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.

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References


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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.

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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.

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FIG 1 Pedigree.
Case reports

Chromosome analysis with trypsin banding showed a 46,XX normal female karyotype.

Weight gain from birth to 4 months of age was at the 25th centile. At 4 months of age, she had a seizure and on examination was noted to be dehydrated and hypotonic. Pertinent additional findings included urine output of low specific gravity and hypernatraemic dehydration. Pitressin injection decreased urine output and raised the specific gravity. Her electrolyte imbalance was corrected and the diabetes insipidus treated with IM pitressin. At 5½ months of age her lip and hard palate were surgically closed. At 7½ months of age she was found dead in her crib.

The proband’s 8-year-old half brother was born on 15.11.67 with a bilateral complete cleft lip and palate (fig 3). He had small, malformed ears, soft tissue syndactyly between the second and third fingers of the right hand, ectrodactyly and syndactyly of both feet, and undescended testicles.

An intravenous pyelogram showed normal kidneys and ureters. Chromosome analysis showed a 46,XY normal male karyotype. His intelligence is normal.

The mother denies having taken any medication or suffered any illness during either pregnancy.

Discussion

The association of cleft lip and palate (CLP) and ectrodactyly has been described by Walker and Clodius in three families. Atresia and other deformities of the lacrimal duct were present in some of their affected cases. Both of our patients had intact lacrimal ducts. Wiedermann reported two sibs with bilateral CLP and absence of the fifth rays on both hands and feet. It has also been suggested that CLP and ectrodactyly represent the incomplete form of the EEC syndrome, as compared to patients having the complete form, showing evidence of ectodermal dysplasia as well as ectrodactyly and CLP. Five of the previously reported familial cases of the incomplete form showed an autosomal dominant inheritance pattern. Preus and Fraser have suggested variable penetrance and expressivity of a single gene inherited in an autosomal dominant manner.

Our two patients resemble the cases reported to have ectrodactyly with cleft lip and palate with many more features noted in the proband. The type of cleft was identical in both patients but the limb malformations differed in severity. The proband also showed evidence of dominantly inherited tremors, in her case passed on by her biological father. Permission to confirm paternity by blood grouping was refused.

The observation of this syndrome in two half sibs who are the offspring of the same mother is of great interest and is difficult to explain if the mother shows no clinical evidence of the syndrome. One explanation is that the mother had the (dominant) trait expressed in a minimal form and passed it on to both of her children in whom the gene was expressed in a much more severe manner. In the family described, the mother showed no sign of even a microform of a
cleft and the x-rays of her hands and feet showed normal bony components. The common parent could be considered to be a non-expressing heterozygote and an obligate carrier. Another explanation would be to assume that the mother had a balanced chromosomal translocation and that, in the children, an unbalanced form of the translocation is present, resulting in the anomalies. In the absence of any detectable changes in the karyotype of either child, this interpretation becomes hypothetical. A fourth explanation would be that the mother had a gonadal mosaicism which could result in repeated births of children with similar congenital malformations not present in the maternal phenotype, but this assumption is also speculative and cannot be demonstrated.

If these two sibs had been the children of the same parents, the cases would have been quoted as 'suggesting' that these anomalies were attributable to homozygosity of an autosomal recessive gene, an explanation that is unlikely in view of the different fathers. In the case of a common mother and different fathers, X linked recessive inheritance can be involved if the affected children are males. An exception to this rule is the rare possibility that a female has an X linked recessive disorder (Lyon hypothesis).

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Case reports

18p− syndrome with a single central maxillary incisor

SUMMARY A child with a single central maxillary incisor and a deletion of the short arm of chromosome 18 (18p−) is presented. He is the first patient in whom this association has been found.

A syndrome of short stature and single central maxillary incisor has been described by Rappaport et al. Five of the seven patients in the original report had cytogenetic studies, all of which were normal. Four of these five patients were growth hormone deficient.

We are reporting a child with short stature and a single central maxillary incisor who was found to be missing the entire short arm of chromosome 18 (18p−). To our knowledge, he is the first patient in whom this dental anomaly has been associated with an abnormal karyotype.

Case report

A 28-month-old male was referred for evaluation of short stature, dysmorphic facies, and developmental delay. He was born after an uncomplicated 37 week pregnancy. The birthweight (2.4 kg) and length (45 cm) were at the 25th and 50th centiles, respectively, for this gestational age. Overlapping of the second and third toes was noted in the newborn period.

His early linear growth rate, weight gain, and cranial growth were normal, but he had fallen off since the age of 6 months. At 9 months of age his third tooth, a large single central maxillary incisor, appeared.

The parents report that his early developmental milestones were normal; he rolled over at 4 months and sat at 6 months. His language development has been delayed. Although he spoke his first word at 1 year, he does not combine words at 28 months.

The mother (aged 24 years), father (aged 25 years), and a sister (aged 7 years) are of normal stature and dentition. There is no consanguinity or history of similarly affected relatives. The home environment is stable.

The patient has had no other admissions to hospital for serious illnesses. His diet is appropriate for age.

At 28 months, his height (79 cm), weight (8.8 kg), and head circumference (44 cm) were below the 3rd centile for age. Pertinent craniofacial features included prominent simply-formed ears, downward slanting palpebral fissures, mild epicanthal folds.