Probable de novo 17q duplication (q11.2→q21.1): a newly recognised chromosomal syndrome in a child with Klinefelter's syndrome

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Abstract

A child is described with a previously unreported probable trisomy for a segment of the long arm of chromosome 17 responsible for some distinct clinical features. These include craniofacial and skin abnormalities, failure to thrive, partial malrotation of the gut, malabsorption, gastro-oesophageal reflux, neurodevelopmental delay, autonomic disturbance, and cardiac and CNS abnormalities. The coexistence of Klinefelter's syndrome (47,XXY) is of minor significance in relation to this child's phenotype.

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Several cases of distal trisomy 17q have been published since Berberich *et al*¹ originally described three related patients (cousins) with common phenotypic features delineating a new cytogenetic syndrome. We report a new case resulting from a previously unreported abnormality of the proximal part of chromosome 17q.

Case report

This male infant was the second child of 21 year old, healthy, non-consanguineous Caucasian parents. There is a healthy 3 year old female sib. The pregnancy was unremarkable and the patient was born at 37 weeks by vaginal delivery with breech presentation (birth weight 2300 g, 3rd centile; Apgar scores

4 at one minute, 7 at five minutes, 8 at 10 minutes). Minor initial resuscitation with facial oxygen was required and the patient spent four days in an incubator because of poor temperature control. Presumed physiological jaundice was treated by phototherapy from days 3 to 8 (maximum level of serum bilirubin = 275 $\mu\text{mol l}^{-1}$). No obvious dysmorphic features were noted at this time.

At 2 weeks of age he was treated with topical antibiotics for sticky eyes. At 10 weeks of age he presented with recurrent cyanotic episodes and respiratory difficulty. Odd facies, hypotonia, bilateral undescended testes, and a cardiac murmur were noted. On subsequent admissions at 5 and 8½ months of age he presented with an apnoeic episode associated with a presumed viral respiratory illness, and stridor with a viral croup-like illness. During these admissions, brief (1 to 20 minutes) intermittent episodes of paroxysmal sinus tachycardia (rate 200 to 250 per minute) were observed. These were usually nocturnal, associated with sweating and coughing, and have persisted subsequently, though with reduced frequency. Chest x ray changes suggested an aspiration syndrome. Failure to thrive (weight at 5 months 3.8 kg, << 3rd centile; head circumference 78.5 cm, << 3rd centile) and developmental delay became apparent, and the following dysmorphic features were noted: thin vermillion border of the upper lip; flat nasal bridge; hypertelorism; epicanthic folds; short palpebral fissures; dry scaly skin; and thin, sparse scalp hair but synophrys and generalised hirsutism (fig 1). Abnormal posturing of the hands, truncal hypotonia, lower limb hypertonia, and a soft grade 2/6 systolic murmur at the left sternal edge were noted. Neither testis was palpable. Developmental level was assessed to be between 2 and 4 months at a chronological age of 8 months. Severe visual immaturity was manifest, function being at a 14 week level at a chronological age of 11 months. On further follow up he has been reported to develop clinical seizures and problems with his upper airway attributed to a floppy larynx.

Radiological investigation showed partial midgut malrotation with an abnormal small intestinal mucosal pattern. Fat malabsorption was suggested by low serum vitamin A and E levels, and by fat globules observed on stool microscopy. Moderate gastro-oesophageal reflux was confirmed by 24 hour pH monitoring. Head ultrasound and CT brain scan were normal, but the EEG showed marked non-specific bilateral temporal lobe abnormalities.

Figure 1 The proband.

Brain stem evoked response (BSER) indicated bilateral 50 dB mid-high frequency sensorineural hearing loss. Echocardiography showed a small muscular ventriculoseptal defect, and a 24 hour ambulatory ECG showed episodes of sinus tachycardia. Other tests, including those for familial dysautonomia, catecholamines, urinary VMA/HMA, α -1-antitrypsin, immunoglobulins, and thyroid function, and a congenital infection screen were normal.

CYTOGENETICS

G banded (Giemsa-trypsin) analysis of chromosomes from PHA stimulated peripheral blood lymphocyte cultures showed the child to have an extra sex chromosome (47,XXY). In addition, the long arm of one chromosome 17 was observed to be slightly longer than normal. C banding showed this additional material to be euchromatic in nature. Using high resolution banding, the extra euchromatin was thought most probably to be the result of a small duplication of the region 17q11.2→q21.1. The child's karyotype was thus interpreted as 47,XXY,dup(17)(q11.2→q21.1) (fig 2). The parents were shown to have normal chromosome complements. No cell line is available from this patient.

Discussion

No previous case involving partial trisomy of the proximal part of the long arm of chromo-

some 17, q11.2→q21.1, has been described. Since Berberich *et al*¹ originally reported three cases of distal trisomy of the long arm of chromosome 17, several other cases have been published.²⁻¹¹ In these cases the trisomic segment varies between q21 and q25.1, thus accounting for the variability of clinical expression of the described syndrome.¹⁰

The current case manifests some clinical features in common with previous descriptions. These include abnormally rough, dry skin and bilateral cryptorchidism³; thin upper vermillion and generalised hirsutism¹¹; and bushy eyebrows, short palpebral fissures, temporal lobe EEG abnormalities, and sensorineural deafness.⁸ Postnatal failure to thrive, psychomotor retardation, and visceral anomalies are also features in common.¹⁰

Autonomic dysfunction is a unique and prominent feature of this case, with unexplained paroxysmal episodes of tachycardia and sweating occurring frequently. These episodes may, however, reflect abnormal seizure activity in the brain without alteration in consciousness or obvious fits at the time. Energy expenditure by such a process, together with malabsorption associated with gut malrotation, provides an explanation for the failure to thrive despite a more than adequate calorie intake (160 to 180 Kcal/kg/day). The other major problems are those relating to seizures and neurodevelopmental delay, including hearing and vision.

This case illustrates some of the specific problems that may be encountered in a child with a duplication of chromosome 17 (q11.2→q21.1). There are both similarities and dissimilarities in clinical expression when compared with other descriptions of partial trisomy for the long arm of chromosome 17.

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Figure 2 Karyotype of the proband.

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