65. A Case of a Female Infant with Terminal Deletion of the Long Arm of No. 4 Chromosome

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Up to date, the deletions of the long arm of no. 4 chromosome were reported on 23 cases by the several authors (Ockey *et al.* 1967; Golbus *et al.* 1973; Ferrier and Freund 1974; v. Kempen 1975; Back *et al.* 1977; Serville and Broustet 1977; Frias *et al.* 1978; Rethoré *et al.* 1979; Townes *et al.* 1979; Davis *et al.* 1981; Fryns *et al.* 1981; Mitchell *et al.* 1981; Yu *et al.* 1981; Lech *et al.* 1982; Lipson *et al.* 1982; Stamberg *et al.* 1982). Of these, 5 cases had the interstitial deletions of 4q, and 18 cases had the terminal deletions of 4q. In this paper, we reported on an additional female infant with the terminal deletion at 4q31.

Case report. The propositus was a female infant of 15 days after delivery, and she was born as the first child between a 25-year-old mother and 34-year-old father. There was no history of abortion, still birth, congenital malformations, consanguinity, and the atomic bomb exposure in this couple. The clinical examination revealed her both parents were phenotypically normal showing no evidence for the mental deficiency.

The birth weight of the propositus was 2900 g at 38 weeks of the gestation. Her remarkable clinical findings were short neck, hypertelorism, epicanthus, low set ears, low nasal bridge, saddle nose, cleft lip and cleft palate, hypoplastic mandible, low voice, wide spaced nipples, clinodactyly of the 4th and 5th fingers of her right hand, peculiar overlapping at her right hand, poorly developed flexion creases in the 5th finger of her right hand, low set in the 5th fingers, deep D-lines of both palms, flat feet, abnormal positions of toes, hypotonia, sinking breathing due to the upper airway stenosis (Figs. 1, 2).

Cytological findings. Chromosome slides for this study were prepared from the leucocyte cultures established from the propositus and her parents. The G-banding differential staining was applied for the chromosome identification. The chromosome numbers were determined with 124 well-delineated metaphases. Karyotypes were analysed in 12 cells each following the conventional Giemsa and the G-banding procedures.

The karyotype of the propositus based on the conventional Giemsa specimen showed 46 chromosomes including a no. 4 chromosome having an unusually shortened long arm. By the analysis of G-banding methods, it was revealed that an unusual element corresponded to the segment q31→qter of no. 4 chromosome. Then the chromosome formula of the propositus was given as 46,XX,del(4)(q31) (Fig. 3). Both parents of the propositus were chromosomally normal with no slight evidence for the aberration, based on 12 cells karyotyped in each case.

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Fig. 1

Fig. 2

Figs. 1-2. 1: Clinical features of the propositus. 2: X-ray finding of the propositus' hands.

Fig. 3. G-banding karyotype of the propositus (46,XX,del(4)(q31)).

Remarks and conclusion. The first initial case of del(4q) was reported by Ockey *et al.* (1967). Thereafter additional cases for the deletion of the long arm of no. 4 chromosome using the G-bands were reported by several authors (Golbus *et al.* 1973; Ferrier and Freund 1974; v. Kempen 1975; Back *et al.* 1977; Serville and Broustet 1977; Frias *et al.* 1978; Rethoré *et al.* 1979; Townes *et al.* 1979; Davis *et al.* 1981; Fryns *et al.* 1981; Mitchell *et al.* 1981; Yu *et al.* 1981; Lech *et al.* 1982; Lipson *et al.* 1982; Stamberg *et al.* 1982).

The deleted portions of the long arm of no. 4 chromosome were divided into two groups which were the interstitial deletion and the terminal deletion

Table I. The case of deletion of the long arm of no. 4 chromosome

Part of deletion	No. of cases	Authors
Interstitial deletion:		
q12→q21	1	Lech <i>et al.</i> (1982)
q21→q25	1	Mitchell <i>et al.</i> (1981)
q21→q26	1	Mitchell <i>et al.</i> (1981)
q24→q32	1	Serville & Broustet (1977)
q27→q31	1	Mitchell <i>et al.</i> (1981)
Terminal deletion:		
q3 or q31→qter	15	Ockey <i>et al.</i> (1967), Golbus <i>et al.</i> (1973), Ferrier <i>et al.</i> (1974), v. Kempen (1975), Back <i>et al.</i> (1977), Frias (1978), Townes <i>et al.</i> (1979), Yu <i>et al.</i> (1981), Davis <i>et al.</i> (1981), Mitchell <i>et al.</i> (1981), Lipton <i>et al.</i> (1982), Present case
q32→qter	2	Rethoré <i>et al.</i> (1979), Fryns <i>et al.</i> (1981)
q33→qter	2	Mitchell <i>et al.</i> (1981), Stamberg <i>et al.</i> (1982)

(Table I). On the interstitial deletion, it was reported on 5 cases: One case with the deleted segment of q12→q21 (Lech *et al.* 1982), one case of q21→q25 (Mitchell *et al.* 1981), one case of q21→q26 (Mitchell *et al.* 1981), one case of q24→q32 (Serville and Broustet, 1977), and one case of q27→q31 (Mitchell *et al.* 1981). On the terminal deletion, it was reported on 19 cases: 15 cases with the deleted segment of q3→qter or q31→qter (Ockey *et al.* 1967; Golbus *et al.* 1973; Ferrier *et al.* 1974; v. Kempen 1975; Back *et al.* 1977; Frias *et al.* 1978; Townes *et al.* 1979; Yu *et al.* 1981; Davis *et al.* 1981; Mitchell *et al.* 1981; Lipson *et al.* 1982; the present case), two cases of q32→qter (Rethoré *et al.* 1979; Fryns *et al.* 1981), and two cases of q33→qter (Mitchell *et al.* 1981; Stamberg *et al.* 1982).

The deleted segment of 4q3→qter and the manifestations of all those reported cases are summarized in Table II. Male cases were seven of them and female cases were twelve. All the patients were born at full term or near full term with the normal birth weight except for one case by Townes *et al.* (1979) in which the deletion resulted from a paternal translocation.

According to Table II, the characteristic features of 4q-syndrome were retrognathia or micrognathia (89%), cleft lip and/or cleft palate (79%), flat nasal bridge (79%), short nose (74%), low set and/or malformed ears (74%), displacement of toes (68%), clinodactyly of fingers and/or toes (58%), hypertelorism (58%), epicanthus (53%), cardiac anomalies (53%) and the growth retardation (53%). In parental karyotypes, 17 cases out of 19 cases with the terminal deletion were normal. One case reported by Townes *et al.* (1979) had the abnormal karyotype and resulted from a paternal translocation between no. 4 and no. 20 chromosomes. And on one case reported by Fryns *et al.* (1981), the chromosomal examination of her parents was not cooperated.

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Table II. Manifestations of the deletion of the long arm of no. 4 chromosome

Symptoms and findings	Ockey <i>et al.</i> (1967)	Golbus <i>et al.</i> (1973)	Ferrier & Freund (1974)	v. Kempen (1975)	Back <i>et al.</i> (1977)	Frias <i>et al.</i> (1978)	Townes <i>et al.</i> (1979)	Yu <i>et al.</i> (1981)	Davis <i>et al.</i> (1981)		
Deletion	4q	4q3	4q3	4q31	4q31	4q31	4q31	4q31	4q31		
Sex	M	F	F	M	F	M	M	M	F		
Gestation (weeks)	40	40	40	36	40	38	30	37	40		
Birth weight (g)	3600	3390	3120	2430	2900	2600	1295	2400	3530		
Age at death	3.5 m.		4 m.	(6 y.)	(5 y.)	6 m.	1 hr.	17 d.	(19 m.)		
Growth retardation			+	+	—	+		+	+		
Mental retardation		±	±	+	+	+			+		
Abnormal/asymmetric head			+	+	+	+	+	+			
Microcephaly			—	+	+				—		
Short neck								+			
Upward slanted palpebral fissure	+		+	—	—	+		+	+		
Hypertelorism	+			+	+		+	+	+		
Epicanthus			+	+	+	+		+			
Low set and/or malformed ears	+		+	—	—	+	+	+	+		
Soaring ears		+		+	—	+	+	—			
Flat nasal bridge	+		+	+	+	+		+	+		
Short nose	+	+	+	—	—	+	+	+	+		
Cleft lip and/or cleft palate		+	+	+	+	+	+	+	+		
Retro-/Micrognathia		+	+	+	—	+	+	+	+		
Facial bone hypoplasia		+	+	+		+	+				
Poorly developed flexion creases in the 5th fingers		+	+	+	—	+	+	—	+		
Simian creases			+	+	+	+	+	+	—		
Clinodactyly (fingers, toes)			+	+		+	+	—	+		
Syndactyly (fingers, toes)	+			+	+	+					
Displacement of toes	+	+	+	—	—		+		+		
Cardiac anomalies	+	+	+	+	—			+	+		
Renal anomalies	+	+	+	—				—	—		
Parental karyotype	Normal	Normal	Normal	Normal	Normal	Normal	t(4;20)pat	Normal	Normal		
Symptoms and findings	Mitchell <i>et al.</i> (1981)				Lipson <i>et al.</i> (1982)	Present case (1986)	Rethoré <i>et al.</i> (1979)	Fryns <i>et al.</i> (1981)	Mitchell <i>et al.</i> (1981)	Stamberg <i>et al.</i> (1982)	Total (%)
Deletion	4q31.3	4q31.5	4q31.5	4q31.5	4q31	4q31	4q32.1	4q32	4q33	4q33	
Sex	F	F	F	F	F	F	M	F	F	M	
Gestation (weeks)	36	40	40	39	40	38	37	38	40	32	
Birth weight (g)	2300	3200	2720	2600	3100	2900	2800	2000	3100	2000	
Age at death	1 hr.	(21 m.)	15 m.	23 d.	(9 y.)	(15 d.)	3 m.	(12 y.)	(12 y.)	(11 m.)	
Growth retardation	+	+		+					+	+	10/19 (53)
Mental retardation	+	+		+				+	±		11~8/19 (58~42)
Abnormal/asymmetric head									—	+	7/19 (37)
Microcephaly		+		+					—	+	5/19 (26)
Short neck	+	—	—	+		+	+	—	—		5/19 (26)
Upward slanted palpebral fissure	—	+	—	—					+		7/19 (37)
Hypertelorism	+	+	—	—		+	+		—	+	11/19 (58)
Epicanthus	—	+	+	—		+	+		+	—	10/19 (53)
Low set and/or malformed ears	+	+	+	+	+	+	+	+	—	—	14/19 (74)
Soaring ears					+				—		5/19 (26)
Flat nasal bridge	+	+	+	+	+	+		+	+	+	15/19 (79)
Short nose	+	+	+	+			+	+	+		14/19 (74)
Cleft lip and/or cleft palate	+	+	—	+	+	+	+	+	—	—	15/19 (79)
Retro-/Micrognathia	+	+	+	+	+	+	+	+	+	+	17/19 (89)
Facial bone hypoplasia	—	—	+	+	+				—		8/19 (42)
Poorly developed flexion creases in the 5th fingers						+	+		—	+	9/19 (47)
Simian creases	+	+	+	—		—			—		9/19 (47)
Clinodactyly (fingers, toes)		+	+		+	+	+		—	+	11/19 (58)
Syndactyly (fingers, toes)					—	—			—	+	5/19 (26)
Displacement of toes	+	+	+	+		+	+		+	+	13/19 (68)
Cardiac anomalies	—	+	+	+	—	—	+	—		—	10/19 (53)
Renal anomalies	—	+	—	—					—		4/19 (21)
Parental karyotype	Normal	Normal	Normal	Normal	Normal	Normal	Normal		Normal	Normal	

(): Alive. y., years; m., months; d., days; hr., hours.

References

- Back, E. *et al.* (1977): *Ann. Génét.*, **20**, 294-296.
Davis, J. M. *et al.* (1981): *Amer. J. Med. Genet.*, **9**, 113-117.
Ferrier, S., and Freund, M. (1974): *Arch. Genet.*, **47**, 16-26.
Frias, J. L. *et al.* (1978): *Birth Defects*, XIV, 355-358.
Fryns, J. P. *et al.* (1981): *Ann. Génét.*, **24**, 187-188.
Golbus, M. S. *et al.* (1973): *J. Med. Genet.*, **10**, 83-85.
Lech, H. *et al.* (1982): *Klin. Pädiat.*, **194**, 117-119.
Lipson, A. *et al.* (1982): *J. Med. Genet.*, **19**, 155-157.
Mitchell, L. A. *et al.* (1981): *Amer. J. Med. Genet.*, **8**, 73-89.
Ockey, C. H. *et al.* (1967): *Arch. Dis. Child.*, **42**, 428-434.
Rethoré, M. O. *et al.* (1979): *Ann. Génét.*, **22**, 214-216.
Serville, F., and Broustet, A. (1977): *Hum. Genet.*, **39**, 239-242.
Stamberg, J. *et al.* (1982): *Clin. Genet.*, **21**, 125-129.
Townes, P. L. *et al.* (1979): *Am. J. Dis. Child.*, **133**, 383-385.
van Kempen, C. (1975): *J. Med. Genet.*, **12**, 204-207.
Yu, C. W. *et al.* (1981): *Ann. Génét.*, **24**, 158-161.