significant enough to make amniocentesis available to a normal carrier.

We share the feeling that the presence of these variants is significant, and may have an aetiopathological role in causing non-disjunction. However, it seems to us that carefully controlled studies are necessary before one can support a recommendation for amniocentesis in an otherwise normal carrier.

MOSE FRYDAN, FIORELLA SHADAI, ISAAC HALBRECHT, AND EZRA ELIAN
Departments of Pediatrics and Human Cytogenetics, Hasharon Hospital, Petah-Tiqva; and Tel Aviv University Sackler School of Medicine, Israel

References
11. Wang HS, Hamerton JL. C-band polymorphisms of chromosomes 1, 9, and 16 in four subgroups of mentally retarded patients and a normal control population. Hum Genet 1979;51:269-75.

Requests for reprints to Dr M Frydman, Division of Medical Genetics, Harbor-UCLA Medical Center, 1000 West Carson Street, Torrance, California 90509, USA.

Absence of constitutive heterochromatin in a partially identified supernumerary marker chromosome

SUMMARY A retarded child with multiple malformations was found to have a karyotype 47,XY,del(11)(11pter→q21:),+mar(11qter→q21::?). The mitotically stable centric marker had no demonstrable C heterochromatin. Phenotype-karyotype correlation and the role of C heterochromatin in phenotypic effects are discussed.

Supernumerary chromosomes of unknown origin are not uncommon in phenotypically abnormal subjects. When they occur in normal subjects, they are presumably composed of only genetically inert heterochromatin. The supernumerary marker we describe here was found in a malformed child and is unique because of a complete deficiency of demonstrable heterochromatin along its length.

Case report

The proband was born to a healthy, young, non-consanguineous black couple after an uncomplicated term gestation. He weighed 3.2 kg at birth and showed the following malformations: left sided complete cleft lip and palate, hypotelorism, sinus over right pinna, umbilical hernia with diastasis recti, anal stenosis, tapering fingers, and a distal axial triradius. During 18 months of observation, his height and development were slow. His fontanelle closed early, a ridge along the metopic suture became palpable, the skull showed bitemporal narrowing and trigonocephaly, esotropia became evident, the nose was short with a wide low bridge, and cafe-au-lait spots appeared over his face and chest (fig 1). No internal malformations were discovered. Radiographic appearance of the skeleton was not unusual except for trigonocephaly. Several laboratory studies, including lactate dehydrogenase levels in the serum and isotope patterns, were normal.

CYTOGENETIC DATA

Cultured lymphocytes showed 47 chromosomes in each of 50 orcein stained cells. The extra chromosome was the size of a chromosome 16 and appeared metacentric to submetacentric in morpho-
FIG 1  Facies of the proband at 18 months of age. His cleft lip and palate have been surgically repaired.

FIG 2 A. Partial G banded karyotypes showing deleted 11 and the marker beside the normal 11. B and C. C banded metaphase spreads showing the absence of heterochromatin on the marker (arrows).

None of the other chromosomes of the proband or his parents showed unusual polymorphisms with quinacrine, Giemsa, and Wright stains.

Discussion

Variations in the quantity and staining properties of centromeric heterochromatin are common polymorphisms in the human karyotype. Abnormal location of the heterochromatin through structural alteration of chromosomes, such as pericentric inversion and isochromosome formation, are also relatively common. On the other hand, total deficiency of C heterochromatin on any chromosome, normal or abnormal, has been reported rarely. In one such case reported by Buys et al. a metacentric chromosome 9 found in amniotic fluid cells and the father of the baby was shown to be devoid of heterochromatin by the DAPI and Giemsa staining methods. The father and the baby after its birth were phenotypically normal.

In our patient several clinical features, for example, trigonocephaly, short nose with a flat wide bridge, hypotelorism, and strabismus, are reminiscent of the 11q deletion syndrome. Cyogenetically the proband is not missing any part of 11q. Position effect or a submicroscopical deletion of a critical region because of the break on 11q may explain these findings. The child showed additional malformations which are undoubtedly the result of the presence of the unidentified piece of chromosome, which made up about one half of the marker. Thus it appears that the absence of C heterochromatin on the marker had no detectable influence on its phenotypic effects. The mitotic stability of the marker, as demonstrated by its consistent presence...
in repeated studies over an 18-month period, and the lack of mosaicism shows that the absence of C heterochromatin does not interfere with centromere function.

G S Pai, George H Thomas, and Paul J Benke
\*Department of Pediatrics, The Johns Hopkins University School of Medicine, Baltimore, Maryland; and †the Mailman Center, University of Miami School of Medicine, Miami, Florida, USA

References


Requests for reprints to Dr G S Pai, Division of Medical Genetics, Medical University of South Carolina, 171 Ashley Avenue, Charleston, South Carolina 29425, USA.

Ectrodactyly, cleft lip and palate in two half sibs

SUMMARY Two half sibs with bilateral complete cleft lip and complete cleft of the palate associated with ectrodactyly of the hands and feet, born to the same phenotypically normal mother, are reported. The younger of the two sibs also has dominantly inherited tremors (also referred to as essential heredofamilial tremors) as did her biological father. Possible genetic causes to explain the recurrence of the facial and limb malformations in the half sibs with additional central nervous system malformations in the younger sib are discussed.

Received for publication 5 November 1980

Cleft lip with or without a cleft of the palate is occasionally a component of an inherited malformation syndrome. In such cases, the pattern of inheritance and the risk of recurrence may be higher than the multifactorial type and is the same as that of the syndrome itself. Rarely, the associated anomalies may differ from previously described entities making the diagnosis, inheritance, management, and prognosis more unpredictable. We report two half sibs with multiple congenital anomalies associated with bilateral complete cleft lip, complete cleft of the palate, and ectrodactyly (fig 1).

Case reports

The proband, born 9.2.76, is a female of French Canadian and Polish descent, born to unrelated parents. The mother was 33 years and the father 27 years of age at the time of birth. She was a term infant with a birthweight of 2.9 kg. She had a complete bilateral cleft of the lip and palate (fig 2a) and small malformed ears. She had four digits on her hand (fig 2b), four toes on each foot, and a pilonidal dimple which was not associated with any vertebral anomalies.

Tremors manifested by horizontal nystagmus and horizontal rhythmic movements of the head, hands, and arms were present when the infant was awake and disappeared when asleep. The neurologist who evaluated the infant and her father made the diagnosis of dominantly inherited tremors (also known as essential heredofamilial tremors). A grade 3/6 systolic murmur was heard on auscultation and the diagnosis of an atrial septal defect was made by the cardiologist.

A CT scan of the brain was consistent with agenesis of the corpus callosum. An intravenous pyelogram showed normal kidneys and ureters.

Routine blood work including serum BUN, creatinine, and electrolytes, and urine analysis were normal.

X-rays of the hands and feet showed a missing digit on the left hand and a missing ray on each foot.

FIG 1 Pedigree.

I

II

Bilateral CLP + Essential heredofamilial tremors

Proband

DI = Diabetes insipidus