7qter DELETION WITH NORMAL HAGEMAN FACTOR

Hiroko KAWASHIMA and Noboru TANIGUCHI

*Department of Pediatrics, School of Medicine, Kanazawa University,
Kanazawa 920, Japan*

Summary A 10-month-old boy with a 46,XY,del(7)(pter → q32:) karyotype is presented. Many of the clinical features of the patient are common with 11 previously reported cases except for the presence of congenital cardiac anomaly. There have been conflicting views as to the assignment of Hageman-factor locus to band 7q35. In the present case, the factor showed normal activity.

INTRODUCTION

In 1973 Shokeir *et al.* described the first case with terminal deletion (q32 → qter) of the long arm of chromosome 7. Thereafter, 11 cases with similar chromosomal abnormalities were reported (de Grouchy *et al.*, 1968; de Grouchy and Turleau, 1974; Harris *et al.*, 1977a; Harris *et al.*, 1977b; Kousseff *et al.*, 1977; Biederman and Bowen, 1978; Friedrich *et al.*, 1979; Bernstein *et al.*, 1980).

In the present paper, a boy with del(7)(pter → q32:) is presented. The karyotype and clinical features of this patient are compared with those of previously reported cases. Results of Hageman-factor assay were also described.

CASE REPORT

The patient, boy was the second child of healthy nonconsanguineous parents. The maternal age was 27 years and paternal age 33 at the time of the child's birth. There was no family history of congenital malformation and mental retardation. His birth weight was 1,390 g and product of 34 week uncomplicated gestation. He received an exchange transfusion at 7th day of his life and was placed in an incubator for 3 months. He was fed by tube. He was referred to the University Hospital at 10 months of age because of heart murmur and failure to thrive. On admission his height (62.6 cm), weight (5,060 g) and head circumference (38.7 cm) were all significantly below the 3rd percentile. Physical examination revealed a small and hypotonic infant without head control. Physical abnormalities included microcephaly, frontal bossing, strabismus, prominent nose with bulbous tip, malformed ears, micrognathia, high arched palate, widely spaced nipples, heart murmur, sacral

Received December 1, 1980

Fig. 1. Patient at 10 months of age.

Fig. 2. Karyotype of the patient. Arrow indicates chromosome 7 with terminal deletion.

dimple, bilateral cryptorchidism and hypospadia with small penis (Fig. 1).

Routine laboratory data were within normal ranges. Cardiac catheterization revealed patent ductus arteriosus with pulmonary hypertension. He was operated at 10 months of age. Since then, he became much active and there was some weight gain. He was still floppy without head control at the age of 13 months.

CYTOGENETIC STUDY

G-band analysis of chromosome on cultured lymphocytes revealed a probable terminal deletion of the long arm of a chromosome 7. The karyotype was interpreted as 46,XY,del(7)(pter → q32:) (Fig. 2). The parents had normal karyotypes with no evidence of translocation, insertion nor any other structural rearrangements.

GENE MARKER STUDIES

The activity of Hageman-factor was assayed by the method described by Biggs (1976), normal value being 50–200%. The activity of Hageman-factor was 170% in the patient, 145% and 76% in his mother and father, respectively. They were all within the normal range.

DISCUSSION

A total of 15 cases of distal 7q monosomy have so far been described. It is noteworthy that in 12 of them, points of breakages were located at band 7q32. Ten cases, including the present case, had a seemingly identical karyotype, del(7)(pter → q32:) (Harris *et al.*, 1977a; Harris *et al.*, 1977b; Koussef *et al.*, 1977; Biederman and Bowen, 1978; Friedrich *et al.*, 1979; Bernstein *et al.*, 1980). In two cases, deletion was associated with reciprocal translocation, *i.e.*, t(6;7)(p12;q32) and t(6;7)(q25;q32), respectively (de Grouchy *et al.*, 1968; Bernstein *et al.*, 1980). In 11 of these cases, karyotype of the parents was examined and revealed a normal complement in 10 cases and t(6;7)(p25;q32) in the mother of Bernstein *et al.*'s case. In a case of Shokeir *et al.* (1973), parents were not examined.

Phenotypic features of these 12 cases were summarized in the Table 1. The present case appears to share most of the features with the other. Cardiac anomalies, however, was not observed in any other cases.

In the fifth issue of Human Gene Mapping (Evans *et al.*, 1979) several genes were assigned to chromosome 7. Hageman-factor locus was included in them, however, it was ranked as inconsistent, *i.e.*, conflicting results had been published. In 1974, de Grouchy and Turleau (1974) tentatively assigned it to 7q, presumably 7q35. On the other hand, in three cases of del(7)(q32), normal Hageman factor was observed (Biederman and Bowen, 1978; Bernstein *et al.*, 1980). In two cases it was decreased (de Grouchy and Turleau, 1974; Friedrich *et al.*, 1979), however, in one of them, both 7q— propositus and the phenotypically normal father showed

Table 1. Clinical features of distal 7q deletion.

	Shokeir <i>et al.</i> (1973)	de Grouchy <i>et al.</i> (1974)	Harris <i>et al.</i> (1977)			
			case 1	case 2	case 3	case 4
Sex	F ^a	M ^b	F	M	F	M
Mental retardation	+	+	+	+	+	+
Growth retardation	+	+	+	+	+	+
Microcephaly	?	?	?	?	+	—
Prominent forehead	?	+	+	+	—	?
Hypertelorism	+	?	?	?	?	—
Eye anomalies	+	+	+	+	?	?
Ear anomalies	?	+	+	+	+	+
Bulbous nasal tip	?	+	+	+	+	?
Abnormal nasal bridge	—	+	?	+	?	+
Large mouth	?	?	?	+	+	?
Cleft lip, palate	—	?	?	?	+	+
Micrognathia	—	—	?	?	+	?
Cardiac anomalies	—	?	?	?	?	—
Inguinal hernia	?	+	?	?	+	+
Genital anomalies	—	—	+	+	+	?
Distal limb anomalies	+	?	+	+	+	+
Hageman factor	?	↓ ^c	?	?	?	?
Karyotype	t(2;7)→ del(7)	t(6;7) (p12;q32)	del(7) (q32)	del(7) (q32)	del(7) (q32)	del(7) (q32)

	Kousseff <i>et al.</i> (1977)	Biederman & Bowen (1978)	Friedrich <i>et al.</i> (1979)	Bernstein <i>et al.</i> (1980)		Present case (1980)
				case 1	case 2	
Sex	M	F	F	M	F	M
Mental retardation	?	+	+	+	+	+
Growth retardation	?	+	+	+	+	+
Microcephaly	+	+	+	+	+	+
Prominent forehead	?	?	?	+	+	+
Hypertelorism	?	—	?	+	+	—
Eye anomalies	?	+	+	?	?	+
Ear anomalies	?	+	+	+	+	+
Bulbous nasal tip	?	+	?	?	+	+
Abnormal nasal bridge	?	+	?	+	+	—
Large mouth	?	?	?	?	+	+
Cleft lip, palate	?	—	?	+	?	—
Micrognathia	?	?	?	+	?	+
Cardiac anomalies	?	—	?	?	?	+
Inguinal hernia	?	?	?	?	?	—
Genital anomalies	+	+	?	+	?	+
Distal limb anomalies	+	+	+	+	+	+
Hageman factor	?	→ ^d	↓	→	→	→
Karyotype	del(7) (q32)	del(7) (q32)	del(7) (q32)	t(6;7) (p25;q32)	del(7) (q32)	del(7) (q32)

^a Female, ^b male, ^c decreased, ^d normal.

a very low activity of Hageman factor (Friedrich *et al.*, 1979). It was postulated that this particular case presented familial deficiency of the factor. In additional two cases, normal level was observed. In both of them the breakages were at band 7q35 (Francke, 1978; Turleau *et al.*, 1979). It is possible that a part of this band, proximal to the break point, escaped deletion.

In the present case, the point of breakage was at band 7q32 and Hageman factor was within the normal limits in agreement with the concept that the factor was not located on 7q35 (Francke, 1978).

Acknowledgements The authors wish to express their thanks to Mr. H. Takai for performing the Hageman factor assay.

REFERENCES

- Bernstein, R., Dawson, B., Morcom, G., Wagner, J., and Jenkinson, T. 1980. Two unrelated children with distal long arm deletion of chromosome 7: clinical features, cytogenetic and gene marker studies. *Clin. Genet.* **17**: 228-238.
- Biederman, B., and Bowen, P. 1978. Balanced t(8;9)(q12;p33)pat carrier with phenotypic abnormalities attributable to a *de novo* terminal deletion of the long arm of chromosome 7. *Hum. Genet.* **41**: 101-107.
- Biggs, R. 1976. Human Blood Coagulation, Hemostasis and Thrombosis, 2nd Ed., Blackwell Scientific Corp.
- De Grouchy, J., Veslot, J., Bonette, J., and Roidot, M. 1968. A case of ?6p— chromosomal aberration. *Am. J. Dis. Child.* **115**: 93-99.
- De Grouchy, J., and Turleau, C. 1974. Tentative localization of a Hageman (factor XII) locus on 7q, probably the 7q35 band. *Humangenetik* **24**: 197-200.
- Evans, H.J., Hamerton, J.L., Klinger H.P., and MuKusik V.A. 1979. Human Gene Mapping 5. *Cytogenet. Cell Genet.* **25**: no 1-4.
- Fancke, U. 1978. Hageman (Factor XII) Locus on 7q? *Hum. Genet.* **45**: 363-367.
- Friedrich, U., Osterballe, O., Stenbjerg, S., and Jorgenson, J. 1979. A girl with karyotype 46,XX, del(7)(pter→q32:). *Hum. Genet.* **51**: 231-235.
- Harris, E.L., Wappner, R.S., and Palmer, C.G. 1977a. 7q deletion syndrome? New syndrome (The National Foundation—March of Dimes, Birth Defects; Original Article Series, Volume XIII number 3B), Alan R. Liss Inc., New York. p. 244.
- Harris, E.L., Wappner, R.S., Palmer, C.G., Hall, B., Dinno, N., Seadhore, M.R., and Breg, W.R. 1977b. 7q deletion syndrome (7q32→qter). *Clin. Genet.* **12**: 233-238.
- Kousseff, B.G., Hus, L.Y., Pacious, S., and Hirshhorn, K. 1977. A partial long arm deletion of chromosome 7: 46,XY,del(7)(q32). *J. Med. Genet.* **14**: 144-147.
- Shokeir, M.H.K., Ying, K.L.L., and Pabello, P. 1973. Deletion of the long arm of chromosome no. 7: tentative assignment of the Kidd(JK) locus. *Clin. Genet.* **4**: 360-368.
- Turleau, C., de Grouchy, J., Perignon, F., and Lenoir, G. 1979. Monosomie 7qter. *Ann. de Genet.* **22**: 242-244.