De novo interstitial direct duplication of 15q: 46,XY,dir dup(15) (pter→q24::q14→q21·1::q24→qter)

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SUMMARY A profoundly retarded, slightly dysmorphic male was re-examined cytogenetically by high resolution GTG banding and found to have a de novo interstitial direct duplication of 15q.

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Case report

The patient reported here (fig 1) is a 12-year-old Caucasian male, the product of a 41-week gestation of a 34-year-old gravida 2 para 2 woman and her 36-year-old non-consanguineous husband. During the eighth and ninth months of pregnancy, hydrochlorothiazide (Hydrodiuril) for significant
dependent oedema was used three times a week, with dietary salt restriction. The pregnancy was otherwise without complication and a spontaneous vertex delivery was achieved following a labour of approximately 3 hours. Oxygen and mucous aspiration were required to attain an Apgar score of 8 at 5 minutes. Birth weight was 2670 g and the child was noted to have cryptorchidism.

At 4 months of age chromosome analyses were done on peripheral blood from the proband and his parents, but no abnormality was detected. At 8 months a right orchiectomy was performed because of impaired cord blood supply. At 18 months the patient had a left orchiopexy and received a prosthetic implant (ultimately extruded spontaneously). Shortly after his surgery, he was referred for orthopaedic consultation because of skeletal problems with his back and feet; these were treated symptomatically. An infant-parent stimulation programme was suggested for his developmental retardation following assessment. Psychological evaluation at 22 months indicated a mental age of 10 months, with an IQ of 47 on the CIIS.

We continued to follow the patient at 6-month to yearly intervals. When he was 7 years old chromosome analysis (which had previously been done elsewhere) was repeated. Again, no structural abnormalities were detected in Giemsa banded metaphase cells. Following a seizure at the age of 11 years, EEG, thyroid and growth hormone assays, and other laboratory studies were done. With the exception of the EEG, which was compatible with a seizure disorder, the tests were normal and the diagnosis remained 'syndrome of unknown aetiology'. At 12 years, by which time a clinical geneticist had been added to the staff, it was felt that syndrome identification should be re-explored, and a genetics consultation was requested.

Physical examination revealed short stature, although the exact height could not be measured due to hyperactivity. Head circumference of 49.1 cm was below 2 SD for age. The face was distinctive, with a narrow forehead, high nasal bridge, narrow palate, dental malocclusion, small ears, and micrognathia. Additional findings included lumbar kyphosis, bell-shaped chest, mild scoliosis, scrotal hypoplasia, and micropenis (2.5 cm long, 1.5 cm wide). There was no cardiomegaly and no thrills or murmurs were heard. The abdomen was protuberant but could not be adequately examined for organomegaly owing to poor cooperation. Mental retardation was profound and intelligible speech was absent.

FIG 1 Proband aged 12.
A repeat cytogenetic analysis, using high resolution GTG banded prometaphase chromosomes, revealed an interstitial direct duplication in the long arm of chromosome 15 (fig 2). We interpret the karyotype as 46,XY,dir dup(15) (pter→q24::q14→q21.1::q24→qter), in accordance with the International System for Human Cytogenetic Nomenclature. The proband is therefore trisomic for a small interstitial segment of 15q. Repeat studies of the parents confirmed 46,XX and 46,XY karyotypes.

Discussion

A number of reports have been published on partial trisomy of 15q resulting from parental translocation or inversion. Yip et al compared eight such cases with a ninth case of de novo tandem duplication. In all but one, the most proximal breakpoint was q21 and all were trisomic to qter. The case reported here is only the second de novo case observed and the first 15q interstitial direct duplication. It is of interest that although the trisomic segment in our case is more proximal than in the majority of the other cases, the physical findings are very much in agreement.

While we would not advocate high resolution banding as a routine procedure nor suggest that every suspect patient with a normal karyotype be re-analysed, it would seem prudent to apply this newer technique in certain special instances. More cases with minor structural abnormalities are obviously needed before a precise picture of 15q trisomy evolves.

References


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