A case of twin chimerism

Summary. A case of twin chimerism is presented and shown by cytogenetic studies, red cell grouping, and white cell HL-A typing. The sex of each twin is confirmed by examination of buccal smears and their chimeric state is confirmed by non-reactivity in the mixed lymphocyte culture system. The results of these investigations are discussed.

Chorionic vascular anastomoses are usually present between dissimilar bovine twin embryos, and when Owen (1945) published his work on 'Immunogenetic consequences of vascular anastomoses between bovine twins' it was realized that primordial red cells belonging to one twin take root in the other twin. This occurrence is rare in the human situation. The first example of human chimerism in twins was reported by Dunsford et al (1953). It was discovered when the propositus Mrs McK was found to have a mixture of two kinds of blood. Since this first case there have only been 12 further examples reported, 8 of these cases of twin chimeras are excellently summarized by Race and Sanger (1968). Gundolf described a Danish pair (1970) Ducos et al (1970) a French pair, Crookston et al (1970) a Canadian pair, and Kasser and Nennstiel (1971) a German pair.

The case to be presented differs from the majority of previously reported cases in that it was discovered after cytogenetic studies and not through blood grouping. As there was no mixture involving the ABO blood group system this example of twin chimerism could easily have been missed.

Case report

AK and PK are a pair of dissimilar, unlike sexed twins. At the age of 2 months the girl, AK, was suspected of having hypothyroidism; this was confirmed at 3 months. She responded to appropriate treatment and is now euthyroidic. The boy, PK, has shown a normal developmental pattern, apart from bilateral undescended testes, which are still impalpable at the age of 21 months. In addition to the hypothyroidism AK was noticed to have an odd facies, and for this reason a chromosome analysis was carried out.

Cytogenetic studies

Chromosome studies from short-term lymphocyte cultures were carried out on three separate occasions on the twins, and once on their elder female sib, and parents. Chromosome analyses of the parents and sib yielded normal results. A total of 100 cells from each twin were karyotyped, and the results of these studies can be seen in Table I.

![Table I](http://jmg.bmj.com/10.1136/jmg.13.6.528)

Buccal smears were made on several different occasions to try to ascertain with certainty the sex of each twin.

Red cell grouping: secretor status and HL-A typing

Standard serological techniques were used in the determination of the red cell groups and secretor status. HL-A typing of the lymphocytes was carried out using the lymphocyte cytotoxicity technique. The results are shown in the Fig.

Despite the extensive red cell grouping carried out, a chimeric mixture showing mixed field agglutination was only obtained with anti-s sera. Separation of the two populations was attempted with difficulty, as the anti-s serum only reacted by the indirect antiglobulin technique. 26% of AK's red cells and 10% of PK's red cells had the genotype Ss. 74% of AK's and 90% of PK's red cells had the genotype SS. Both twins were shown to have two populations of lymphocytes which could be separated into major (strong reacting) and minor (weak reacting) groups. Taken together these two populations showed all the HL-A antigens detectable in the mother and father, giving further confirmation of
twin chimerism. The mixture of HL-A antigens in PK's lymphocytes was much more difficult to show, as the percentage of lymphocytes belonging to the minor HL-A groups was much less than for AK. From the results of the chromosome analysis, where in AK 34% and in PK 25% of the lymphocytes had the karyotype 46,XX, it is reasonable to suppose that the genotype of the 46,XX cells is 3/7, W18 (the minor groups), and that the genotype of the 46,XY cells is 1,11/5, W15 (the major groups).

**Mixed lymphocyte reactivity**

As a mixture was found in the HL-A system of both twins it was decided to confirm the presence of twin chimerism by using the mixed lymphocyte culture technique. These were very kindly carried out by Dr Jillian A. Need, Department of Obstetrics and Gynaecology, University of Leeds. Six-day cultures of peripheral blood lymphocytes were used, tritiated thymidine is added during the last 16 hours of culture, and the amount incorporated is used as an indication of the amount of DNA synthesis, hence the degree of lymphocyte transformation in response to antigenic stimulation. Both twins' lymphocytes alone showed a normal response to then on specific stimulation of phytohaemagglutinin (PHA). AK had a stimulation index of 66.7 and PK had a stimulation index of 37.9.

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\text{stimulation index} = \frac{\text{cpm with PHA}}{\text{cpm without PHA}}
\]

When their lymphocytes were mixed and cultured together no reaction occurred, the stimulation index being calculated at 0.95. As anticipated, this technique showed complete lack of reactivity between AK's and PK's lymphocytes, i.e. neither twins' lymphocytes regard the other's lymphocytes as antigenically foreign.

**Discussion**

The majority of previously reported cases of twin chimerism have been discovered during routine blood grouping, the mixture of red cells usually involving the ABO blood group system. The interesting feature of this case is that had blood grouping alone been carried out, this case of human twin chimerism would have been overlooked. Only one mixture involving the MNS blood group system was found, despite careful and extensive blood grouping studies of 12 different systems. It was the karyotype analysis that first alerted us to the possibility, followed by the demonstration of mixed HL-A antigens, which helped confirm the presence of chimerism in this case. Is it possible, therefore, that twin chimerism is commoner than at first thought, and missed in the ABO compatible situation?

For the chimeric state to occur, the exchange of blood must take place in early fetal life, i.e. the immigrant primordial cells are not regarded as foreign.
A case of ring chromosome G22

Summary. A girl with a G22 ring chromosome is described. There are few physical abnormalities, performance quotient is in the low normal range but verbal skills are much more retarded.

Many patients with ring G chromosomes have been reported since that of Lejeune et al (1964), but until chromosome banding techniques were available the specific identity of the ring was in doubt. Only four cases of definite ring G22, identified by Q- or G-banding, have been published to our knowledge—two by Crandall, et al (1972) and a set of twins by Lindenbaum, Bobrow, and Barber (1973). Three other cases are known, two by B. Noel (personal communication 1975) one of which is a mosaic 46,XY/46,XY,22r, and one by R. Nelson (cited by Lindenbaum et al, 1973).

We wish to report a further patient identified by G-banding who is less retarded than those previously described.

Case report

The patient, a girl, was born in June 1971 and was initially admitted to Alder Hey Children's Hospital at the age of 8½ months with an upper respiratory tract infection and bilateral otitis media. A week previously she had developed measles. The otitis media resolved with ampicillin and she was discharged from hospital after eleven days.

While she was in hospital it was noted that she had distinct epicanthic folds and a rounded face with prominent large ears. Her fontanelle was closed and her head circumference was below the third centile at 42.5 cm. Her weight was on the twentieth centile at 7100 g. The hands, including palmar creases, and feet were normal.

The patient's birth was normal and she was a vertex delivery. The pregnancy was uneventful and she weighed 3000 g at birth. Her mother was aged 25 years and was in good health. Her father was aged 29 years and was employed as a crane driver until six months.