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A female infant case with tetrasomy 18p

Bir dişi infant tetrazomi 18p olgusu

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SUMMARY

Tetrasomy 18p is a rare chromosomal anomaly that can affect different systems. It is caused by an abnormal extra chromosome, called isochromosome 18p. This condition usually causes growth retardation, intellectual disability, abnormalities in muscle tone, and specific facial features. A dysmorphic female child with microcephaly and mental-motor retardation was referred to our department. After physical examination, we researched the problem of this patient using conventional cytogenetic procedure. Her karyotype was 47, XX, +mar. In order to determine the origin of marker chromosome, we performed fluorescence in situ hybridization (FISH) method on metaphase cells. Tetrasomy 18p was detected in this patient. Her signs and symptoms were consistent with this disorder.

Keywords: Tetrasomy 18, isochromosome 18p, marker chromosome

ÖZET

Tetrazomi 18p farklı sistemleri etkileyen seyrek bir kromozom anomalisidir. İzokromozom 18p denilen anormal ekstra bir kromozom nedeniyle oluşur. Bu rahatsızlık genellikle gelişme geriliği, entelektüel bozukluk, kas tonusu anomalileri ve spesifik fasiyal bulgulara neden olur. Mikrosefali ve mental-motor retardasyonu olan dismorfik bir kız çocuğu bölümümüze sevk edildi. Fizik muayene sonrası konvansiyonel sitogenetik yöntemle hastanın problemini araştırdık. Karyotipi 47, XX, +mar olarak tespit edildi. Marker kromozomun orijinini belirlemek için metafaz hücrelerine FISH çalışması yaptık. Hastada tetrazomi 18p tespit edildi. Hastamızın bulgu ve semptomları bu hastalıkla uyumluydu.

Anahtar sözcükler: Tetrazomi 18, izokromozom 18p, marker kromozom

INTRODUCTION

Tetrasomy 18p is a chromosome anomaly results from an isochromosome consisted of two copies of the short arm of chromosome 18. In the most of cases, the isochromosome is de novo. The patients have no family history concerning this disease. Tetrasomy 18p was reported by Froland et al.[1] firstly in 1963. It is a rare chromosomal disorder[2]. The prevalance of this anomaly is 1/140.000 and the disease affects males and females equally[1, 2]. Tetrasomy 18p syndrome is characterised by mental retardation, microcephaly, low birth weight, growth retardation, hypotonia or hypertonia and some dysmorphic features like low-set ears, small mouth, micrognathia, high palate, strabismus, scoliosis or kyphosis etc.[3, 4]. Additional features of tetrasomy 18p may implicate seizures, vision problems, hearing loss, recurrent ear infections, gastrointestinal and urogenital problems (cryptorchidism, hypospadias) and heart defects[3]. Babies with tetrasomy 18p also have feeding difficulties. Some patients have spinal deformity like scoliosis or kyphosis and different psychiatric conditions, such as attention deficit hyperactivity disorder and anxiety may be.

Source of this phenotype and symptoms is a small marker chromosome, isochromosome 18p[5]. Tetrasomy 18 is an anomaly rarely seen in the world but clinical signs may be important. So, we report a child with tetrasomy 18p from Sivas, Turkey.

CASE REPORT

A nine months old female was referred to our genetic department because of her dysmorphic signs. She was premature and she had a story of intrauterin growth retardation. Her father was 29 and her mother was 28 years old and there was no consanguinity. She had 46cm height, 2260 gr weight and 30 cm head circumference at birth. In the last measurement, this values were 63 cm, 6850 gr and 40 cm respectively (all of the values were under the third percentile). She was microcephalic and her mental and motor development were delayed. Controlling of the head was possible at six months of age, and sitting unsupported at eight months. Her facial symptoms were hypertelorism, broad based nose, high palate, upslanted palpebral fissure, low-set ears and strabismus. She was hypotonic and she had a sacral dimple. There were bilateral Sydney lines in her palms. Her heartbeats were bradycardic. A moderate mitral regurgitation was determined with echocardiography. Abdominal and urinary USG of this patient were normal. TFUSG was performed and several cysts were observed in both choroid plexus. There was no any abnormal finding in EEG. In this patient, 47, XX, +mar karyotype was detected in conventional cytogenetic analysis. In order to determine the origin of marker chromosome, fluorescence in situ hybridization (FISH) analysis was performed. Tetrasomy of chromosome 18p was determined by FISH method applied to metaphase cells from peripheric blood. Marker chromosome was isochromosome 18p (subtelomeric region of the short arm). Test reliability was estimated 95%. Parental karyotype analysen were normal.

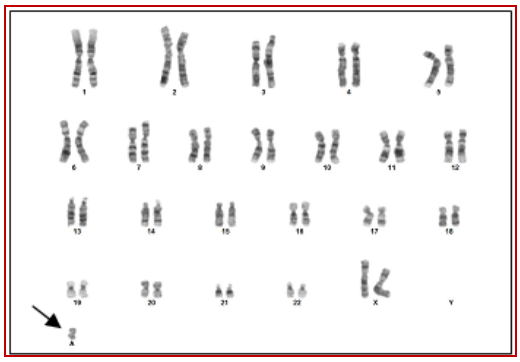

Figure 1: Karyotype of our patient, including a supernumerary markerchromosome (47, XX, +mar).

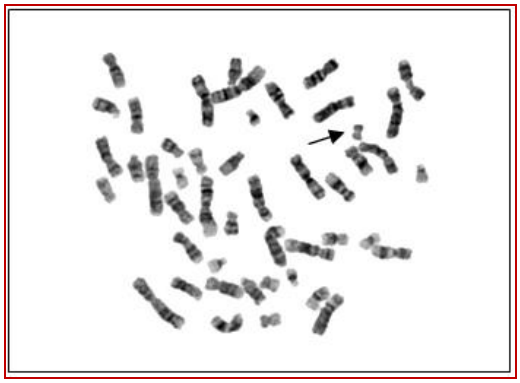

Figure 2: The metaphase image of the same patient.

DISCUSSION

In order to access accurate diagnosis of a genetic condition, researchers need to substantiate with molecular methods. m-FISH is an important procedure to determine the origin of the chromosomal fragment in the marker i.e., tetrasomy of 18p[6]. Tetrasomy 18p is a rare chromosomal abnormality that occurs due to isochromosome 18p which is supernumerary marker chromosome consists of two copies of the short arm of chromosome 18. An isochromosome with the normal chromosome pair leads to a tetrasomy of the arm for a chromosome[7]. Cases of Tetrasomy 18p may have variable phenotypic characteristics. The cause of different phenotypic features may be chromosomal origin, euchromatin content, mosaicism, parental origin and genomic imprinting[8]. Callen et al.[9] suggested that parental age might be advanced in the isochromosome 18p syndrome. In a study by Hook and Cross, mean maternal age of mutant cases was 37.5 + 2.9, a bit greater than the controls[10]. Ages of our

patient's parent did not support these data. Her father was 29 and her mother was 28 years old. Most of the I (18p) cases are sporadic, de novo meiotic events[11]. However, familial and somatic mosaic cases have also been reported[12]. Takeda et al.[13] reported a family with an 18p trisomic mother and two 18p tetrasomic daughters. The mother is phenotypically normal and healthy but the older sister has dysmorphic features and mental retardation and the younger sister was stillborn with extensive defects. Mosaic tetrasomy 18p cases in the literature are rare[3]. Mental retardation is the most common clinical sign of tetrasomy 18p (100%). The rate of microcephaly is 74% and heart defects is 24%[14]. The features of our patient were consistent with the literature (mental retardation, microcephaly, low set ears, high palate, growth retardation, heart defect). An interesting symptom in this patient was sydney line. This hand marker may also be in Down's syndrome, childhood leukemia, congenital rubella, Alzheimer, Fragile X-syndrome, Marfan syndrome, Rubinstein-Taybi syndrome and achondroplasia. The exact identification of the supernumerary marker chromosome may provide important diagnostic and prognostic information. Microdissection libraries for FISH may contribute to specific diagnostic approachs for marker chromosomes[15]. In conclusion, we report a rare chrosomal anomaly, tetrasomy 18p in a nine months old female child from Sivas, Turkey. She needs specific treatment and rehabilitation.

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