Case reports

TABLE

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<th>CASES OF RING G22 IDENTIFIED BY CHROMOSOME Q- OR G-BANDING</th>
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<td>High palate</td>
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The main interest in this case is the level of intelligence, for all previous G22 ring cases have indicated severe mental retardation. On the Griffiths Mental Development Scale our patient has a performance quotient in the low normal range (71) but her quotient for verbal skills was much lower (47). Though in this case the latter may be depressed by home environment it is in agreement with the pronounced slowness in speech development in other recognized ring G22 cases. The two patients of Crandall et al (1972) had IQ's of 10 and 22 on the Binet scale, one showing no speech and the other very slow speech development. The twins described by Lindenbaum et al (1973) had IQ's of 35 to 40 by the Merrill-Palmer test, they were hyperkinetic and often resorted to 'low-pitched cries than to recognizable words'. The case of Nelson, cited by Lindenbaum et al (1973), and the two cases of Noel (personal communication 1975) also had severe mental retardation. Neither of the two latter cases had any speech.

The intelligence of the girl reported here is within the subnormal range with an overall DQ of 59 and above those cases of ring G22 previously described. As with all chromosomal deletions the possible variable amount of chromatin loss in different cases could account for the variability in expression.

For the palm prints, and to Mr W. T. A. Donohoe and Miss P. Ball for technical assistance.

D. S. K. BROOKFIELD* and S. WALKER

Institute of Child Health, Alder Hey Hospital and Cytogenetics Unit, University of Liverpool

REFERENCES


Familial Ebstein's anomaly

Summary. A family is described in which both a father and son are affected with Ebstein's anomaly, while several other family members manifest different cardiac malformations. Five additional instances of familial Ebstein's anomaly

We are grateful to Dr R. J. Derham for access to his patient, to Dr L. Rosenbloom and Miss E. J. Horn for the developmental assessments, to Dr D. W. Fielding for the palm prints, and to Mr W. T. A. Donohoe and Miss P. Ball for technical assistance.

D. S. K. BROOKFIELD* and S. WALKER

Institute of Child Health, Alder Hey Hospital and Cytogenetics Unit, University of Liverpool

* Present address: c/o Department of Child Health, Faculty of Medicine, University of Dar es Salaam, P.O. Box 20693, Dar es Salaam, Tanzania.
were found in the literature and compared with our family. Inspection of possible modes of inheritance in this group of families suggests that Ebstein's anomaly is probably inherited as a polygenic character with a threshold phenomenon.

Ebstein's anomaly of the tricuspid valve is a rare condition which constitutes approximately 1% of all congenital cardiac malformations (Nadas and Fyler, 1972). Only a few familial cases were found among more than 500 cases reported by Watson (1974). We wish to present a family in which father and son were affected with Ebstein's anomaly and to review the familial cases already published in order to establish the possible mode of inheritance of this cardiac malformation.

**Family history**

The parents (I.1, I.2) of the proband II.2 (Fig.) are not consanguineous and are of East European (Polish) origin. The father (II.2), the first proband, had an older sister (II.3) who died of uninvestigated congenital cyanotic heart disease at the age of 1 month. Of his two sons (III.1 and III.2) one (III.1) was affected with cor triloculare biaatriale and the other (III.2) with Ebstein's anomaly. All other living family members are healthy.

**Report of cases**

**II.2.** The proband, a 28-year-old man, was referred to the Department of Human Genetics after finding cor triloculare biaatriale during the necropsy of his 4-month-old son (II.1). The proband has been cyanotic most of his life and experienced recurrent thrombotic episodes related to polycythaemia. At the age of 20, he underwent detailed cardiac investigation. Catheterization showed a bidirectional shunt at the atrial level, with displacement of the right valve into the right ventricle. The 'three bubble effect', characteristic of Ebstein's anomaly of the tricuspid valve, was evident on cineangiography. The atrial septal defect was surgically repaired thereby alleviating the severe polycythaemia.

Since his operation the patient has suffered from recurrent attacks of atrial tachycardia and dyspnoea.

His son (III.2), the second proband, weighed 3.8 kg at birth after an uneventful full-term pregnancy and a normal delivery; he was persistently cyanotic from birth. Investigation at the age of 4 days revealed tachycardia and tachypnoea without murmurs or any indication of cardiac failure. The electrocardiogram showed axis +90°, PR interval of 0.12 s, and signs of an enlarged left ventricle. Chest x-ray examination showed an enlarged right atrium and poor vascular markings of the lungs, cardiac catheterization showed a greatly enlarged right atrium, downward displacement of the tricuspid valve, a small right ventricle, and a large atrial septal defect. Progressive amelioration of his cardiac condition was noted during the following months.

**Discussion**

Although the vast majority of instances of Ebstein's anomaly are sporadic in nature (Watson, 1974), five familial cases, in addition to that reported here, were found in the literature (Table). In three of these families, two sibs each had Ebstein's anomaly (Gouffault, Le Damany, and Lenegre, 1960; Gueron et al., 1966; Simcha and Bonham-Carter, 1971), while in the remaining two families a father and his daughter and an uncle and his nephew were affected. Gouffault et al. (1960) described Ebstein's anomaly of the tricuspid valve and a similar malformation of the mitral valve in sibs. This mitral valve deformity is considered to be the left counterpart of classic Ebstein's anomaly (Gouffault et al., 1960; Donegan et al., 1968).

The occurrence of identical congenital cardiac deformities in several family members has been documented (Nora, 1968; Emanuel, 1970; Fuhrman, 1968). In addition, different congenital cardiac deformities also can occur within families (Zetterqvist, 1971; Kumar et al., 1971). The proband of our family had a son who died of cor triloculare biaatriale which is embryologically and anatomically different from Ebstein's anomaly (Streeter, 1951; Goerttler, 1958), and his elder sister died of a congenital cyanotic heart disease, the exact nature of which was not established.

The familial cases of Ebstein's anomaly strongly suggest an hereditary basis whose mode of inheritance is not clear. Watson (1974) found an equal occurrence of affected males and females in his series of 505 cases; however, a preponderance of females affected has also been reported (Simcha and Bonham-Carter, 1971). In the cases summarized in the Table, the female-to-male ratio is 3:9 which does not differ statistically from unity \( x^2 = 3.0 \) 0.05 < \( P < 0.10 \). Since in the series of 505 cases both sexes are equally affected and male-to-male
transmission was noted in family VI, sex limitation and/or sex linkage can be effectively ruled out. The remaining possible modes of transmission are, therefore, autosomal recessive, autosomal dominant with reduced penetrance, or polygenic inheritance with a threshold. It is not possible to pool the six families and to compare them with the series of about 500 cases (Watson, 1974) in order to test the mode of inheritance, since data concerning family size and number of possible additional patients in this large series are grossly inadequate. On the other hand, the sample of the six families alone is also too small for a significant genetic analysis. In families I, II, IV, an autosomal recessive inheritance is possible as only sibs were affected and furthermore the parents of family II were second cousins. The pedigree of families V and VI in which both a parent and child were affected suggest autosomal dominant inheritance. Incomplete penetrance of a mutant dominant gene may explain the occurrence of the anomaly in the nephew and uncle (family III) without an affected parent. If a common hereditary basis is sought in all 6 families, one must seriously consider polygenic inheritance with a threshold phenomena resulting in an increased risk to both first and second degree relatives. In several other isolated congenital heart malformations, e.g. ventricular septal defect, pulmonary stenosis, atrial septal defect, and persistent ductus arteriosus (Fuhrman, 1968; Nora, MacNamara, and Fraser, 1967; Nora, McGill, and MacNamara, 1970), multifactorial inheritance is considered to be the most probable mode of transmission. We suggest that Ebstein’s anomaly also is a threshold character transmitted through multifactorial inheritance, a mechanism that explains the recurrence of this anomaly in the various families described above.

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A. ROSENMANN, I. ARAD, A. SIMCHA, and T. SCHAAP

From the Departments of Human Genetics and Pediatrics, Hadassah Hebrew University Medical Center, Jerusalem, Israel

REFERENCES


Partial trisomy D: a diagnostic and cytogenetic dilemma*

Summary. An 18-month-old proposita with psychomotor retardation and other congenital abnormalities is presented. Chromosomal analysis of both parents proved normal. However, the karyotype of the proposita contained 47 chromosomes in both lymphocytes and cultured fibroblasts. The marker chromosome proved to be a deleted No. 14 or 15. Comparison of the reported cases of partial trisomy D indicates that a definitive clinical syndrome is not apparent in either case.

With the institution of chromosome banding techniques, many new 'partial trisomy' syndromes have been identified (Lewandowski and Yunis, 1975). The majority of these cases result from clinically abnormal, chromosomally unbalanced segregants of reciprocal translocations. Therefore, karyotypic analysis allows the identification of the additional chromosomal material so that phenotypic-karyotypic correlations are possible. However, other instances of partial trisomy are the result of non-disjunction of apparently deleted chromosomes, leading to an extra abnormal marker chromosome.

We wish to describe a child with psychomotor retardation and congenital anomalies possessing 47 chromosomes with partial trisomy 'D'. Banding revealed that the marker chromosome was definitely not a No. 13 and its assignment to either No. 14 or 15 was difficult.

Case report and family history

The proposita is the only child of healthy, unrelated parents, the mother being 26 years old and the father 27. The mother had had one previous miscarriage. During the present pregnancy, she received hormone therapy because of vaginal bleeding in the second month. The proposita was born at term after a normal delivery and weighed 2700 g. Bilateral congenital dislocation of the hip was diagnosed shortly after birth.

The baby was referred to the Department of Human Genetics at 18 months of age because of psychomotor retardation, generalized hypotonia, seizures during the last two months, and additional congenital anomalies. On physical examination a left epicanthal fold and divergent strabismus of the right eye were observed (Fig. 1a). The ears were small with very small antehelices. Scars from the removal of preauricular skin tags were evident. The nares were anteverted; the palate was high and arched. A low hair line was observed on a short neck. A large cavernous haemangioma was present on the right forearm (Fig. 1b). The fingers and toes seemed short and somewhat large. Hypotonia was pronounced and head lag was present. Fundoscopy, audiometry, electroencephalogram, x-rays of skull and chest, and bone age, as well as haematological examination and urinary screening tests for mucopolysaccharidosis and amino acids were all within normal limits.

Cytogenetic studies

Chromosomes, from phytohaemagglutinin (PHA) stimulated peripheral lymphocytes, were studied in the proposita and her parents. In addition, cultured skin fibroblasts of the proposita were examined. The initiation, culture, and harvest of cells for cytogenetic evaluation were according to standard methods. G-banding patterns were achieved by the 'hot-plate' Giemsa pH 9 technique of Patil et al (1971).

The karyotypes of the parents were numerically and structurally normal. In both lymphocytes and fibroblasts, the proposita had a modal chromosome number of 47 with an extra small acrocentric chromosome, the same size and morphology as a G group element. This marker participated in satellite association with other acrocentrics in 40% of the metaphases. After G-banding (Fig. 2), it became apparent that the marker was not a member of Group G, but did fit the pattern of either a deleted No. 14 or 15. However, without the presence of the distal portion of the long arm, allowing distinction between these two chromosomes, precise identification of the marker was difficult. None the less, based on the proximity to the centromere and size of the proximal darkly staining wide band (14q21), we felt that this

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A Rosenmann, I Arad, A Simcha and T Schaap

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