Familial haemolytic uraemic syndrome

Since the first report by Gasser et al. (1955) of the haemolytic uraemic syndrome (HUS) in childhood, this condition has remained relatively uncommon in Britain, which is not an endemic area. Reports have recently accumulated of 2 sibs affected, which prompted Kaplan et al. (1975) to review 41 families with 83 affected sibs. In the majority of these pairs the syndrome occurred simultaneously, implying an infective aetiology, as in the environmental study by Van Weringen et al. (1974), or environmental factors, with a mortality of 19%. However, other pairs of similar age of onset, but where the presentation was separated by one or more years, were more likely to have a genetic basis. The mortality in this group was high (68%). Though rare, these genetic cases seem to be relatively more common in areas which are not endemic. We therefore report 4 cases of HUS occurring in the same family in two generations.

Case reports

Case 1. A 5-month-old boy was admitted to hospital on 1 December 1974 with a 7-day history of upper respiratory infection, associated with vomiting and anorexia. For 3 days he had been pale, and his urine blood stained. Examination showed marked anaemia and a blood pressure of 110/60 mmHg. The urine contained red cells. Initial investigations showed haemoglobin 4.5 g/dl, platelets $8 \times 10^9$/l, reticulocytes 8.5%; uraemia 23.3 mmol/l (140.4 mg/100 ml), fibrin degradation products 10-40 µmol/l. Blood film showed schistocytes and burr cells.

He was treated with blood transfusions, heparin, and hypotensive drugs. Urine output continued normally for the first month with the uraemia only slightly raised. A single dose of urokinase (20 000 U) was infused into the left renal artery on the seventh day after admission. The hypertension was extremely difficult to control despite treatment with minoxidil in large dosage (15 mg bd) and beta-adrenergic blockade. Renal failure became progressively more severe. A single peritoneal dialysis was carried out on 24 November 1976, but he steadily deteriorated and died on the 5th of January. Permission was not obtained for an necropsy.

Case 3. A 26-year-old woman was admitted in October 1966, 5 weeks after a normal pregnancy and delivery with a 1-week history of anorexia, diarrhoea, and vomiting. 3 weeks previously stilboestrol had been given for 10 days to suppress lactation. She was pale with a puffy face. Initial investigations: Hb 8.5 g/dl, platelets $142 \times 10^9$/l, reticulocytes 11%, and blood urea 57 mmol/l (345 mg/100 ml). A progressive downhill course followed, despite conventional heparin and dialysis therapy, and complications included convulsions and epistaxis, pulmonary oedema, and pericarditis. She died 2 months after admission. Histology: both biopsy and necropsy showed the characteristic thrombi in glomerular tufts and afferent arterioles of HUS or thrombotic thrombocytopenic purpura.

Case 4. The 23-year-old sister of Case 3 was admitted, in January 1963 with an acute history of nausea, vomiting, facial and ankle oedema. During the next week she became oliguric and blood urea rose to 53.8 mmol/l (324 mg/100ml). Blood pressure was 180/120 mmHg. Subsequently she became anuric and had convulsions and pulmonary oedema. Despite dialysis, she died 2 weeks after admission. At post-mortem the kidneys were large and firm and histology again showed thrombotic microangiopathy and the typical lesions of HUS or thrombotic thrombocytopenic purpura.

Family history

The relevant portion of the family tree is shown in the Fig. The affected boys' parents did not appear to be related, and the father's relatives had no history of HUS. The maternal great uncle died at
the age of 24 with the diagnosis of Bright’s disease. Perhaps today’s diagnosis would have been thrombotic thrombocytopenic purpura or HUS. The son of Case 3 is reported to be in good health.

Discussion

The fatal outcome in this family, the study by Farr et al. (1975), and the reports of 3 infant sibs (Kaplan et al., 1975) and 4 sibs from Zurich (Blättler et al., 1975) all of whom died, together indicate a grave prognosis in cases where more than 2 family members are affected. It seems likely that the stronger the genetic evidence, the worse the prognosis. This family and its case pattern strongly support a genetic predisposition as an aetiological factor in some cases of HUS. Farr et al. (1975), however, were unable to identify red cell or HLA genetic markers in their family study. The inheritance pattern in this family, where first-cousin marriages were frequent, would fit an autosomal recessive rather than dominant mode of transmission. Dialysis and renal transplantation offer survival prospects to some victims, but it is doubtful whether conventional therapeutic measures for HUS can alter the outcome in these cases.

Summary

Two pairs of cases of HUS are reported from two generations in a family where first-cousin marriages have been frequent. All 4 died. We suggest that there is a high expected mortality in those familial cases of HUS where genetic factors are strongest. An autosomal recessive inheritance pattern is suggested in this family.

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References


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Congenital heart block and hypothyroidism

Complete heart block has been reported in association with thyrotoxicosis (Stern et al., 1970; Kernoff et al., 1973; Fairfax and Leatham, 1975), and hypothyroidism (Singh et al., 1973; Fairfax and Leatham, 1975) in adults. Autoimmunity (Zoob and Smith, 1963) and myocarditis (Hudson, 1965) have been implicated. I describe a case here in which hypothyroidism was associated with congenital heart block. I have not been able to discover another such case in the literature.

Case report

The mother of the patient, aged 30, blood group B Rh positive, had a previous normal child. She developed rheumatoid arthritis after his birth and was treated with aspirin alone. She became pregnant again soon after diagnosis. There is no relevant family history.

In this pregnancy polyhydramnios was noted by the obstetrician at 36 weeks and she had mild oedema of the legs at 38 weeks’ gestation, treated with hydrochlorothiazide, reserpine, and potassium chloride.