A rare sex chromosome aneuploidy: 48,XXYY syndrome

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Abstract

48,XXYY syndrome is a rare sex chromosome abnormality. Although some physical features are similar to Klinefelter syndrome(47,XXY), 48,XXYY is typically associated with different neuropsychiatric symptoms and phenotypic findings. Approximately 100 cases with 48,XXYY have been reported to date. In this report, a patient who was diagnosed with 48,XXYY syndrome with clinical evaluation and cytogenetic analysis is presented. A 6-year old male patient was hospitalized due to recurrent respiratory tract infections, recurrent abdominal distention and dyspepsia. He was the first and only child of nonconsanguineous parents. He had a history of mild developmental retardation. In his history, it was learned that he received treatment for gastroesophageal reflux and his symptoms improved with treatment. On physical examination, his weight was found to be 31 kg (>97 centile) and his height was found to be 123 cm (90 centile). He had upslanted palpebral fissures, depressed nasal bridge, long philtrum, incomplete cleft lip and micrognathia. Clinodactylia was found in the fifth fingers in both hands and large big toes and adduction in the second and third toes were found in both feet. Karyotype analysis showed a chromosomal composition of 48,XXYY. The patient presented here is the second Turkish case of 48,XXYY syndrome. (Turk Pediatri Ars 2016; 51: 106-9)

Keywords: Klinefelter syndrome, sex chromosome abnormality, XXYY syndrome

Introduction

48,XXYY syndrome which is one of the sex chromosome aneuploidies was described by Muldal et al. (1) in 1960 for the first time as a rare type of Klinefelter syndrome (47,XXY) because of presence of one more Y chromosome compared to Klinefelter syndrome. Currently, it is considered a separate clinical and genetic condition. Although it is phenotypically similar to Klinefelter syndrome in many aspects, it is especially differentiated with mental retardation and psychiatric disorders (2, 3).

Here, a patient who was hospitalized because of dyspepsia and underwent karyotype analysis because of minor dysmorphic findings and borderline intellectual disability and whose karyotype was found to be 48,XXYY has been presented.

Case

A six-year old male patient presented with attacks of abdominal swelling which recurred in the last one year and frequent upper respiratory infections. He was the only

child of the parents who were not consanguineous born at term by normal spontaneous vaginal delivery with a birth weight of 2 800 g. It was learned that he sat with support at the age of eight months, walked at the age of 18 months and spoke single words at the age of 16 months. It was reported that he previously had two simple febrile convulsions. He had been treated for abdominal distension and flatulence with a diagnosis of gastroesophageal reflux and benefited from this treatment. On physical examination, his weight was measured to be 31 kg (>97p) and his height was measured to be 123 cm (90p). The dysmorphic findings on the patient's face included a wide forehead, slightly upward-slanting palpebral fissures, wide and prominent nasal root, long philtrum, cleft-lip (incomplete in the upper lip), externally rotated lower lip, horizontal streaks on the chin, plump cheeks, retrovert ears and small chin. Truncal obesity was present. Clinodactyly was found in the fifth finger in both hands, large thumbs and introverted appearance of the second and third toes were found in both feet, joint laxity was found in the upper and lower extremi-

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Received: 24.08.2013

Accepted: 20.02.2014

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DOI: 10.5152/TurkPediatriArs.2016.1551

ties and narrow nail folds were found. Genital examination was found to be normal (Figure 1). Complete blood count, liver function tests, renal function tests and ions were found to be normal. Abdominal ultrasonography and esophago-gastro-duodenal and colonographies were found to be normal. Fundoscopic examination and hearing assessment were found to be normal. On psychiatric evaluation which was requested because of aggressive behaviors, it was reported that he had separation anxiety and borderline mental retardation was found (IQ was measured to be 85). On cranial magnetic resonance imaging, multiple small hyperintense formations were observed in the subcortical region in the brain, whereas cranial magnetic resonance angiography was found to be normal. Chromosomal analysis performed using high-resolution G-banding technique was found to be 48,XXYY. Informed consent was obtained from the patient's family for publication of the clinical findings, laboratory test results and pictures of the case (Figure 2).

Discussion

While Klinefelter syndrome is observed in one of 650 male births, the incidence of 48,XXYY syndrome has been calculated to be 1/18 000-1/40 000. More than 100 cases have been reported up to today. The case presented here is the second case reported from our country (4).

Recently, 48,XXYY syndrome has been accepted to be a different picture like some other rare sex chromosome aneuploidies (48,XXXY and 48,XXXXY). Long height is one of the most important physical findings in 48,XXYY syndrome similar to Klinefelter syndrome. Tartaglia et al. (5) reported that increase in height accelerated especially

from the period of puberty. While long height has also been reported in 48,XXXY syndrome, individuals with 48 XXXXY syndrome are mostly short (6). Although our patient was in the prepubertal period, his height was in the 90th percentile. It can be predicted that his height will increase to the 97th percentile or above with the pubertal growth spurt.

It is controversial if descriptive facial dysmorphic findings are present in 48,XXYY syndrome. In most cases, anomalies including hypertelorism, epicanthus, upward-slanting palpebral fissures, clinodactyly in the fifth finger, short nail folds, pes planus, joint laxity, dental problems and radioulnar synostosis have been identified (4, 7). In the study of Tartaglia et al. (5) conducted with 95 male patients, the most common dysmorphic findings in patients aged younger than 10 years were reported to be hypertelorism, upward-slanting palpebral fissures, micrognathia, clinodactyly in the fifth finger and pes planus. In the same study, obesity was found in 12.5% of the patients. The above-mentioned dysmorphic findings and truncal obesity were present also in our patient. Submucosal or hidden cleft palate have been reported previously, whereas incomplete cleft lip found in our patient has not been identified in previous cases (6). Toe deformities found in our patient are another dysmorphic finding which has not been identified before. Borghgraef et al. (8) reported that the reason directing to chromosomal analysis in at least half of the cases of 48,XXYY syndrome before puberty was presence of one or multiple dysmorphic findings.

While mental retardation is observed rarely in Klinefelter syndrome, 26% of the subjects with 48,XXYY syndrome have mental retardation and almost all have learning difficulty. Delayed speaking and motor developmental retardation is found with a rate of 75-92%. In our patient, delayed speaking was found in addition to a mild retardation in motor developmental stages. In addition, aggressive behaviors matched up with the psychiatric findings described previously for this syndrome (5, 9, 10). T2 hyperintense lesions in the white matter (45.7%), enlarged ventricles (22.8%), corpus callosum agenesis (5.7%) and cortical dysplasia (8.6%) may be observed on cranial magnetic resonance imaging in individuals with 48,XXYY syndrome. T2 hyperintense lesions found on cranial magnetic resonance imaging in our patient were considered compatible with this syndrome in this aspect (5).

Finally, one of the complaints at presentation in our patient was recurrent upper respiratory tract infections

Figure 1. Peripheral blood karyotype result belonging to the subject: compatible with 48,XXYY

Figure 2. Dismorphic findings of the patient: (a, b) wide forehead, upward-slanting palpebral fissures, wide and prominent nasal root, long philtrum, cleft-lip (incomplete in the upper lip), externally rotated lower lip, horizontal streaks on the chin, plump cheeks, retrovert ears, micrognathia (c) clinodactyly in the fifth finger in both hands (d) simian line in the left hand (e, f) deformities in the toes in both feet

and dispeptic complaints which recurred in the last one year. In this context, it was reported that gastroesophageal reflux was observed with a rate of 19.3%, recurrent otitis was observed with a rate of 12.9% and history of hospitalization because of respiratory tract infection was observed with a rate of 46.2% in all age groups in a large series of 95 cases (5).

Informed Consent: Written informed consent was obtained from patients' parents who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - T.A., Ö.Ç., F.Ö.; Design - T.A., F.Ö.; Supervision - Ö.Ç., F.Ö.; Data Collection and/or Processing - T.A.; Analysis and/or Interpretation - T.A., Ö.Ç., F.Ö.; Literature Review - T.A.; Writer - T.A., F.Ö.; Critical Review - Ö.Ç., F.Ö.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study has received no financial support.

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