an interstitial duplication of the 7q22→q32 region in patients with frontal bossing, strabismus, large wide ears, and hypotonia. Turleau *et al*² proposed two syndromes based on these distinctive characteristics. More recently, Schmid *et al*⁸ suggested a third syndrome as their patients had asymmetry of the skull, small dysplastic ears, kyphoscoliosis, and seizures, as well as strabismus and hypotonia.

Despite apparent specificity there is some phenotypic overlap and certain common features are described in all cases. These include mental retardation, low set ears, hypertelorism, small palpebral fissures, a short upper lip, and a short neck.

Almost all reports of partial trisomy 7q result from a familial reciprocal translocation or insertion translocation. In addition to trisomy, partial monosomy of a variety of other chromosomes is represented.³ There are also reports of derivative chromosomes resulting from pericentric inversions of chromosome 7. The first de novo report was by Wahrman *et al*.⁴ A very large chromosomal segment was duplicated and involved the 7q11→qter region. This was also the first case reported with genitourinary and renal anomalies. Our patient is similar clinically in that he had an atrophic kidney, a ureteral anomaly, and cryptorchidism, as well as the similar facial features that are characteristic of 7q trisomy. The specificity of renal anomalies is further illustrated by Ramirez and Uribe⁹ as they report full trisomy 7 in an infant who presented with Potter's syndrome. The pathological examination revealed an absent left kidney and a right polycystic kidney.

Although a gene dosage effect could not be demonstrated by enzymatic assay or blood group linkage analysis, high resolution banding suggested a duplication of the 7q11→q22 region as compared to the other 7q bands. The phenotypic similarities to full and partial trisomy 7 make it unlikely that the

extra material is derived from another chromosome. The most likely mechanism producing the derivative chromosome is three breaks resulting in an insertion of the region in question or an unequal cross over in meiosis.

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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

FIG 1 *Proband aged 12.*

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 2 (a) *Chromosomes 15 from proband;* (b) *diagram of duplicated chromosome 15.*

A repeat cytogenetic analysis, using high resolution GTG banded prometaphase chromosomes,¹ 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.² 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*³ compared eight such cases with a ninth case of de novo tandem duplication. In all but one,⁴ 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.

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