

Double aneuploidy: A unique case of trisomy 21 with XYY

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ABSTRACT

The double aneuploidy or two chromosomal abnormalities occurring in an individual are relatively uncommon. It mainly arises due to non-disjunction at either first or second meiotic division. The double aneuploidy 48, XXY, +21 was described for the 1st time in 1959, and the incidence is reported to be 0.4–0.9/10,000 male births. Chromosomal abnormalities are seen in 1–2% of live births. We report a case of newborn with the clinical features of Down's syndrome, the most common aneuploidy and genetic cause of moderate intellectual disability. Cytogenetic analysis showed karyotype of 48, XYY, + 21. Our case had double aneuploidy (48, XYY, +21) with congenital heart disease and hypothyroidism.

Key words: Aneuploidy, Dysmorphic features, Hypothyroidism, Intrauterine growth restriction, Trisomy 21

Chromosomal abnormalities are observed in about 1% of live-born infants. The occurrence of double aneuploidy, the existence of two chromosomal abnormalities in the same person, is a relatively rare phenomenon. Double aneuploidy leading to trisomy and/or monosomy of two different chromosomes arises due to non-disjunction at either first or second meiotic division. Aneuploidies are the most common structural chromosomal abnormalities detected in fetuses [1]. Down's syndrome (DS) is the most common aneuploidy seen in live-born infants. The incidence of DS in live births is 1:733 in West and 1:920 in India [2]. In 1959, the first case with autosomal and sex chromosomal anomalies, 48, XYY, + 21, was presented by Ford *et al.* [3], and till date, 29 cases with 48, XYY, + 21 have been reported [4].

CASE REPORT

The patient was born at 39 weeks gestation and was delivered by the lower segment cesarean section in view of fetal distress with pregnancy-induced hypertension. He was the second child of non-consanguineous parents. The mother was 41 years old at conception and father's age was 47 years. The antenatal period was uneventful. The child weighed 1.92 kg at birth and was small for gestational age. The older sibling was normal and there was no significant family history.

The clinical examination of the infant revealed hypotonia, flat facial profile, depressed nasal bridge, right preauricular sinus, downward slanting of eyes, saddle gap, and bilateral congenital talipes equinovarus. The birth weight was <3rd centile, length was 43 cm (10th–23rd centile), and head circumference was 31 cm (<3rd centile). The phenotype of the child resembled autosomal aneuploidy.

A number of laboratory investigations were carried out. The hematocrit value was 66.6% and platelet count was 148,000/mm³. Thyroid screening showed elevated TSH (21 µIU/ml) levels. Cardiac abnormalities (partial atrioventricular [AV] canal defect, atrial septal defect, ventricular septal defect, patent foramen ovale, and patent ductus arteriosus) were also detected on echocardiography. Chromosomal analysis was performed using modified whole blood and microtechnique method followed by GTG banding. Thirty metaphase spreads technique was analyzed at 500 levels of bands and was reported. The karyotype of the case was identified as 48, XYY, + 21. The partial exchange was performed. Polycythemia recovered in a short course of time.

DISCUSSION

Double aneuploidy was first described in a patient with both DS and Klinefelter syndrome (48, XXY, +21) by Ford *et al.* [3]. The incidence is reported to be 0.4–0.9/10,000 male births [4]. This is also the most common described double aneuploidy [5]. Non-disjunction during maternal meiosis 1 is the most common cause of trisomy 21. The XYY occurs when 24, YY spermatozoa are formed due to non-disjunction either at paternal meiosis 2 or mitosis [6]. The literature depicts that there is no specific chromosome association in double aneuploidy formation; however, the most frequently involved chromosomes are the sex and acrocentric chromosomes [7]. Most double aneuploidies are associated with an increased maternal age and pregnancy loss at a very early gestational age [8]. Unlike DS, the XYY is not associated with increased paternal age [9]. In patients with double aneuploidies, phenotype resembles autosomal aneuploidies.

Compatible with the literature, the clinical phenotype of DS was predominant in our case. Polycythemia may be present in autosomal aneuploidies. It is thought to be associated with erythropoietin increase in intrauterine chronic hypoxia. The incidence of congenital heart disease in DS is 50%. AV canal defects, atrial septal defect (ASD), ventricular septal defect, patent ductus arteriosus (PDA), and tetralogy of Fallot are the most commonly seen cardiac defects. The present case had partial AV canal defect, ASD, patent foramen ovale, and PDA.

Our case also had elevated TSH. Transient mild TSH elevation with normal thyroxine (T4) levels is the most commonly seen pattern of thyroid dysfunction in DS [10,11]. The incidence of congenital hypothyroidism in DS is 1%. Besides transient thyroid dysfunction, DS is also associated with long-term thyroid dysfunction. Several studies have stated a remarkably higher prevalence of persistent primary congenital hypothyroidism in DS [12].

An XYY sex chromosome complement, without an abnormal phenotypic component, may be found in general population. However, patients may have long stature, large teeth, prominent glabella, asymmetric, and long ears and fingers, dull mentality, relative weakness, poor fine coordination, and learning disabilities. Behavioral problems such as hyperactivity and anger onset may be prominent at childhood or adolescence which may be found at a later age, so these patients should be followed regularly for the evaluation of behavioral problems. However, the behavioral changes appear to be variable and may be modified by the environment in which these children live. Similar case reports have been presented earlier by Shen *et al.* and Shu *et al.* [13,14].

CONCLUSION

A 48, XYY, + 21 is a very rare disorder. In addition to the features mentioned in the literature, our case had congenital heart disease and hypothyroidism. Therefore, it is important to recognize the XYY abnormality at the earliest so that the children can be evaluated periodically and given appropriate care and interventions for learning and behavioral needs.

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