

LOW IgA ASSOCIATED WITH SHORT ARM DELETION OF CHROMOSOME 18

İbrahim Keser, Ph.D.* / Güven Lüleçi, Ph.D* / Özlem Akça, M.D.**

* Department of Medical Genetics, School of Medicine, Akdeniz University, Antalya, Turkey.

** Department of Pediatrics, School of Medicine, Akdeniz University, Antalya, Turkey.

ABSTRACT

A one-year-old boy with the short arm deletion of chromosome 18 is reported. The case has IgA deficiency and facial dysmorphism. Chromosome analysis showed that his father had 32% premature centromere division (PCD). The deletion of short arm of chromosome 18 in our case may have occurred because of PCD in the father. Our case might be an important example for concurrent appearance of these chromosomal abnormalities.

Key Words: Chromosome 18, Chromosome 18p deletion, IgA deficiency, Premature centromere division

INTRODUCTION

Deletion of the short arm of chromosome 18 (18p-) was first reported in men (1). However, sex ratio is in favour of females. Pregnancy is of normal duration (2). Over one hundred patients with 18p- have been reported till now. The clinical findings of these patients are variable, but most of them have common features of the syndrome. The frequently noted findings are low birth weight, short stature, mental retardation, wide mouth, ptosis, dental anomalies, round face, broad detached ears and autoimmune disorders (2). Long-term survival is not expected. Mortality can occur in the first days of life, but a 61 years old case has been reported (3). In these patients fertility is possible, mental retardation is variable. We report here deficiency of IgA and the short arm deletion of chromosome 18 in a boy whose father has premature centromere division (PCD).

CASE REPORT

A one-year-old boy was referred to our department for chromosome analysis because of dysmorphic facial features, malabsorption and IgA deficiency. Following a complicated pregnancy of 40 weeks under the threat of spontaneous abortion he was born through vaginal delivery. Mother was 29 years old and father was 27 at birth. Mother had a spontaneous abortion in the first trimester of her first pregnancy. Birth was normal with a high Apgar score. Patient's birth weight was 2300 g, height 47 cm, and head circumference 33 cm. He could not sit and crawl until he was one-year-old. The first tooth erupted at 10 months. At one year of age his height was 64 cm, weight 5.5 kg and head circumference 42.5 cm, all below 3rd percentile. The dysmorphic facial appearance associated with physical retardation was apparent. Clinical findings were featured as prominent forehead, low set ears, inverted mouth, micrognathia, hypertelorism, big tongue, and short neck. Also, he had low posterior hairline and widely set nipples (Fig.1).

Blood and urine analysis were within normal ranges. Creatinine, calcium, phosphate and sodium were also within normal levels.

Liver, kidneys, spleen and gall bladder were reported to be normal at ultrasonographic examination. Craniography has confirmed micrognathia, and ECG results were normal.

Immunoglobulin levels as measured by nephelometric technique were as follows; IgA 4.67 g/dl (69-392), IgM 150 g/dl (61-277), IgG 943 g/dl (723-1625). Immunological test results indicated deficiency of



Fig. 1.: The patient aged one year.



Fig. 2.: Partial karyotype of proband showing deletion of the short arm of chromosome 18;18p(11.1--pter).

serum IgA. His father had normal immunoglobulin levels.

Chromosome preparations were made from peripheral blood lymphocytes using standard culture techniques. Using the high resolution banding of the karyotype of case has been determined as 46,XY,del (18p)(p11.1--pter) (Fig.2). When cytogenetic analysis were done in his parents, mother was normal, father had the PCD in 32%. The rate of PCD has not changed in different medium, time, with/without colcemid treatment in culturing lymphocytes.

DISCUSSION

IgA deficiency has been reported in the short arm deletions and ring form of chromosome 18 (4). One of the most common primary immunodeficiencies is IgA deficiency where IgA levels are lower than 5 g/dl in general (adult normal value: 90-450 g/dl). All 18p-cases do not have IgA deficiency. In 16 out of 27 patients IgA were absent or markedly decreased (5). In the saliva and blood of patients with 18p- abnormality IgA levels were decreased, 11% and 50%, respectively indicating that chromosome 18 is responsible for IgA secretion (6).

However, chromosomes 6 and 14 may also be involved in IgA synthesis (5). In addition, IgA deficiency has also been found in other chromosomal abnormalities, such as i(Xq), a variant of Turner syndrome, and Klinefelter syndrome (7,8). Immunodeficiencies are also seen in ICF (immunodeficiency, centromeric heterochromatin instability, facial anomalies) syndrome (9). In four cases of growth hormone deficiency and 18p-syndrome, two had also IgA deficiency. Although, we could not observe it in our case, 18p- has been associated with midline (10-13). It is suggested that PCD has been involved with subfertility, aneuploidy (non-dysjunction), spontaneous abortions and in some cases malignancy (14-16).

The level of growth hormone could not be determined, because the family refused this investigation. The deletion of short arm of chromosome 18 in our case may have occurred because of PCD in the father. Our case might be an important example of both deletion occurrence of 18p and clinical features.

REFERENCES

1. de Grouchy J, Iamy M, Thieffry S, Arthuis M, Salmon C. *Dysmorphie complexe avec oligophrenie: deletion du bras court d'un chromosome 18. CR Acad Sci (Paris) 1963;256:1028-1029.*
2. Emery AEH. *Principles and practice of medical genetics. Second Edition. Edinburgh: Longman Group UK Ltd 1990:265-266.*
3. Schinzel A. *Catalogue of unbalanced chromosome aberrations in man. New York: Berlin de Gruyter, 1984:300-304.*
4. Lewkonja RM, Lin CC, Haslam RHA. *Selective IgA deficiency with 18q+ and 18q- karyotypic anomalies. J Med Genet 1980;17:436-453.*
5. Lakhanpal S, O'Duffy JD, Homburger HA, Moore SB. *Evidence for linkage of IgA deficiency with the major histocompatibility complex. Mayo Clin Proc 1988;63:461-465.*

6. de Grouchy J, Turleau C. Atlas des maladies chromosomiques. Paris: Expansion Scientifique Française 1982;310-315.
7. Choudat D, Taillemite JL, Hirsch-Marie H, Choubrac P, Lebas FX. Relation entre isochromosome Xq et deficit serique en immunoglobine A. *Nouvelle Presse Med* 1979;8:2419-2426.
8. Silver HKB, Shuster J, Gold P, Hawkins D, Freedman SO. Endocrinopathy and IgA deficiency. *Clin Immunol Immunopathol* 1973;1:212-214.
9. Tiepolo L, Marashio P, Gimeli G, Cuoco C, Gargani GF, Romano C. Multibranched chromosomes 1,9 and 16 in a patient with combined IgA deficiency. *Hum Genet* 1979;51:127-139.
10. Leisti J, Leisti S, Perheentupa J, Savilahti E, Aula P. Absence of IgA and growth hormone deficiency associated with with a short arm deletion of chromosome 18. *Arch Dis Child* 1973;48:320-322.
11. Gül D, Saylı BS, Gök F, Gökçay E. IgA deficiency associated with growth hormone deficiency in a boy with shortarm deletion of chromosome 18(46,XY,18p-). *Ann Genet* 1994;37:82-85.
12. Kane HA, Borgaonkar D, McDermott M, Septimus S, Movahhedian H. 18p monosomy syndrome. *Pediatr Cadiol* 1991;12:133-146.
13. Taine L, Goizet C, Wen ZQ, Chateil JF, Battin J, Saura R, Lacombe D. 18p monosomy with midline defect and a de novo satellite identified by FISH. *Ann Genet* 1997;40:153-163.
14. Bajnoczky K, Mehes K. Parental centromere separation sequence and aneuploidy in the offspring. *Hum Genet* 1988;78:286-288.
15. Gaborrón J, Jimenez A, Glover G. Premature centromere division dominant inherited in a subfertile family. *Cytogenet Cell Genet* 1986;43:69-71.
16. Keser İ, Lüleci G, Gündüz G. Premature centromere division in three unrelated families. *Ann Genet* 1996;39:87-90.