Short report

Cornelia de Lange syndrome with ring chromosome 3

Prema Lakshminarayana, P Nallasivam

This report describes a known pattern of malformation in association with a rare chromosomal abnormality, a combination which, to our knowledge, has not been reported so far.

A 4 month old male infant was referred to the genetic clinic for investigation of 'odd facies'. He had been admitted to the paediatric ward with respiratory infection and septicaemia. He was the first child of consanguineous parents (first cousins), born after 40 weeks of gestation. There was no history or suggestion of exposure to teratogens or infection during the pregnancy and delivery was normal. His mother and father were 26 and 40 years old, respectively, at conception. The infant was born one year after marriage and there had been no preceding fetal loss. No physical abnormality was reported in family members.

At birth he was 48 cm long, weighed 2400 g, and his Apgar scores were 8 and 10 at five and 10 minutes. Excess lanugo hair was also noted as well as synophrys.

On physical examination at 4 months of age, his length, weight, and head circumference were below the 3rd centile. The anterior fontanelle measured 1×1 cm and was flat. Skull transillumination was negative. He had a small head, bushy eyebrows, and synophrys, and the hairline was low. Generalised hirsutism and cutis marmorata were noted. His eyes were small. He had large ears (4.5 cm, 97th centile) with a preauricular sinus on the right side. The nasal

bridge was wide, the nostrils were upturned, and the philtrum was long (1 cm, 97th centile). The mouth was downturned and the upper lip was thin. He had retrognathia and a high arched palate.

The phallus was short with hypospadias. There was a pilonidal sinus. The elbows and knees could not be extended fully. He had short fingers with brachymesophalangy and clinodactyly of the little fingers.

His dermatoglyphic analysis showed short and interrupted main creases and absent triradius *b* on both sides. The second digits had an arch pattern with ulnar loops in the rest. Examination of the cardiovascular system indicated normal heart sounds with a short, soft systolic murmur in the third left space. The respiratory system was normal. The liver was just palpable. He has not yet attained head control or social smile.

Radiographs showed delayed skeletal maturation and normal heart contour. ECG was within normal limits. Ultrasonography of the abdomen was normal.

Figure 1 Ring chromosome 3.

Institute of Child Health and Hospital for Children, Dr ALM PG Institute of Basic Medical Sciences, Madras, India.

P Lakshminarayana, P Nallasivam

Correspondence to Dr Lakshminarayana, Reader in Medical Genetics, Institute of Obstetrics and Gynecology, Commission Office Road, Madras 600 008, India.

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Figure 2 Clinical photograph of the proband.

Scan of the brain showed a dilated cisterna magna. Peripheral lymphocyte culture showed a karyotype of 46,XY,r(3) (fig 1). This anomaly was not present in either parent.

The above clinical picture (fig 2) corresponds to Cornelia de Lange syndrome, but a dilated cisterna magna has not been reported in this syndrome before. Various chromosomal abnormalities have been reported in Cornelia de Lange syndrome. Luzzarti¹ reported chromosomal anomalies in 11 out of 38 patients, but no consistent pattern was noted. The association of ring chromosome 3 has not been reported so far, but deletion 3p was noted in one case. Three cases of ring chromosome 3 have been reported so far,² but none in a case of Cornelia de Lange syndrome. The reported cases had large ears, a short, upturned nose, growth retardation, and renal anomalies.

It has been suggested by McKusick³ that the presence of chromosomal anomalies in Cornelia de Lange syndrome may indicate a predisposition to chromosomal change induced by point mutation.

This case has been presented because of the rare combination of clinical, sonographic, and cytogenetic findings.

- 1 Luzzarti CAP. Translocation in De Lange syndrome. *Lancet* 1965;ii:445-6.
- 2 Schinzel A. *Catalogue of unbalanced chromosomal abnormalities in man*. Berlin: de Gruyter, 1984:133-4.
- 3 McKusick VA. *Mendelian inheritance in man. Catalog of autosomal dominant, autosomal recessive, and X-linked phenotypes*. Baltimore: Johns Hopkins University Press, 1979:461.