Case reports


**A probable case of mutation in Huntington’s disease***

Summary. A patient is described in whom Huntington’s disease was diagnosed at the age of 34 years. No evidence of the disorder was found in either parent. Their parentage of the alleged mutant could not be excluded from a study of the inheritance of 25 genetic markers.

It is rare for signs of Huntington’s disease to appear in offspring before it manifests itself in one of the living parents. When such a case occurs, it is reasonable to suspect a mutation. Because of the possibility of very late onset of symptoms, few cases have been reported in which the parents of the alleged mutant are both alive. For such reasons, Reed and Neel (1959) do not believe that specific instances of mutation in the disorder can be demon-
progressive choreoathetosis or rigidity, dementia, and autosomal dominant inheritance (genocopies, such as that described by Cederbaum et al (1971), should be excluded). The latter is important since the disease produced by the mutation should be shown to occur in more than one generation.

(ii) Both parents of the propositus must have lived to such an age that it can be reasonably assumed that the disease would have appeared had they carried the abnormal gene.

(iii) Sufficiently reliable information about the health of both parents must be obtained to ensure their freedom from the disease.

(iv) The apparent mutant must be the offspring of both the alleged parents and not the issue of an unknown parent who bore the abnormal gene.

The present case cannot fulfil the requirement of dominant autosomal transmission in criterion (i) because the children of the propositus were born in 1961 and 1972. This deficiency was counter-balanced by the ability to examine personally both parents, thus meeting criterion (iii) and overcoming the common problem—noted by Reed and Neel (1959)—of having to rely upon other than direct observation. It is virtually impossible for a single person to examine the three generations of a family (unaffected parents, supposed mutant, and affected offspring) ideally envisaged by the requirements. The only other area of possible dispute would be the ages of the parents; it can be argued that Huntington’s disease could still affect one of them. There is a small chance of this eventuality occurring, since cases having an age of onset up to 75 years have been reported in Norway (Orbeck and Quelprud, 1954). In Victoria the latest onset of symptoms found was at 63 years of age (Brackenridge and Telscher, 1975).

As the father of the propositus was a professional soldier who was seldom home, it was necessary to exclude illegitimacy. This was done to a high degree of probability by using 25 genetic markers.
Unfortunately it was not possible to estimate the probability of excluding parentage because phenotype frequencies for many of the polymorphisms have not been reported for southern Italy. The present case bears some similarities to two Norwegian sisters, whose apparently unaffected parents were aged 62 and 64 years at the time of reporting (Haugerud, 1968), and whose red-cell antigens in 8 systems provided no evidence for excluding parentage. The alleged mutants both had histories of chronic progressive chorea.

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References

Trigonocephaly and associated minor anomalies in mother and son

Summary. A mother and her son are described with neonatal trigonocephaly, multiple suture synostosis; shallow orbits; unusual nose; deviation of the terminal phalanges of fingers 1, 2, and 5; and broad toes which radiologically may show duplication of the terminal phalanx. Untreated, the condition leads to a disfiguring oxycephaly with hypertelorism.

This appears to be the first documented instance of autosomal dominant trigonocephaly. The importance of the minor anomalies in its recognition and its good prognosis are emphasized.

Recent progress in facial corrective surgery has resulted in large numbers of children with craniostenosis being seen in single centres. This growth provides a new opportunity for the study and recognition of increasing numbers of subtypes of craniostenosis. Ultimately this will result in improved counselling for parents and patients. We describe here a mother and her son who are affected by trigonocephaly in association with multiple suture synostosis and other minor anomalies. We are unable to find previous reference to the transmission of trigonocephaly from an affected individual to the offspring.

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The propositus was referred to the Hospital for Sick Children in Toronto for evaluation of trigonocephaly. Birth had been complicated by a cephalohaematoma and linear parietal fracture, but development was normal.

On examination at 6 months, length was 71 cm (97%), weight 8500 g (80%), and head circumference 42.5 cm (30%). He had trigonocephaly with a prominent metopic ridge, shallow orbits, epicantlic folds, and minimal ptosis (Fig. 1). The inner canthal, outer canthal, and interpupillary distances were 2.5 cm (97%), 7 cm (50%), and 4 cm (3%), respectively. The nose was hooked with the septum extending below the alae, and the philtrum attached anteriorly on the septum. He had a large mouth with a down-turned upper lip.
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