report was published in 1991 on mental development in DS mosaicism[7]. It showed that the mean IQ of the mosaic group was 12 points higher that the mean IQ of the non-mosaic group Baliakova and Gavrilov (1975) also demonstrated mainly milder forms of mental retardation in mosaicism[8]. The psychologist assessed the study patient and mild mental retardation was found. The IQ score was within the average range (70-51). The boy was a student of class I studying in a school for the Developmentally Disabled known as Kalyani (Mirpur, Dhaka) run by Bangladesh Protibondi Foundation (BPF) and performed well at school. This finding could be explained by the relatively low trisomic cell frequency, which may have less effect in the critical tissues for intellectual development. Other factors, such as strong family support and continued intervention programmes with thorough educational process provided by the school also helped in the development of the cognitive potential of the subject.

The percentage of mosaic DS is less and the risk to recur is also less than 1% , until the maternal age of 40. After 40, the risk for chromosome abnormalities to occur in a pregnancy is based on the mother's age at the time of delivery. In this study the age of the mother of the mosaic patient was below 40 i.e. 25 years at the time of delivery. Moreover, in this series the mean of maternal age of all the DS cases was found 27.0 ±5.9 years with a high frequency (78%) in the mothers <30 years of age. So, the chance of recurrence is more and karyotyping should be done for proper genetic counseling and to provide good support as the mosaics show variable phenotypic features with mild mental retardation.

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