band p21 was involved in the deletion. Therefore, deletion of 7p21.1–p21.2 would be compatible with the association with premature craniosynostosis.

Our case and the patient of Baccichetti *et al*⁴ are the only two reported pure terminal deletions of 7p22. Neither patient had signs of craniosynostosis and they therefore provide additional evidence that partial or complete deletion of band 7p22 is not necessarily associated with craniosynostosis.

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A non-centromeric C band variant on chromosome 11q23.2

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SUMMARY An extra G band was found inserted into chromosome 11q23.2 in a boy who had severe developmental delay and anal stenosis. Cytogenetic characterisation of this extra band showed that it was composed of Q band brilliant, C band heterochromatin. It was also present in clinically normal subjects in two other generations and was therefore presumed to be unrelated to the clinical abnormalities in the proband. Although rare, this cytogenetic anomaly may be useful as a genetic marker for 11q23.2.

Chromosome polymorphism has been well described in the human genome and includes differences in amount, location, and type of pericentromeric constitutive heterochromatin.¹ These variations are attributed primarily to gain or loss of repetitive DNA sequences that have synonymously been referred to as satellite DNA.² Changes in the

amount of this material are believed to be caused by unequal recombination or over-replication or both.³ Occasionally, pericentromeric inversions of this genetically inert material are observed, most commonly on chromosome 9.⁴ There also appear to be different types of constitutive heterochromatin on different chromosomes as these can be distinguished cytochemically. For example, chromosome 9 contains a large block of heterochromatin that can be distinguished using the Giemsa 11 technique and has been used to determine the mechanisms responsible for rearrangement.⁴ Other regions of the genome can also be distinguished with a montage of other cytochemicals.

To date, very few chromosome variants have been described that involve translocation to parts of the genome other than those in which they are commonly found. Watt *et al*⁵ described a normal subject who had an insertion of the nucleolus organising region (NOR), normally found on the acrocentric chromosomes, along with some adjacent heterochromatin into chromosome 12p. The NOR, while differing from satellite DNA in that it is highly active transcriptionally, may also show a tremendous degree of variation in copy number without any

FIGURE Pedigree showing the inheritance of the chromosome 11 containing the extra band on q23.2. In addition, chromosomes from the proband's mother are shown below using G banding, Q banding, and C banding for comparison.

known clinical consequences. This variant was also found in other family members in three generations. Another brief report described an insertion of similar material into chromosome 11q21.⁶ This chromosome was found in family members in three generations, all of whom were phenotypically normal, suggesting this variant to be of little phenotypic consequence.

We describe a variant chromosome 11 that has an insertion of C band heterochromatin at q23.2 and was found in three family members in three generations. We suspect that this variant will be useful to examine the effects that constitutive heterochromatin have on recombination, since pairing is known to be reduced, or even absent in such regions of the genome.

Case report

The proband was a 20 month old child who was referred for genetic evaluation because of a history

of anal stenosis and global developmental delay. He was the 3600 g product of an uneventful 42 week pregnancy of a 30 year old primigravida, delivered by caesarean section because of failure to progress. For the first seven months the proband was constipated and irritable and it was not until that time that he was diagnosed as having a nearly imperforate anus with a massively dilated bowel proximal to the stenosis. The anal stenosis required colostomy, followed later by a sacroperineal pullthrough procedure. The proband was developmentally assessed to be at a six to eight month level at 15 months of age. He also had a small head circumference (2nd centile), the outer canthal distance was on the 75th centile, and the inner canthal distance on the 50th centile. Also noted were bilateral epicanthic folds and a prominent crease under the lower eyelids, a prominent lower lip, and a flat nasal bridge. Owing to the minor facial dysmorphism, global developmental delay, and imperforate anus, blood was obtained for chromosome analysis.

At follow up at the age of three years three months, the proband was found to have severe developmental delay and self-stimulating behaviour with head banging. Psychological testing using the Bayley Mental Scale of infant development placed his functioning within the severely retarded range. He was again noted to have a head circumference on the second centile. His facial appearance suggestive of mild relative hypertelorism resembled that of his mother. Interpupillary distance was between the 3rd and 25th centile. The remainder of the physical examination was normal. Other diagnostic laboratory studies, including brain CT scan, urine and plasma quantitative amino acids, and urine organic acids, were normal.

Materials and methods

High resolution chromosome preparations⁷ were examined with GTW,⁸ QFQ,⁹ CNG,¹⁰ and AgNOR¹¹ banding methods.

Results

Cytogenetic examination of G banded preparations on the proband showed an unusual extra band at 11q23.2. A parental translocation was suspected and blood samples from both parents were obtained for analysis. While the same anomalous chromosome 11 was found in the mother the remainder of her karyotype appeared to be normal, arguing against a reciprocal translocation.

Further analysis of this variant chromosome using C banding showed that this extra band was composed entirely of constitutive heterochromatin and Q banding showed it to be brilliantly staining, not unlike the intensity encountered on chromosomes 3 and 4 and the short arms of the acrocentrics. Examination with the AgNOR technique, which stains darkly those NORs that were transcriptionally active, did not identify anything unusual in the karyotype, indicating that if this band were derived from heterochromatin from an acrocentric it did not include active NOR sequences (data not shown). As shown in the figure the maternal grandfather was also found to have this chromosome in addition to the proband and mother. The father and maternal grandmother were cytogenetically normal.

Discussion

An unusual familial insertion segregating in three generations was ascertained through a proband with severe developmental delay and anal stenosis. Since phenotypically normal family members had the same chromosome variant, this unusual insertion is presumed to be genetically benign and, therefore, merely coincidental with the clinical findings in the

proband. This presumption is supported by previous studies.¹² One cannot, however, rule out the possibility that the proband's father is a carrier for a recessive genetic disorder that is located at 11q23 and that insertion on the variant 11 in the proband has disrupted its normal allele.

Based on the combined staining characteristics, the most likely origin of this extra material is chromosome 3 or 4; the distal portion of the Y chromosome, as well as the perinucleolar heterochromatin on the acrocentrics, can stain intensely with Q banding, but generally are not very dark with G banding. A survey of published reports failed to find similar cases, indicating that this is a newly described non-centromeric variant. Unusual cases such as this provide superb opportunities for studying the recombinational effects of heterochromatin that has been inserted into a euchromatic portion of the genome.

We thank Dr Stephen Schochat for referring the patient, Susan Schelley for coordinating the acquisition of the samples, and Professor Albert Schinzel for helpful discussions.

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