Pelvic examination showed that it was normal and adequate for vaginal delivery. Her haemoglobin at the time of booking was 12 g/dl, group O, rhesus positive. Haemoglobin electrophoretic pattern was A + C. Serological test was negative. Urine analysis showed no abnormality.

The pregnancy progressed normally and she went into labour spontaneously at term. On 18 February 1976, after being in labour for 9 hours 45 minutes, she delivered a normal, healthy, infant weighing 2830 g with an Apgar score of 7. The puerperium was uneventful. Both mother and the baby were in a satisfactory condition.

Comment

Nephroblastoma is a malignant condition of infancy and childhood. The tumour is usually unilateral, though it may rarely be bilateral. The survival rate in this disease has improved in recent years, but cytotoxic and radiation therapy usually affect fertility. In our patient such treatment did not affect fertility.

We thank Mr Elliot Philipp for permission to report this case.

2 British Medical Journal, 1976, 1, 1166.

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Congenital factor XIII deficiency in a neonate

Congenital factor XIII deficiency is rare. Only two cases have been described in the newborn. The diagnosis is simple and important, since the condition is readily treated with prophylactic factor XIII concentrate. We present a further case.

Case report

A girl was born at term by normal delivery weighing 3034 g. There was no family history of a bleeding disorder or consanguinity. When 7 days old the cord stump separated and she started to bleed from her umbilicus. The bleeding slowly worsened, leading to her admission at 10 days. Examination showed a healthy looking infant, not shocked or anaemic. Venous blood oozed from the base of her umbilicus, oozing which was a friable clot. Local measures failed to stem the bleeding. Initial routine coagulation screening (Thrombotest, Normotest, prothrombin time, kaolin cephalin clotting time, and thrombin time) were all normal. Fibrin clot solubility tests showed a rapid solubility in 5 min uroso solution, so factor XIII deficiency was provisionally diagnosed. The bleeding arrested without recurrence during a transfusion of 80 ml stored bank blood.

Prophylactic treatment was started after one month with an infusion (4 ml/kg) of fresh frozen plasma (FFP). Regular intravenous injections (4 ml) of factor XIII concentrate (Hoechst) were started the following month at intervals determined by the results of preinjection clot solubility tests. Apart from a small epistaxis the day before the first factor XIII injection, no bleeding episodes occurred. The table shows results of the clot solubility studies. The diagnosis was confirmed by the absence of factor XIII subunit A on immunoelectrophoresis and the return to normal of the clot solubility with reappearance of subunit A after FFP and specific factor XIII concentrate injection.

Salicylate hepatotoxicity in systemic lupus erythematosus: a common occurrence?

Acetylsalicylic acid (ASA) can induce abnormalities of liver function in patients with rheumatic fever, juvenile (and adult) rheumatoid arthritis, and systemic lupus erythematosus (SLE). How often this happens in SLE is not known, but it may be commoner than realised. We report our experience of aspirin hepatotoxicity in SLE.

Patients and results

During the 18 months to June 1978, 74 patients were admitted for SLE and eight for mixed connective tissue disease (MCTD). All had high titres of either anti-ds DNA antibody (Farr assay) or anti-RNP antibody (by counter-immunoelectrophoresis). All patients had at least one sequential multiplex analysis (SMA 12), which included serum albumin, globulin, bilirubin, alkaline phosphatase, and aspartate transaminase (serum AST; SGOT). Eight SLE and two MCTD patients had abnormal liver function tests. Three patients (SLE with lymphoma, SLE with pneumococcal pneumonia and raised bilirubin concentration, and MCTD with active myositis and raised serum alkaline phosphatase concentration) were not taking salicylate. Of the other seven, five had started taking acetylsalicylic acid (ASA) recently, two had not. The two who had not developed salicylate hepatitis were taking the drug for a shorter period (7 months and 1 month) than those who had developed the syndrome (7 months, 2 months, and 2 weeks).

Comment

Factor XIII deficiency was first described in 1960, although the existence of a plasma factor responsible for fibrin stabilisation has been known since 1944. Since then about 100 cases have been reported. Factor XIII is composed of two subunits. Subunit A carries the enzymatic activity and subunit S is the support unit. Inheritance is autosomal recessive and heterozygotes may be identified by measuring subunits A and S. We have shown the carrier state in both parents of our patient. No other family members are homozygotes.

Apart from wound bleeding, typically delayed, and easy bruising, umbilical bleeding is the commonest manifestation occurring in over 80% of reported cases. Unlike the more common hereditary coagulation disorders, intracranial bleeding is a frequent (25%) complication. Prophylactic treatment, recommended because of this risk, is feasible since factor XIII has a relatively long half-life of 12-14 days and is active in low concentrations (0-5-10), of normal. Factor XIII concentrate has superseded FFP in the management of congenital deficiency because of its higher activity (1 ml = 60 ml FFP) and a lower risk of hypersensitivity and hepatitis. We believe our patient is the youngest to start prophylactic treatment with factor XIII concentrate.

In only two other reported cases has the diagnosis been made in the newborn, despite its common presentation at that time. Delay in diagnosis occurs for two main reasons. Firstly, the stability of factor XIII in stored bank blood has resulted in haemostasis during transfusion and failure to pursue investigation. Secondly, the diagnosis has not been considered. Indeed, a recent review on neonatal bleeding failed to mention factor XIII deficiency. If the diagnosis is considered laboratory confirmation by clot solubility studies is simple and rapid.

We thank Dr L G Evans-Jones for his help and encouragement in reporting his patient.

2 Duckert, F, Jung, E, and Shmerling, D H, Thrombosis et Diathesis Haemorrhagica, 1960, 8, 179.
5 British Medical Journal, 1977, 2, 915.

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salicylic acid (1.8-3.6 g/day) in hospital (figure). The two other patients had taken acetylsalicylic acid before admission and had raised serum AST concentrations, which were subsequently normal. Serum AST concentrations were affected in all, and gamma-glutamyltransferase and glutamic-pyruvic transaminase concentrations were also affected in four patients. All other liver function tests were normal. No patient was taking other drugs (including alcohol) known to influence liver function tests, and all had negative tests for hepatitis B antigen.

Comment

The characteristics of aspirin hepatotoxicity have been clearly defined from this and previous studies. It is dose-dependent (generally requiring a blood concentration of 25 mg/100 ml) and is independent of the form of salicylate given. The biochemical changes (mainly affecting serum AST and serum alanine transaminase (ALT; SGPT)) concentrations are much more striking than structural changes in the liver, and the abnormalities are quickly reversible on stopping the drug. The liver damage due to salicylate seems to be a direct toxic effect of the drug. There are few markers of allergy in patients, either clinically, on histological examination of the liver, or on peripheral blood examination. In one study an associated rise in eosinophil count was noted in all of six patients with juvenile rheumatoid arthritis. In only one was this rise pronounced. None of our patients showed a peripheral blood eosinophilia. Liver biopsy was not performed in any of the patients with salicylate-related abnormalities. The histological changes are non-specific and resolve rapidly on aspirin withdrawal. Biopsy was therefore unjustifiable on ethical grounds. Similar arguments apply to rechallenge with aspirin to confirm the diagnosis, which has been shown to reproduce a predictable response without yielding further information (even when combined with biopsy).

The epidemiology of aspirin hepatotoxicity is not fully known, but the seven patients in this series who developed hepatotoxicity were the only ones known to be taking regular, high-dose salicylate treatment. This suggests that a substantial proportion of patients with SLE or MCTD will develop abnormalities of liver function when exposed to salicylates. Several of the patients reported in this study have required further analgesia and we have substituted diflunisal, an aspirin derivative without the ortho-acetyl group. Four patients were treated with diflunisal 500 mg twice daily. Over a two-month follow-up period no patients showed a rise in serum AST or other enzymes and the drug was well tolerated. This suggests that hepatotoxicity may be associated with the ortho-acetyl moiety of aspirin, and that diflunisal might be a useful alternative anti-inflammatory agent in SLE.

5. Wolff, J D, Metzger, A L, and Goldstein, R C, Annals of Internal Medicine, 1974, 80, 74.

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Sarcoid lesion in breast after probable sarcoidosis in lung

Sarcoid lesions in breast tissue are rare. Scadding1 described one case in which they occurred and cited five others, in one of which the diagnosis was considered doubtful.

Case report

A 22-year-old white woman was seen because of wheeze, but no cause was found. At follow-up three months later a chest radiograph showed nonspecific linear shadowing confined to the right upper lung. She had been a non-reactor to tuberculin at school but had not had BCG. At the time the x-ray shadow appeared she did not react to 10 TU but did react to 100 TU (20 mm). Laryngeal swabs were negative for acid-fast bacilli. She was given para aminosalicylic acid-isoniazid for eight months without any change in the radiological appearances. She subsequently underwent a Kveim test, which gave a negative result. Gas exchange was not impaired. Lung biopsy was not thought to be justifiable. The radiological abnormality regressed spontaneously and slowly over the next five years.

Seven years after her first appearance she was found to have a nodule in her right breast. This was excised and was seen to show the characteristic...