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Case Report

Tetrasomy X, a Rare Cause of Epilepsy and Behavior Disorder

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Abstract

Introduction: Tetrasomy X is an extremely rare condition that affects only women. This syndrome was described first in 1961 and about 50 cases were reported then.

Aim: In this article, we aimed to present a 15-year-old female patient who presented with seizure and self-harm behaviours and diagnosed as tetrasomy X.

Case Report: A 15-year-old female patient without perinatal problems was brought to our clinic with the complaint of seizure and self-harm behaviours. She was a full-term third-born of a 31-year-old mother and a 34-year-old father, there was no kinship between the parents. She had history of febrile seizures at 3 months of age and had mental motor developmental delay. At 7 months of age, epilepsy was diagnosed and treatment was initiated. She was still being followed up by pediatric psychiatry clinic because of her self-injurious behavior. On physical examination, she was conscious and mentally retarded. There were dysmorphic findings on the face. Cranial nerve, motor, cerebellar and sensory examinations were normal. The patient, whose hearing was normal, started newly to form sentence while speaking. She had hyperactive movement pattern and aimless movements in the hands. Metabolic screening and cerebral MRI were normal. EEG showed generalized epileptiform discharges. Standford-Binet test showed severe mental retardation.

Results: Tetrasomy X is caused by inadequate separation of chromosomes during meiosis. Clinical manifestations may range from mild to severe. Delay in speech, learning disabilities, growth retardation and dysmorphic facial appearance are frequently observed. Behavioral disorder can be as severe as much as mild. Panic attacks, manic depression, bipolar disorder can be seen. However, these problems can be controlled with medication. Other anomalies such as tooth anomalies, heart defects, joint laxity, radio-ulnar synocytosis, hip joint dysplasia, renal anomalies and ovarian dysfunction may also be seen. In addition, increased sensitivity to infections in childhood is reported. Therefore, if a tall female patient approaches due to behaviour disorder and epilepsy, tetrasomy X should be considered.

Keywords: *Dysmorphic Findings; Mental Retardation; Epilepsy; Tetrasomy X*

Introduction

48, XXXX is a rare and poorly characterized aneuploidy syndrome. Neurocognitive delays, delayed speech and poor speech perception, skeletal and facial abnormalities, atypical behaviors, and attention deficit hyperactivity disorder (ADHD) can be seen. There is no common clinical findings and phenotype as it is rare, but high forehead, flat nasal bridge, ocular hypertelorism, short neck, clinodactyly in the fifth finger, decreased muscle tone in the extremities and oral-facial regions, long stature, tooth anomalies, menstruation disorders and ovarian dysfunction have been reported [1-3].

In this article, we present a 15-year-old female patient who presented with seizure and self-harm behavior and diagnosed as Tetrasomy X.

Case Report

A 15-year-old female patient with history of uncomplicated pregnancy and delivery was brought to our clinic with the complaint of seizure and self-harm behaviours. She was a full-term third-born of non-consanguineous 31-year-old mother and 34-year-old father. She had a history of febrile seizures at 3 months of age and had mental motor developmental delay. At 7 months of age, epilepsy had been diagnosed in another clinic. Physical examination revealed a height of 170 cm (75-90p) and weight of 66 kg (50-75p). She was conscious, and mentally retarded. There were dysmorphic findings such as hypertelorism and flattened nose on the face (Figure 1). She was being followed up by the ophthalmology department for myopia. Cranial nerves, motor, cerebellar and sensory examinations were normal. The patient, whose hearing was normal, started newly to form a few sentences. She had hyperactive movement pattern and aimless movements in the hands. The tooth structure was normal, regular menstruation cycle present, and external genital structure was normal. Metabolic screening and cerebral MRI were normal. EEG showed generalized epileptiform discharges. Sandford-Binet test showed severe mental retardation. Pelvic USG was performed and both ovaries were seems normal. No cardiac anomaly was detected on cardiologic examination and tests.

Figure 1

Cytogenetic and molecular analysis

Chromosomal preparations were made from peripheral lymphocytes stimulated with phytohemagglutinin using RPMI1640 medium and standard culturing. 48 XXXX chromosome aneuploidy syndrome was detected.

Discussion and Conclusion

Tetrasomy X or 48, XXXX chromosome is an extremely rare aneuploidy syndrome. The first case reported from India in 1961, since then, 100 cases have been diagnosed, but 50 cases have been reported as scientific publications. Tetrasomy X is caused by inadequate separation of chromosomes during meiosis [4,5].

Tetrasomy X may have a wide range of mild to severe clinical signs. Delay in speech, learning disabilities, growth retardation and dysmorphic facial appearance are frequently observed. The average IQ is between 60 and 80, but Neilson., *et al*. reported an IQ scale of 30-101 in a study on 27 cases with tetrasomia. Only one patient with normal IQ in the 90 - 110 range was reported. However, despite normal IQ, she had severe articulation problems, delayed perception and poor speech skills. IQ level decreases 10 - 15 points with each X added chromosome, Patients usually start talking at the age of 3 years. Coarse motor lag is more prominent than fine motor skills. Linden., *et al*. described a 48,XXXX patient with facial asymmetry, delayed development and poor motor coordination, delayed speech, poor speech skills, limited expression and perception, fine and coarse motor delays, and frontal lobe dysfunction [6,7].

Behavioral disorder can be as severe as it is mild. Some of the 48, XXXX individuals are pleasant, friendly, open to co-operation, while others are aggressive and emotionally indecisive. Schizophrenic symptoms, panic attacks, manic-depression, and bipolar disorder can also be seen.

The phenotypic findings in tetrasomy X are very heterogeneous. The presence of extra sex chromosomes has a detrimental effect on growth, development and overall phenotype. Most often affected organs are skeletal, heart and gonadal systems. Facial dysmorphism is detected in varying degrees. Cammarata., *et al*. reported mid-face hypoplasia, hypertelorism, myopia and iridochiasis, elevated palpebral fissures, epicantal folds, low nose bridge, micrognathia, short neck, clinodactyly of the fifth finger and metaphyseal enlargement of the long bones in a patient with tetrasomy X [8,9].

Loss of an X chromosome results in short stature and often primary ovarian failure. However, an extra X chromosome in tetra-

somy is responsible for being tall. The average height of 48, XXXX patients are 169 cm. While there were growth and weight gain problems in the early ages, the average height of these patients is higher than the population average in the following years [10,11].

Other anomalies such as tooth anomalies, heart defects, joint laxity, radio-ulnar synocytosis, hip joint dysplasia, decreased muscle tone in the upper extremity and oral-facial regions, renal anomalies and ovarian dysfunction may also be seen. 48, XXXX girls have usually normal external genitalia, but some cases with irregular menarche, absence of ovaries and early ovarian failure have been reported. Three women with tetrasomy X syndrome conceived and gave birth to children with normal karyotype, with omphalocele and with trisomy, respectively. Half of the 48, XXXX cases have normal menarche and menstruation periods, while others have menstrual dysfunction. Patients who have functional ovaries and regular menstrual cycles can become mothers. Estrogen therapy may be necessary for breast development, to stop longitudinal growth, prevent osteoporosis and maintain bone health [11-14].

In conclusion, if a tall female patient approaches due to behaviour disorder and epilepsy, tetrasomy X should be considered.

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