The Partial 4q Monosomy

Report of a 5-year-old Boy with Deletion 4q31.3→4qter

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Abstract. A terminal deletion of the long arm of chromosome 4 with a break at 4q31.3 is reported in a 5-year-old boy. The features expressed by the patient and 11 previously published cases, especially the peculiar dysmorphic face with long flat nasal saddle, hypertelorism, upturned nares, micrognathia, clinodactyly, joint contractures and absence of the flexion crease of the 5th finger, cardiac and kidney malformations and mental deficiency, confirm the existence of a recognizable clinical syndrome associated with this partial autosomal monosomy.

Key words: Human chromosome 4 - Terminal deletion - Phenotype

Introduction

The clinical and cytogenetic features of terminal deletion of the long arm of chromosome 4 are little known in contrast to the well defined classic anomalies of chromosome 4 such as the 4p- syndrome (Wolf et al. 1965; Hirschhorn et al. 1965). The first patient with this chromosome abnormality was identified by Ockay et al. (1967) with the prebanding methods of autoradiography and arm-length measurements. Since this time at least a further 11 cases have been extensively reported (for reviews see Reithö 1977; Mitchell et al. 1981). In most cases the terminal segment 4q31→qter was deleted. The characteristic morphological features allow delineation of a new phenotypic entity. The mortality is very high and only a few patients have survived the first months of life.

In this paper we provide further understanding of this chromosomal syndrome with the description of a 5-year-old mentally retarded boy with multiple physical abnormalities.

Case Report

A boy weighing 3900 g and 53 cm in length was born normally to a 20-year-old healthy primiparous mother following an uncomplicated pregnancy. The father was 22-year-old and healthy and there was no history of abortion or of malformations among relatives. Early postnatal progress was uneventful, but subsequently motor and mental development have been severely impaired. He did not sit alone until the age of one year, and only walked at the age of 18 months. At 5½ years he only speaks a few words. There have been no convulsions. He was admitted to hospital at the age of 18 months for surgical removal of an extra digit on the left hand and at 4 years for repair of a cleft soft palate. He has attended a kindergarten for mentally handicapped children for the last year.

Clinical Findings at 5½ years (Fig. 1, 2 and 3): Height 105 cm (10th percentile), weight 17.4 kg (25th percentile), head circumference 51 cm (50th percentile). He was severely mentally retarded. The head was brachycephalic with thick straw-like hair and the neck short. The face was flat with a broad nasal bridge and relatively long philtrum. The eyes had marked epicanthic folds and an antimongoloid slant. Fundal examination showed slightly prominent papillae, particularly on the nasal side. The nasal orifices were upturned, there was microgenia and a repaired cleft palate. The extremities were short and thick. The fifth fingers of both hands were stiff and the flexion creases were missing. There was palmar and planter dyskeratosis and evidence of the surgically removed extra left digit. No gonads were palpable. Cardiological examination suggested a ventricular septal defect; phonocardiography revealed an early to mid systolic high-pitched diamond-shaped murmur at the 3rd and 4th left intercostal spaces. Electrocardiogram showed temporary junctional rhythm with slow sinus action.

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**Fig. 3.** The patient's hands. Note hypoplastic 5th fingers

**Fig. 4.** Dermatoglyphics and palmer flexion creases of the patient

**Fig. 5.** GTG-banded karyotype from patient's cultured lymphocytes. The arrow indicates the 4q deletion

**Fig. 6.** Partial karyotype from 2 different metaphases showing the abnormal chromosome del(4)(q313). The arrow indicates the 4q deletion

**Radiological Examinations:**

- **Chest:** showed a wide pedicle with increased hilar vascular markings.
- **Skull:** showed no intracerebral calcification and the sella was normal.
- **Hand:** Ossification corresponded to the lower normal limit for chronological age.
- **Urography:** There was a double left renal pelvis with duplex ureter, and pyelectasia on the right with a tortuous right ureter.

**Laboratory Findings:**

Blood count, urine-analysis, E.S.R., aminotransferases, alkaline phosphatase, serum cholesterol, excretion of glycosaminoglycans and amino acids in the urine were all normal.

Electroencephalogram: The tracings were pathological with focal signs and disturbed brain activity.

**Dermatoglyphics:**

- Pearlstring at the hypothenar region. Numerous white lines with strong furrowing (Fig. 4)
- Palms: right: 11.11.10.4. t'-L'. o.0. L.0.
  left: 11. 9. 7.5. "-t" -0. 0.0. L.0.
- Std-angle: right 53°, left 75°
- Hallux: right: small distal loop (L²)
  left: tibial arch (A³)

**Discussion**

In view of the rarity of terminal deletion of the long arm of chromosome 4 the phenotypic features of the 4q monosomy have so far not been clearly delineated. Even in 1977 Rethoré in a review of three cases noted that it seemed too early to define a new syndrome for this chromosomal abnormality, because it was not clear that the deleted segment was the same in all published cases. This conclusion was based on the reports by Ockay et al. (1967), Golbus et al. (1973) and van Kempen (1975). However, further cases (Ferrier and Freund (1973), Back et al. (1977), Rethoré et al. (1979), Townes et al. (1979) and Mitchell et al. (1981)), confirm the existence of a typical and recognisable syndrome of terminal 4q monosomy (4q−). The main features of these cases with 4q deletion are summarized in Table 1.

This syndrome is characterised by a combination of marked craniofacial dysplasia and limb anomalies as well as general features characteristic of all autosomal aberrations, such as postnatal growth retardation, defects of internal organs, convulsions and severely retarded mental development. The typical craniofacial signs are microcephaly with a long flat nasal saddle and snub nose, hypoplasia of the midface, micrognathia and retrognathia. The faun-like ears which are especially mentioned by de Grouchy (1978) and others (van Kempen (1975), Rethoré et al. (1979) and Townes et al. (1979)), are not always present.