MONGOLISM, LEUKEMIA AND SEX CHROMATIN ANOMALIES*

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Cytological characteristics of both Down's syndrome and Klinefelter's syndrome have been described in the same individual (Hoffenberg and Jackson 1957, Ford et al. 1959, Lanman et al. 1960, Hustin et al. 1961, Kaplan 1961, Hamerton et al. 1962). Klinefelter's syndrome and Down's syndrome are associated together more often than can occur purely by chance and sometimes these conditions occur with leukemia in the same sibship (Mosier et al. 1960, Baikie et al. 1961, Bergmann 1963, Polani 1963). A correlation between sex chromatin abnormality and acute leukemia is being increasingly noted (Harnden 1960, Baikie et al. 1961, Kemp et al. 1961, Bergmann 1963), although its statistical significance is dubious. An attempt has been done in the present study to determine the association between sex chromatin anomalies, mongolism and leukemia.

Material and Methods

One hundred normal healthy males and one hundred females were studied initially as controls. Patients with Down's syndrome were selected on the basis of clinical features, particularly mental deficiency, upward slant of the eyes and the typical dermatoglyphics such as a distal axial triradius, presence of ten ulnar loops or radial loops in the fourth or fifth finger, a third interdigital loop in the palm and an arch tibial or loop distal in the foot. The normal sibs of these patients and both parents were also studied. Eighteen families were studied in this group and the total number of persons studied was one hundred and three.

Four cases of acute lymphoblastic leukemia and one of chronic myeloid leukemia and their sibs were also examined.

The staining method of Klinger and Ludwig, as modified by Barr (1960) was used for study of sex chromatin.

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Results

In the healthy females, sex chromatin positivity was found to vary between 28% and 64% with a mean of 41.96%. In the healthy males, sex chromatin positivity was found to vary from 0 to 3%, with a mean frequency of 0.9%. Of 19 patients with Down's syndrome, one male patient was found to have 15% chromatin positive nuclei. His family members were normal.

This child Papoo, aged 11 years, somatically male, was mentally retarded since early infancy. The mother's age at the time of his birth was 37 years. The child had many features seen in mongolism, viz. upward slant of eyes, epicanthic folds, low set ears, low hair line, incurving of little fingers, an arch tibial with a deep cleft between first and second toes, hypotonia and gross mental deficiency. Submandibular glands were seen to be enlarged, firm and matted together. There was a soft systolic murmur over the third left parasternal region. His standing height was 45 inches, arm span 45 inches, sitting height 23 inches, head circumference 19½ inches, ratio of upper segment to total height was 51%. All the seven siblings of this child were normal.

No abnormalities of nuclear sex were found in the other patients with Down's syndrome or their family members.

All the five cases of leukemia and their siblings studied had nuclear sex in conformity with their somatic sex.

Discussion

Cytologic characteristics of both mongolism and Klinefelter's syndrome have been found in the same patient. These patients tend to be born at advanced maternal ages. The average age of the mother in such reported cases was 37.4 years. A pair of monozygotic twins with cytological characteristics of both conditions has been reported (Fuchs and Riis 1954). It would be of interest to know whether they occur more often than could be anticipated by chance, because if so it might suggest that some people have a genetic tendency for non-disjunction. Two surveys covering 133 patients with Down's syndrome have shown two of these persons to have chromatin positive Klinefelter's syndrome (Hamerton et al. 1962). Taking into account the maternal age effect also, it has been estimated that the frequency of Klinefelter's syndrome among patients with Down's syndrome might be of the order of 1 in 100 (Polani 1963).

That there may be a tendency for chromosomal non-disjunction in some persons presumably on a genetic basis is suggested also by a study of ten sibships selected from a population of mental defectives, for having a chromatin positive male. In two, there was also a person with Down's syndrome (Mosier et al. 1960).

In certain families, there is a tendency for chromosomal errors of presumptive non-disjunction origin to occur in several members. In one such instructive family, an XXXY male, a male with leukemia and two 21-trisomic mongoloid females occurred. In another, a sex chromosomal anomaly occurred in one member and leukemia in two in the same sibship (Baikie et al. 1961). In yet another, trisomy for chromosome 13-15 and XO gonadal dysgenesis occurred in two sisters (Therman...