Turgut Özal Tıp Merkezi Dergisi **5(2, 3) 1998**

PARTIAL DELETION OF LONG ARM OF CHROMOSOME 11 [del(11)(q24)] IN A PATIENT PRESENTING WITH BEHAVIORAL DISTURBANCES

Osman DEMIRHAN, Ph.D *
A.Kübra TEMOÇIN, MD *
Ayse AVCI, MD **
Ayse BALAT, MD ***

In this report we present a 10 year-old girl having behavioral disturbances and a deletion on the long arm of chromosome 11 involving the q24 region. We compare our patient manifestations to those associated with the distal 11q2 deletion phenotype.

Key words: *11q deletion, Jacobson syndrome.*

Davranış Bozukluğu Nedeniyle Başvuran Bir Vakada 11. Kromozomun Uzun Kolunun Kısmi Delesyonu

Bu çalışmada davranış bozukluğu nedeniyle başvuran ve kromozom analizinde 11. kromozomun uzun kolunun 24.bölgesinde delesyon saptanan 10 yaşındaki bir kız hasta sunuldu. Hastamızın bulguları literatürdeki 11. kromozom q2 delesyonu olan olgularla karşılaştırıldı.

Anahtar kelimeler: *11q delesyonu, Jacobson sendromu*

* Çukurova University
Medical Faculty , Department of Medical Biology and Genetics
Adana

** Çukurova University
Medical Faculty , Division of Child Psychiatry
Adana

*** Inonü University, Medical Faculty, Department of Pediatrics
Malatya

Since the first patient with partial distal deletion of the long arm of chromosome 11 was described by Jacobson et al[1], more than 35 cases of distal deletion of chromosome 11 have been reported in the literature[2-9] . Most cases were of de novo origin. Some of them has a heritable folate sensitive fragile site[10] . Common clinical features of these patients are growth and psychomotor retardation, trigonocephaly, divergent intermittent strabismus, epicanthus, telecanthus, broad nasal bridge, short nose with anteverted nostrils, carp-shaped upper lip, retrognathia, low-set dysmorphic ears, bilateral camptodactyly, hammertoes, and isoimmune thrombocytopenia.

The patient presented in this study has a chromosome 11q24 deletion with the same clinical features of Jacobson Syndrome. The features of our patient are compared with those of individuals reported in the medical literature having distal 11q deletion.

CASE REPORT

Correspondence Address:
Osman DEMIRHAN, Ph.D
Department of Medical Biology and Genetics,01330 Balcali,
Adana,TURKEY. Tel 322-3386060-3498,Fax 322-3386572

The patient is a 10 year-old girl in the 4th grade of Elementary School who is the 3rd child of unrelated and healthy parents. One of her cousins had mild mental retardation. Her mother was 31 year-old and her father was 34 years -old at the birth of this child. Previous and later pregnancies of her mother resulted with the birth of healthy children. Her sisters showed normal

mother resulted with the birth of healthy children. Her sisters showed normal mental and motor development. Her birth weight and height was 2300 g (5^{th} centile), and 46 cm (5th centile) respectively, suggesting intrauterine growth retardation. She was the product of an unremarkable pregnancy and delivery. She was breastfed for 6 months, walked in 12 months but began to talk fluently when she was 5 years old. Her toilet training was completed diurnally when she was 2 years old, but nocturnal bedwetting is still the problem. Her mother describes her masturbation from her toddler age, and also headbangings in these ages. For that reason, CT scan was taken when she was 5 years old and evaluated as normal. She underwent an eye operation because of strabismus at 5 years-old. She was defined as "slow-learning and childish" by her teachers. Behavioral approaches were attempted because of bedwetting, but failed a few years ago. Her learning performance were decreased in years. Behavioral disturbance emerged and included hyperactivity, attention deficit, difficulty in controlling tantrums. She became socially withdrawn, displayed limited interest with peers. She was brought to the child psychiatry unit with "bedwetting, attention deficit, learning difficulties and masturbation" symptoms. At the time of admission, her height was 141 cm (90th percentile), weight was 38 kg (75th percentile), and had a head circumference of 50.5 cm (50th percentile). She had no growth retardation. She had the following dysmorphic features on physical examination; broad nasal base, slightly up-slanted palpebral fissure, strabismus (operated), low-set dysmorphic ears, moderate retrognathia and micrognathia, clinodactyly in fifth finger of left hand and also transverse palmar crease. Unfortunately, we could not obtain this patient's picture because we did not have her parents permission. The initial DSM-IV diagnosis is, according to the APA (11), Axis I; Stereotype Movement Disorder, Axis II; Mild Mental Retardation. Her performance IQ on The Wechsler Intelligence Scale-Revised was 70, verbal IQ was 69, total was 66. Bender Visual-Motor-Gestalt test shows delay in maturation. Primitive responses are including perseveration, difficulties with and joining the parts of figure. Her EEG and magnetic resonance imaging scan were normal. Because of the mild mental retardation with delayed speech development, cytogenetic studies were requested.

CYTOGENETIC

Routine chromosome preparations from the patient and her parents were obtained from cultures of peripheral blood lymphocytes.

Twenty metaphases from the patient and each parent were analyzed. The chromosome spreads were stained with G-banding and a standard protocol. The proband's karyotype revealed a terminal deletion of the long arm of chromosome 11 in all cells, with break-points at 11q24 [46,XX,del(11)(q24)] (Fig 1,2). Karyotype of her parents is found to be normal.

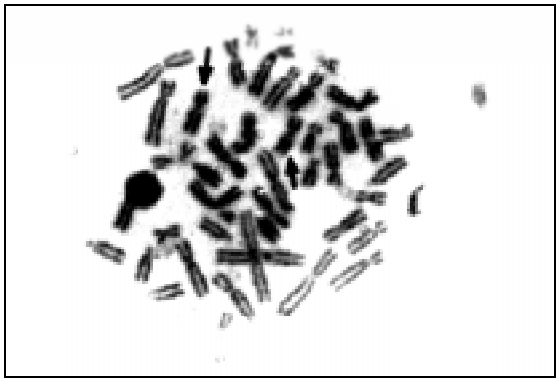

Figure 1. The metaphase of the patient's chromosome.

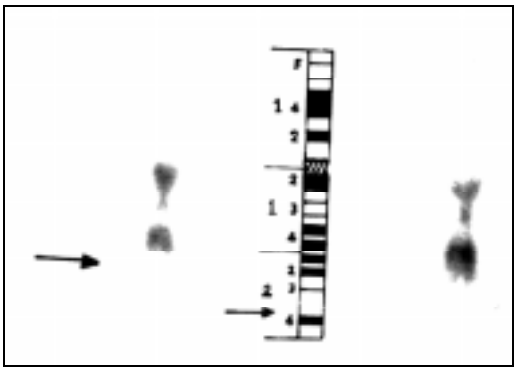

Figure 2. IIlustration of del 11q 24. The schematic and normal appearing of chromosome 11. Breakpoint are marked.

DISCUSSION

More than 35 cases of distal monosomy 11 have been previously described. In spite of the variability in the breakpoint of the terminal deletion between 11q22 and 11q24, the most frequent breakpoint is located at 11 q23 [1,5,12,13] . The clinical features of 11q monosomy consisting

monosomy consisting of prenatal and postnatal onset growth retardation, scaphocephaly or trigonocephaly, prominent metopic ridge, hypertelorism, up-slanted or down-slanted palpebral fissures, strabismus, broad nasal base, short nose with anteverted nares, hypoplastic philtrum, narrow vermillion of upper lip, low-set-posteriorly rotated ears with prominent antihelices, moderate micrognathia, clinodactyly, irregular brachydactly, transverse palmar creases, mild mental retardation with delayed speech development. Our patient had some of these findings. These clinical consequences may be depend on the size of the deleted segment. Differently, our patient had also behavioral disturbances. These phenotypic variabilities may be related to inhibition of expression of a number of gene loci located near 11q24.

The majority of fragile sites on chromosome 11 is folate sensitive. Voullaire et al[6] showed that the origin of 11q23.3 deletion was a familial folate-sensitive 11q23.3 fragility carried by the mother. They suggested that the fragile chromosome 11 was transmitted to the embryo and subsequently broke at the site of fragility. Hausmann et al[7] were unable to identify the folate-sensitive fragile site at 11q23.2 in lymphocytes from either parents. The rare fragile sites were induced in lymphocytes by culturing in folic acid free medium[10] . The chromosomal abnormality of our patient was not obtained by culturing in folic acid free medium but it was obtained de novo during routine chromosome preparations, indicating that it is not from folate sensitive group. Some common fragile sites require specific induction by several mechanisms, but some may occur spontaneously [14] . The origin of the 11q24 deletion of our patient is not familial folate-sensitive, but may be originate simply by chromosome breakage spontaneously, as karyotypes of her parents were normal.

Wardinsky et a[15] and Ono et al[9] found obvious mental retardation and abnormal MR and CT scans in the patients with partial 11q deletions. Our patient had mild mental retardation with delayed speech development. However, MR of her was normal.

Although the mechanism responsible for this illness has not been elucidated, the incidence of mental and motor developmental delay is high in 11q terminal deletions. These phenotypic variabilities appear quite suggestive of the diagnosis with a strong indication for chromosome analysis. For this reason, psychiatrists and pediatricians should be aware of the manifestations of the chromosome 11q deletion syndrome. Genetic evaluation should be recommended to these patients with similar manifestations.

REFERENCES

1. Jacobson P, Hauge M, Henningsen K, Habolth N, Mikkelsen M, Philip J. An (11;21) translocation in four generations with chromosome 11 abnormalities in the offspring: a clinical, cytogenetical,and gene marker study. Human Hered 1973;23:568-85
2. Frank J, Riccardi VM. The 11q- syndrome. Hum Genet 1977; 35:241-6
3. Niikawa N, Jinno Y, Tomiyasu T, Fukushima Y,Kudo K.Ring chromosome 11[46,XX,r(11)(p15q25)] associated with clinical features of the 11q-syndrome. Ann Genet 1981; 3:172-5
4. McPherson E, Meissner L. 11q- syndrome: review and report of two cases. Birth Defects 1982;18:295-300.
5. Fryns JP, Kleczkowska A, Buttiens M,Marien P,vanden Berghe H. Distal 11q monosomy. The typical 11q monosomy syndrome is due to deletion of subband 11q24.1 Clin Genet 1986;30:255-60
6. Voullaire LE, Webb GC, Levers MA. Chromosome deletion at 11q23 in an abnormal child from a family with inherited fragility at 11q23.Hum Genet 1987;76:202-4
7. Hausmann C, Back E, Wolff G, Voiculescu I. Deletion 11q23.3 without familial presdisposition (letter).Hum Genet 1988;80:205
8. Meyer DR, Selkin RP. Ophthalmic manifestations of the chromosome 11q deletion syndrome. Am J Ophthalmology 1993;115(5):673-4
9. Ono J, Harada K, Hasegawa T, Sakurai K, Kodaka R, Tanabe Y, Tanaka J, Igarashi T, Nagai T, Okada S. Case report: Central nervous system abnormalities in chromosome deletion at 11q23. Clin Genet 1994; 45:325-9
10. Sutherland GR, Hecht F. Fragile sites on human chromosomes. New York: Oxford Univ.Press,1985.
11. American Psychiatrie Association. Diagnostic and statistical 36 manuel of mental disorders:DSM-IV, 4th ed,Washington DC, American Psychiatrie Press, 1994.
12. Lippe BM, Sparkes RS, Fass B, Neidengard L. Craniosynostosis and syndactyly: expanding the 11q- chromosomal deletion phenotype. J Med Genet 1980;17:480-3
13. Kuster W, Gebauer HJ, Majewski F, Lenard HG. Report of a deletion 11(qter-q23.3) and short review of the literature Eur J Pediatr 1985; 144:286-8
14. Chudley AE, Ray M, Evans JA, Cheang M. Possible association of rare autosomal folate sensitive fragile sites and idiopathic mental retardation: a blind controlled population study. Clinical Genetics 1990; 38:241-56.
15. Wardinsky TD, Weinberger E, Pagon RA, Clarren SK, Thuline HC. Partial deletion of the long arm of chromosome 11(del(11)(q23.3-qter)) with abnormal white matter. Am J Med Genet 1990; 35:60-3.