Case reports

Partial monosomy 8p with minimal dysmorphic signs

E Blennow, K Bröndum-Nielsen

Abstract

A female patient with a $46,XX,del(8)(p23 \rightarrow pter)$ karyotype is presented. She was mentally retarded and showed a few dysmorphic features. Her red cell glutathione reductase level was within normal limits. This terminal deletion, on the short arm of chromosome 8, appears to be the smallest segment hitherto reported.

Since 1973 11 children have been reported with a partial deletion of 8p. Further cases have had various unbalanced translocations with partial trisomies in addition to monosomy 8p. Some of the features commonly described are mental retardation, growth retardation, a high, narrow forehead, epicanthic folds, short neck, wide set nipples, congenital heart defects, and, in males, genital abnormalities. In one case the level of glutathione reductase was reduced. This locus has a confirmed assignment to p21.1.¹

We describe a case whose appearance is not obviously dysmorphic and whose main features are mental retardation and behavioural problems.

Case report

The female proband was born in 1972 and was the first child of a 28 year old woman and a 30 year old man. Pregnancy and delivery were uneventful. Birth weight was 3430 g and length 50.5 cm. At birth physical examination showed convergent strabismus. She was otherwise considered normal although, according to the mother, she suffered from episodes of shakiness.

She did not walk until 20 months of age. As she grew older the mother found that she was slow in

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Received for publication 31 October 1989. Accepted for publication 6 November 1989. development. Examination at 3 years 9 months showed an overall delay in psychomotor development, but social skills were most delayed (about two years). She was indiscriminate in her contact, could not concentrate, and was easily distracted. At the age of 7 the proband was admitted to a special school. Puberty was normal with menarche at 13 years. Mental retardation was within the moderate range, but according to her parents her memory was remarkable and she speaks two languages (her parents originate from Germany). She was hyperactive.

On physical examination at the age of 16, her appearance was not obviously dysmorphic although her facial features were somewhat coarse with a prominent nose (fig 1). The palpebral fissures had an antimongoloid slant and slight hypotelorism was present. A convergent strabismus was noted. The forehead was narrow and the chin slightly receding. The ears were normal. Her hands were small and slender. The height was 163 cm, weight 61 kg, and head circumference 55 cm. Her body proportions

Figure 1 The proband at 14 years.



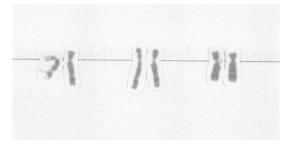


Figure 2 GTG banded chromosomes 8 from three cells with the deleted homologue on the right. The breakpoint is in band 8p23.

were normal and auscultation of the heart and lungs was normal. Her intermamillary distance was normal. EEG showed a diffuse abnormality of moderate degree, but she never had seizures. A CT scan of the brain was normal.

CYTOGENETIC STUDIES

Chromosome analysis was performed on QFQ banded metaphases from peripheral blood lymphocyte cultures when the proband was 13 years old. A terminal deletion of part of the short arm of one chromosome 8 was found in all cells analysed. GTG banding of prometaphases from methotrexate synchronised lymphocyte cultures showed the breakpoint of the deletion to be at 8p23 (fig 2). The karyotypes of the parents were normal.

LABORATORY FINDINGS

Enzyme studies have shown that the red cell level of glutathione reductase was 1.7 mmol/l (normal range 1.5 to 2.4 mmol/l). Serum triglycerides were 1.0 mmol/l (normal range 0.6 to 2.2 mmol/l). The gene for glutathione reductase has been assigned to 8p21.1, and the gene for lipoproteinlipase has a provisional assignment to $8p22.^2$ The normal levels of glutathione reductase and triglycerides indicate that these genes are localised proximally to the deletion.

Discussion

Eleven cases of monosomy 8p have been described since 1973 (table). In addition, a number of unbalanced translocations involving chromosome 8, resulting in both monosomy 8p and partial trisomies, have been published. The first one was by Lubs and Lubs.³

The majority of reported pure deletions have had breakpoints at 8p21-22. In two cases the deletion was interstitial. In only one patient was the cytogenetic diagnosis made in the newborn period, indicating the

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	Taillemite			Breson	Reiohle	Rodewald	Reise	Patil and	Bröcker-V	Bröcker-Vriends et al	Ostergaard	Precent	Total
	et al ³	Craen ⁴	Aula ⁵	et al	et al	et al ⁸	et al	Hanson ¹⁰	I	2	Tommerup ¹²		(12 cases)
Deletion	8p-	(pter→p23: (n21_otter)	$(:p21 \rightarrow qter) (:p22 \rightarrow qter) (pter \rightarrow p21: (:p21 \rightarrow qter) (:p22 \rightarrow qter) (:p21 \rightarrow qter) (:p22 \rightarrow qter) ($:p22→qter) (pter→p21: n11→nter)	(:p21→qter)	(:p22→qter)	(:p2l→qter)	4	$(:p21 \rightarrow qter) (:p21 \cdot 3 \rightarrow qter)$	(:p21·3→	(:p23→qter)	
Sex	W	W	F	. I	E.	W	W	F	н		M W	ц	6F/6M
Age at diagnosis	13y	4mth	3mth 7	7mth 1		6y 10mth	lmth	2y	3y			13y	
Birth weight (g)	2200	3700	2700 2	2770	0062	1900	2500	2250	2600	1930		3430	
Birth length (cm) Postnatal growth		4		4	\$	45	4:5		47			50·5	
retardation		+	+	,	+	+	+	+	+	۸.	+		8/12
Psychomotor													
retardation	+	+	+	+	+	+	+	+	+	+	+	+	12/12
Microcephaly			+	, +	+	+	+	+	+	+	+		9/12
Narrow forehead		+	+				+		+			۸.	4/12
High forehead		+			+	+			+		+		5/12
Epicanthic folds	+	+	+	+			+	+					6/12
Ear anomaly		+	+	, +	+		+	+	+	+	+		9/12
Retrognathia		+					+	+		+		+	5/12
Short neck		+	+		·	+					+		4/12
Wide set nipples	+	+	+	+		+			+		+		7/12
CHD	+		+			+	+		+	+	+		7/12
Genital abnormalities	+		r	+		+					+		4/6M

Clinical findings in patients with monosomy 8p.

paucity of aberrant phenotypic features. Except for two boys described by Taillemite $et al^3$ and Bresson etal,⁶ all these children have shown markedly retarded postnatal growth, and they have all, with one exception,⁴ been small for dates at birth. The clinical picture has varied, but most of them have only had minor dysmorphic features, including epicanthic folds, ear anomalies, and wide set nipples. Other features are short neck, retrognathia, and a narrow, high forehead. Congenital heart defects are common and so are genital abnormalities in the males. All these signs are rather unspecific and the main feature is psychomotor retardation. However, some authors consider these features to constitute a recognisable syndrome.4 8-12

Our case was neither small for dates nor did she show growth retardation. She had very few dysmorphic signs but behavioural problems were present, as reported in the case of Rodewald et al.⁸ The breakpoint of the deletion was more distal than in any of the previously reported cases, and the red cell level of glutathione reductase was normal in our patient, which also indicates that the deletion was terminal rather than interstitial.

The clinical picture of 8p- syndrome seems to show distinct features. The combination of retarded somatic growth, mental retardation, and minor physical abnormalities, including slightly dysmorphic facial features, may suggest a chromosomal aberration, and high resolution banding is indicated in such cases.

- 1 Bootsma D, Ruddle FH. Report of the committee on the genetic constitution of chromosomes 2, 3, 4, 5, 7, 8, 10, 11 and 12 (HGM9). Cytogenet Cell Genet 1978;22:74–91.
- 2 Sparkes RS, Schotz MC, Mohandas T, et al. Human lipase assignments hepatic lipase to 15q21-q23 and lipoprotein lipase to 8p22. HGM9. Cytogenet Cell Genet 1987;46:697
- 3 Taillemite JL, Channarond J, Tinel H, Mulliez N, Roux C. Délétion partielle du bras court du chromosome 8. Ann Genet (Paris) 1975;18:251-5.
- 4 Orye E, Craen M. A new chromosome deletion syndrome. Report of a patient with a 46,XY,8p- chromosome constitution. Clin Genet 1976;9:289-301.
- 5 Leist J, Aula P. A case of deletion of short arm of chromosome 8. Birth Defects 1977;13 (3B):187-94.
- Bresson JL, Noir A, Scherrer M. Délétion partielle du bras court du chromosome 8. Ann Genet (Paris) 1977;20:70-2.
 Beighle C, Karp LE, Hanson JW, Hall JG, Hoehn H. Small
- structural changes of chromosome 8. Hum Genet 1977;38: 113-21
- 8 Rodewald A, Stengel-Rutkowski S, Schultz P, Cleve H. New chromosomal malformation syndromes. I. Partial monosomy 8p. An attempt to establish a new chromosome deletion syndrome. Eur J Pediatr 1977;125:45-57.
- 9 Reiss JA, Brenes PM, Chamberlin J, Magenis RE, Lovrien EW. The 8p- syndrome. Hum Genet 1979;47:135-40.
 10 Patil SR, Hanson JW. Partial 8p- syndrome. J Genet Hum
- 1980;28:123-9.
- Bröcker-Vriends AHJT, Mooij PD, Van Bel F, Beverstock GC, Van de Kamp JJP. Monosomy 8p: an easily overlooked syndrome. *J Med Genet* 1986;23:153-4.
 Ostergaard GZ, Tommerup N. The 8p- syndrome. Ann Genet
- (Paris) 1989;32:87-91.
- 13 Lubs HA, Lubs ML. New cytogenetic techniques applied to a series of children with mental retardation. Nobel Symposia 1973;23:240-50.