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Serum IgG levels in feto-fetal transfusion syndrome

Comments on a discrepancy in the colour of some newborn twins have been made since Biblical times (Genesis xxv, 25), but it is only recently that the phenomenon peculiar to monozygotic twins has actually been defined and become known as the feto-fetal or twin-twin transfusion syndrome. The subject was recently reviewed by Benirschke and Kim (1973).

Details of the haematological picture found in both donor and recipient twin are well known, and Kloosterman (1963) has also discussed some of the consequences of the transfer of plasma proteins between such twins. Little reference, however, has been made to serum immunoglobulin levels, the depletion of which might well result in an imbalance in the immunological status of the two infants. A case which illustrates this problem is presented.

Case report

A 33-year-old Caucasian woman was delivered of twin male infants, by caesarean section, at 38 weeks' gestation. Apart from a transient urinary tract infection in the second trimester, this third pregnancy had been uneventful. A diagnosis of twins was confirmed radiologically in the 28th week.

At birth there was a striking difference in the appearance of the two babies. The first twin (the recipient), weighing 2.7 kg (occipitofrontal circumference 35 cm), was plethoric and vigorous, whereas the second twin (the donor), weighing 1.56 kg (occipitofrontal circumference 30.5 cm), was extremely pale, meconium stained, and showed signs of intrauterine growth retardation.

The appearance of the monochorionic diamniotic placenta was consistent with that found in cases of feto-fetal transfusion (Strong and Corney, 1967), and on microscopical examination the villi of the recipient portion were uniformly mature and deeply congested, whereas those of the donor appeared oedematous, with a well-preserved trophoblast layer and the vessels contained a few normoblasts and white cell precursors. The results of investigations on cord blood and blood samples taken during the first 28 weeks of life are shown in the Table and Fig.

Total proteins were determined by the density column (Lowry and Hunter, 1945). Cellulose acetate electrophoresis was carried out, the strips scanned using a Zeiss absorbance recorder with integrating recorder, and the albumin concentration calculated using the total protein figure obtained from the density column. Transferrin, α1 antitrypsin, and immunoglobulins G, A, and M were determined by radial immunodiffusion. Commercial
antiseras and standards (Behring) were used, the plates were prepared by ourselves, and quality control was carried out using a known pool and the MRC 67/99 standard for immunoglobulins.

They were alike in blood groups (ABO Rhesus, MN, Kell, and Duffy) and red cell enzymes phosphoglucomutase (PGM1), adenylate kinase, adenosine deaminase, and phosphoglucunate dehydrogenase. As a result of these tests, it was estimated that there was 90% probability of monozygosity.

Twin I made good progress. There were no stigmata of intrauterine infection associated with the raised serum IgM and this subsequently fell to normal levels. At birth, twin 2 was severely asphyxiated, pale, and limp, with a heart rate of 80 per minute. After endotracheal intubation and intermittent positive pressure ventilation, regular respirations were established after 10 minutes. On recovery from the asphyxia, though still pale, he was neither shocked (systolic blood pressure 60 mmHg), nor acidicotic (capillary blood pH 7.34, aged 2 hours). He was given a slow transfusion of 26 ml fresh heparinized blood which he tolerated well. However, the following day he became grossly oedematous. The reason for this was uncertain though the low plasma albumin may have been a contributory factor. Urine was free from protein, cells, and casts and there was no sign of congestive cardiac failure. The oedema subsided after the first week. Thereafter, he made slow progress, initially needing gastric tube feeding. During the third week, he was given a 5-day course of antibiotics for a suspected, but bacteriologically unproven, infection and started oral iron twice daily after the first month. He received a second blood transfusion at the age of 5 weeks, after which he became more active and his feeding improved.

At home, both twins made good progress, gaining weight satisfactorily, and the proportionate weight discrepancy decreased. At 10 weeks both infants had upper respiratory tract infections. Twin 1 recovered in a few days but twin 2 developed a chest infection and symptoms persisted for over 2 weeks. Thereafter, there were no further problems.

**Discussion**

Detailed examination of the protein chemistry during the first weeks of life shows some interesting findings. First, total protein, albumin, transferrin, and α1 antitrypsin levels in the cord blood of the donor twin were approximately 46, 54, 30, and 64%, respectively, of those in the recipient twin, and these could be explained as a consequence of the feto-fetal transfusion. However, the immunoglobulin IgG shows a much greater discrepancy, the level in the donor twin being only 13% of that in the recipient, and in two further, but less severe cases of feto-fetal transfusion syndrome (Hb differences of 5·5 and 10·0 g/100 ml) the donor twin again had a much lower level of IgG—50% and 22%, respectively, of that in the recipient. In no other twin pair have we
found such a discrepancy. Factors which may influence the IgG level at birth include birthweight, placental size, and materno-fetal transfer. It has been shown that serum IgG concentrations in newborn singletons have some relation to birthweight. However, Yeung and Hobbs (1968) found that the levels in newborn twins related more closely to gestational age than to birthweight, and in a current study (E. M. Bryan and B. Slavin, unpublished data) we find that the twin of lower birthweight, in some cases, has the higher serum IgG level. Thus, birthweight alone is unlikely to account for the discrepancy. Yeung and Hobbs (1968) also found that small-for-dates babies had significantly reduced serum IgG levels at birth and that of 13 placentas studied the weights of 11 were more than 1 SD below the mean, but in our case the donor twin had the larger portion of the placenta. As the majority of immunoglobulins present in newborn sera are IgG and are of maternal origin, it seems likely that there may be some disturbance in placentation transfer in this condition.

Secondly, the recipient twin showed a rapid fall in all proteins by the third week of life—values in both twins approximating by the ninth week (Table). It appears that the high levels of the recipient twin at birth may have had an inhibitory effect on plasma protein synthesis during the first weeks of life. In their study of the development of immunoglobulins in singleton babies, Vlahovic et al. (1973) found this to be the case with IgG. Those infants with a relatively high serum IgG level at birth had significantly lower mean levels at both 3 and 6 months of age than those whose initial level was relatively low.

Summary

A case of feto-fetal transfusion syndrome is described. All serum protein levels were higher in the recipient twin, but the discrepancy was far greater in the case of the maternally produced immunoglobulin, IgG.

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