Double Aneuploidy: A Case of Trisomy 21 with XYY

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Eur J Gen Med 2011;8(4):338-341

Received: 24.05.2010

Accepted: 30.07.2010

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ABSTRACT

Although aneuploidies are common structural chromosomal abnormalities, double aneuploidies involving chromosomes 21 and Y are very rare. Here we report a case of double aneuploidy involving chromosomes 21 and Y in a 5 day old baby with jaundice and polycythemia. The diagnosis was confirmed by karyotype analysis using modified "whole blood" and microtechnique methods followed by Giemsa-Trypsin-Leishman (GTL) banding technique. The patient had typical features of Down syndrome, however, phenotypic features of XYY was not present. In addition, the patient also had atrial septal defect, multiple trabecular small ventricular septal defect, and moderate degree of pulmonary hypertension. Etiological predisposing factor for 48,XYY,+21 is not known. It is difficult to determine the incidence, phenotypic properties, and recurrence risk of 48,XYY,+21.

Key words: *Double aneuploidy, Down Syndrome, chromosomal anomalies*

Çift Anöploidi: XYY'li Trizomi 21 Olgusu

Anöploidiler yaygın görülen kromozomal anomaliler olmalarına rağmen kromozom 21 ve Y'yi içeren çift anöploidiler çok nadirdir. Burada sarılığı ve polisitemisi olan Kromozom 21 ve Y'yi içeren çift anöploidili beş günlük bir vaka rapor edilmektedir. Tanı, modifiye tam kan ve mikroteknik yöntemle Giemsa-Tripsin-Leishman (GTL) bantlama tekniği kullanılarak yapılan karyotip analizi ile kondu. Olgumuzda Down Sendromu'nun tipik özellikleri mevcuttu. Ancak XYY'ye ait fenotipik özellikler yoktu. Ayrıca olgumuzda atriyal septal defekt, multiple trabeküler küçük ventriküler septal defekt ve orta derece pulmoner hipertansiyon da mevcuttu. 48,XYY,+21'in etyolojisinde yer alan etyolojik faktörler bilinmemektedir. 48,XYY,+21'in insidansının, fenotipik özelliklerinin ve tekrarlama riskinin belirlenmesi zordur.

Anahtar kelimeler: *Çift anöploidi, Down sendromu, kromozomal anomaliler*

INTRODUCTION

Aneuploidies are common structural chromosomal abnormalities. In particular, three of them, trisomy 21, trisomy 18 and trisomy 13 are the most frequently seen autosomal aneuploidies. Other commonly seen gonosomal aneuploidies are Turner syndrome, Klinefelter syndrome and its variants, poly X syndromes and poly Y syndromes. The incidence of trisomy 21, the most frequent autosomal aneuploidy, is 1/600-1/700. Incidence of 47,XYY was reported to be 1/840 live births (1). In 1959, the first case with autosomal and sex chromosomal anomalies, 48,XXY,+21, was presented by Ford et al (2). The case of 48,XYY,+21's are rare with clinical data limited to only 28 reported cases (3). We have reported this case for its rarity and its association to polycythemia and congenital heart defects.

CASE

The case being reported here was delivered by caesarean section at the 39th week of gestation as second child of a 23 year old healthy mother and a 31 year old healthy father. The patient was admitted to our clinic because of jaundice when the baby was 5 days old. The first child of the family then was three years old and he was healthy. The family history revealed no specific abnormality. There was no consanguinity between parents. At physical examination the patient was hypotonic, icteric and plethoric. Flat facial profile, flat nose, bilateral epicanthal folds, enlarged tongue, short neck, loose neck skin, bilateral clinodactyly and simian line were also observed at the examination. The birth weight of the baby was 2740 g (3rd -10th percentiles), he was 49 cm tall (10th -25th percentiles) and his head circumference was 33,5 cm (10th percentiles). Cardiac auscultation revealed grade 2/6 systolic ejection murmur (Figure 1).

Laboratory investigation revealed Hct:66%, plt: 78 000/mm3, blood glucose 36mg/dl, total bilirubin 21mg/dl, negative direct Coombs test, reticulocyte count of 1%, and normal thyroid hormone levels. Two dimensional echocardiography showed an atrial septal defect (ASD) with 3.8mm in diameter, multiple trabecular small ventricular septal defect (VSD) and moderate degree pulmonary hypertension. Partial exchange was performed because of symptomatic polycythemia and continued with intensive phototherapy. Thrombocytopenia and hypoglycemia recovered in a short time after treatment of polycythemia. The patient was discharged from hospital with medication of digoxin and diuretics. At the 4th months of follow up the patient was in a good condition, the body weight was 4700 g (3rd -10th percentiles), his height was 59 cm (10th -25th percentiles), and his head circumference was 39 cm (3rd-10th percentiles). Chromosome analysis was performed using modified "whole blood" and microtechnique methods followed by Giemsa-Trypsin-Leishman (GTL) banding technique. Thirty metaphase spreads were analyzed at 400 band level of bands for chromosomal analysis and was reported according to ISCN nomenclature 1995. The karyotype of the case was determined as 48,XYY,+21 (Fig. 2). Parental chromosomal analyses could not be carried out due to their lack of consent and genetic counselling was done accordingly.

DISCUSSION

XYY syndrome is a common sex chromosomal aneuploidy. Patients characteristically 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 like hiperactivity and anger onset may be prominent at childhood or adolescence. Despite an incidence of 1/840 male births, which almost equals that of Down syndrome, males with XYY genotype are usually detected at a later age (1).

Coincidance of XYY and trisomy 21 is very rare. Al-Aish et al. proposed an incidence of 1/48000 male birth however, the incidence of double trisomy have been reported to range from 0,21 to 2,8 % among the karyotypes of spontaneous abortions (4,5). Furthermore, considering the scarcity of reported cases and the fact that most of the cases ended with first trimester spontaneous abortions (4), it is difficult to determine the real incidence of association of XYY and trisomy 21. Up to now we could found only 28 cases with 48,XYY,+21 reported in the literature (3). Cases with double aneuploidies reflect their chromosomal features to phenotypes. Cases with 48, XYY,+21 may have both phenotypic features of XYY or Down syndrome. The case reported here had typical features of Down syndrome, however phenotypic features of XYY were not present. The incidence of congenital heart disease in Down syndrome is about 40%. Atrioventricular canal defects, VSD, ASD and

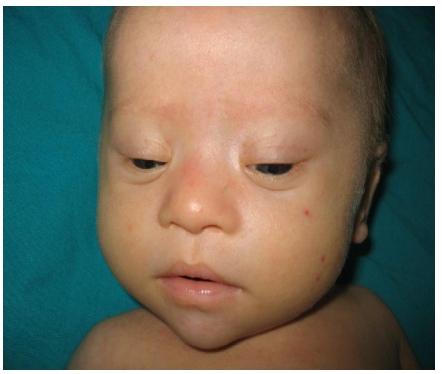

***Figure 1**. Phenotype of the proband.*

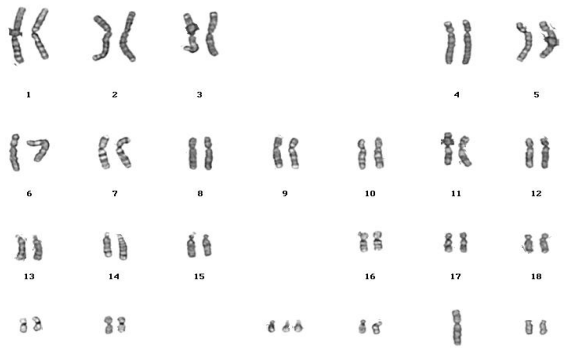

***Figure 2**. Chromose complement and karyotype (48,XYY,+21) of the proband.*

patent ductus arteriosus are the most common signs of congenital heart disease (6). Our patient (this case) had ASD, VSD and pulmonary hypertension. Parmar et al. also reported similar congenital heart disease in previous case (7). Polycythemia may be present in autosomal aneuploidies. Polycythemia is thought to be associated with erythropoietin increase in intrauterine chronic hypoxia (8). In the literature clinical data about patients with double aneuplodies is limited. Our patient is one of few double aneuploidy cases with polycythemia reported in literature.

The behavioral problems which have been seen in XYY, were investigated in patients with 48,XYY,+21 however no significant problem have been observed, probably due to the short duration of follow-up of these patients (5 years). Behavioral problems are seen at late childhood and adolescence in XYY, so these patients should be followed for longer duration of time for evaluation of behavioral problems. In patients with double aneuplodies phenotype is more commonly determined by autosomal aneuplodies. Compatible with the literature; the clinical phenotype of Down syndrome in our patient was dominant as expected (7-9). Classical trisomy 21 results from maternal meiotic nondisjunction. Y chromosome of XYY is always paternal and it occurs by nondisjunction at meiosis II or mitosis after fertilization (3,7,9). Etiological predisposition factor is not known for 48,XYY,+21. Double aneuploidy showed that a 48,XXY,+21 karyotype was associated with advanced maternal age in contrast to a 48,XYY,+21 karyotype which was not. Males with Down syndrome are sterile, it would be reasonable to propose that males with 48,XYY,+21 may also be not fertile. Maternal and paternal karyotypes of these patients were normal in previous literature (3). The parents of our patient did not agree for karyotype analysis, so, it could not be performed. Prenatal diagnosis can be made by conventional cytogenetic methods. When the conventional methods are inadequate, FISH provides a rapid technique for diagnosis. If double aneuploidies have been thought in diagnosis, beside 21st chromosome probe, Y probe must also be used. Otherwise these patients could be diagnosed as Down syndrome and diagnosis of XYY might be missed out.

In conclusion 48,XYY,+21 syndrome is a very rare disorder. So, it is difficult to determine its incidence, phenotype properties and recurrence risk.

REFERENCES

1. *Jones KL. XYY Syndrome. Smith's Recognizable Patterns of Human Malformation 5 th ed. Philadelphia: WB Saunders 1997:70-71.*
2. *Ford CE, Jones KW, Miller OJ, et al. The chromosomes in a patient showing both mongolism and the Klinefelter syndrome. Lancet 1959;1:709-10.*
3. *Kovaleva NV, Mutton DE. Epidemiology of double aneuploidies involving chromosome 21 and the sex chromosomes. Am J Med Genet A 2005;134:24-32.*
4. *Li QY, Tsukishiro S, Nakagawa C, et al. Parental origin and cell stage of non-disjunction of double trisomy in spontaneous abortion. Congenit Anom (Kyoto) 2005;45:21-5.*
5. *Al-Aish MS, Dodson WE, Plato CC. Down's syndrome with XYY: 48,XYY, G+. Am J Dis Child 1971;121:444-6.*

6. McLean SD. Congenital Anomalies. In: Mhairi G. MacDonald MDM, Mary M.K. Seshia, ed. Avery's Neonatology Pathophysiology& Management of the Newborn. 6 th ed. Philadelphia: Lippincott Williams& Wilkins, 2005:893-913.

7. Parmar RC, Muranjan MN, Swami S. Trisomy 21 with XYY. Indian J Pediatr 2002;69:979-81.

8. Widness JA, Pueschel SM, Pezzullo JC, Clemons GK. Elevated erythropoietin levels in cord blood of newborns with Down's syndrome. Biol Neonate 1994;66:50-5.

9. Gollop TR, Naccache NF, Auler-Bittencourt E, et al. Prenatal diagnosis of 48,XYY, +21 ascertained through ultrasound anomalies. Am J Med Genet 1991;39:76-7.