Case Report

Down syndrome child with 48,XXY,+21 karyotype


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Cytogenetic analysis in 60 clinically suspected cases of Down syndrome and their parents was carried out using conventional Giemsa–trypsin-banding technique. Fifty-five individuals (91%) exhibited a free trisomy 21. Robertsonian translocations were seen in three cases and two cases exhibited a normal karyotype. A four-month-old child, the second-born of non-consanguineous parents, possessed an extra X chromosome in addition to trisomy 21. The proband’s parents and his brother showed a normal karyotype. The phenotypic characteristics of this child have been discussed in the light of the published reports on double aneuploidies of XXY and trisomy 21.

Key Words: Down syndrome, Klinefelter syndrome, double trisomy

Introduction

The existence of two chromosomal abnormalities in the same individual is relatively a rare phenomenon. Double aneuploidy leading to trisomy and / or monosomy of two different chromosomes arises because of two meiotic non-disjunctual events. Both these aneuploidies could have the same or different parental origin.[1] The coincidence rate of both Down and Klinefelter syndromes in the same individual is estimated to lie in the range 0.27 to 0.7 × 10⁻⁵.[2] However, neonatal survey data has revealed that the incidence of XXY and trisomy 21 double trisomy at birth is higher than expected from the incidence of either alone.[3] On the other hand, lower values of XXY pattern recorded in older boys and men with Down syndrome suggest that there might be an increased selection against these individuals after birth.[4] Several cases of double aneuploidy of XXY and trisomy 21 have been published since the first report by Ford et al.[5] This abnormality has also been recently described in a pair of monozygotic twins.[6] Further, both the sibs of the proband showing 48,XXY,+21 were found to exhibit trisomy 21 in yet another study.[7] The clinical features of a 4-month-old boy who exhibited the karyotype 48,XXY,+21 have been presented in this paper.

Case History

A 4-month-old male infant was referred for chromosomal analysis because of dysmorphic features suggestive of Down syndrome. He was the second child of an unrelated couple. The mother was 22 years of age and the father was 33 years old at the time of the child’s birth. The couple also has a healthy 1.5-year-old son. The proband showed open fontanelle, microcephaly, flat occiput, slanting palpebral fissures, hypertelorism, low set and malformed ears, thick furrowed protruding tongue, open mouth, hypotonia, short broad hand, clinodactyly, gap between 1st and 2nd toes and plantar furrow. The child was born following a normal gestation and delivery.

Cytogenetics

Chromosomal analysis was carried out in proband,
Chromosomal analysis of proband revealed 48, XXY, +21 [Figure 1] with no evidence of mosaicism. Parental and normal sib’s karyotypes were found to be normal.

Discussion

The proband is a 4-month-old boy who exhibited features typical of Down syndrome and has the karyotype 48,XXY,+21. It is of great interest to note that this case of double aneuploidy is the first case of its kind in more than 1500 cases of Down syndrome referred to our department during the past 25 years. Studies on the incidence of an XXY chromosome pattern among Down individuals have revealed that this double aneuploidy might be more frequent than predicted by multiplying the frequencies of the individual aneuploidies.[8] This observation together with the well-documented increased risk for aneuploidies after the birth of a trisomic child has been attributed to a possibly inherited predisposition to non-disjunction.[9] However, an elucidation of the different factors predisposing to non-disjunction would require determination of the parental origin of the supernumerary chromosomes.[1] This was not feasible in the present study, as the patient was lost for follow-up. Theoretically, 50% of XXY cases could arise from an error in paternal meiosis I and the remaining in maternal meiosis I or II. On the other hand, trisomy 21 can originate in either of the divisions in both parents.

The present case and most of the published cases of 48,XXY,+21 have showed features typical of Down syndrome alone. This is only expected, as features characteristic of Klinefelter syndrome are not apparent until the post-pubertal stage.[10] On the other hand, abnormalities of external genitalia characteristic of Klinefelter syndrome only were observed in a 13-month-old boy probably due to the occurrence of a mosaic pattern of 47,XXY [80.6%] / 48,XXY,+21 [19.4%].[2] This report of double aneuploidy of XXY and trisomy 21 highlighting the clinical characteristics will aid in a better understanding of the phenotype-genotype relationship.

References


Figure 1: GTG-banded karyotype of the proband showing double aneuploidy - 48,XXY,+21