Medical Memoranda

Aplastic Anaemia in Pregnancy Remitting After Abortion

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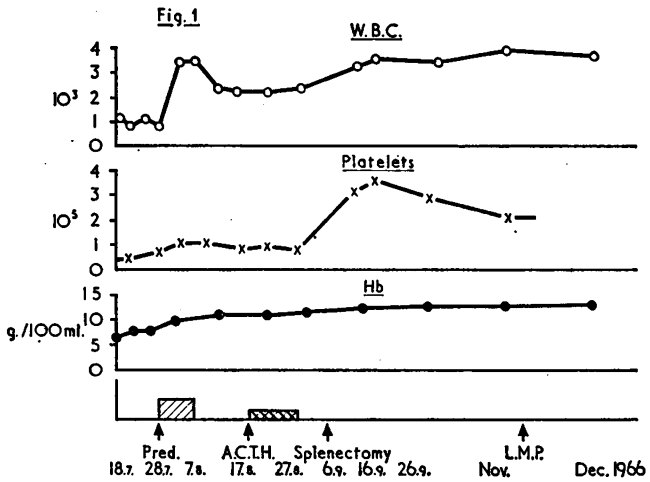
Acute progressive pancytopenia is rare in pregnancy. The following case is particularly interesting in that before pregnancy a somewhat similar though less severe haematological condition improved after splenectomy.

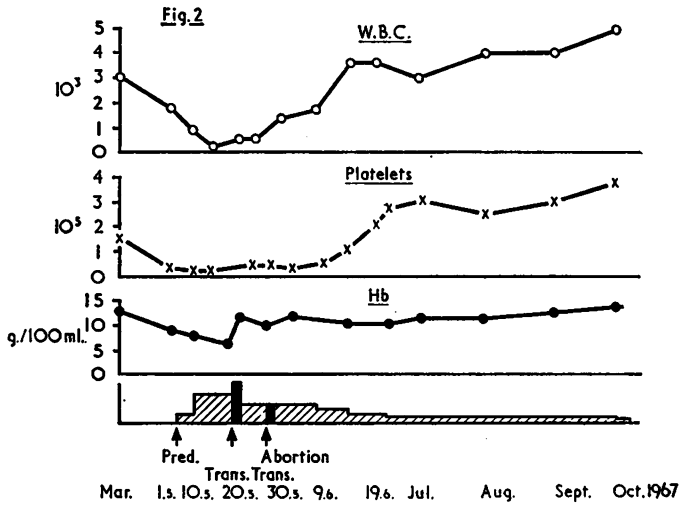
Case Report

First Admission (Fig. 1).—A 22-year-old recently married female clerk was admitted to Glasgow Royal Infirmary in July 1966 with a history suggestive of acute pyelonephritis. On examination she was febrile, with tenderness on pressure over the left hypochondrium and loin. The spleen tip was palpable. Investigations confirmed an acute urinary-tract infection, and in addition a pancytopenia was noted (haemoglobin 6.8 g./100 ml., W.B.C. 1,200/cu. mm., platelets 45,000/cu. mm.). She was iron-deficient (M.C.H.C. 27%, hypochromic, microcytic R.B.C., serum iron 20 μg./100 ml.). Sternal marrow showed active macronormoblastic erythropoiesis with a normal myeloid series. Megakarocytes were abundant. Haemosiderin granules were absent. Treatment with oral iron and ampicillin brought symptomatic improvement and a rise in haemoglobin. Leucopenia and thrombocytopenia persisted, only slightly improved by oral prednisolone. Hypersplenism was thought likely, and splenectomy was carried out in September. The spleen (175 g.) was macroscopically and microscopically normal. However, there was a gratifying if not unexpected improvement in her blood picture, and she was discharged home without any specific therapy.



Second Admission (Fig. 2).—The patient remained well until May 1967, when she complained of lethargy, nausea, anorexia, and recurrent epistaxes. There had been no vaginal bleeding since her last menstrual period in November 1966. The uterus was enlarged consistent with her dates (approximately 24 weeks' gestation). She was again pancytopenic (haemoglobin 8.4 g./100 ml., W.B.C. 1,800/cu. mm., platelets 25,000/cu. mm.). Other investigations showed reticulocytes 1%, serum iron normal, blood group A Rh-positive, neutrophil alkaline phosphatase activity normal, Coombs test negative, whole blood clotting-time (Lee and White) three minutes, prothrombin time normal, factors VIII and IX assay 100%, blood cultures negative, L.E. latex and L.E. cell test repeatedly negative, glucose-6-phosphate screening test normal. Attempts at sternal marrow aspiration were unsuccessful. An iliac crest bone biopsy taken with the Gardner needle showed an extremely hypocellular marrow with no organized erythroid or myeloid tissue. Megakaryocytes were not seen, histiocytes and plasma cells dominating the picture. Her condition deteriorated markedly despite blood transfusion, corticosteroids, and a variety of antibiotics and antifungal agents. She was moribund. Therapeutic abortion was arranged, but she aborted spontaneously. Uterine blood loss was negligible, the foetus (not examined) and membranes being expressed complete. Over the next few days there was an astonishing clinical improvement, haematological improvement following some weeks later.

There has been no evidence to suggest exposure to any agent known to cause aplastic anaemia. The patient remained very well and was aware of the potential hazards of further pregnancy.



Comment

Ehrlich (1888) was the first to describe aplastic anaemia in pregnancy. Since that time over 40 cases have been published, but Rovinsky (1959), after a thorough review of the literature, could find only 16 acceptable cases of primary refractory anaemia in association with pregnancy. He added another, and a further three have since been reported (King and Todd, 1964; Rosner and Sussman, 1964). The present case is unusual in that we were aware of a predilection to a pancytopenic state before pregnancy. On both occasions the cause of the pancytopenia was obscure, though it would appear that pregnancy was a major factor in causing the second and more serious illness. It may be that in susceptible individuals pregnancy excites an immune reaction, with consequent damage to the bone marrow, but this is merely hypothetical.

The report illustrates certain aspects of cardinal importance in management. Firstly, improvement, indeed survival, took place after abortion, and it is noteworthy that of the 20 cases hitherto described maternal survival occurred only after therapeutic or spontaneous delivery. Secondly, in his review Rovinsky noted that uterine blood loss after delivery was often surprisingly slight. This is confirmed in the present case.

Thus ideally treatment should be directed towards maintaining pregnancy so long as the health of the mother is not seriously impaired. If maternal survival is threatened then evacuation of the uterus should be carried out as soon as possible (Lachmann *et al.*, 1954; Lennard-Jones *et al.*, 1958).

I would like to thank Dr. A. Brown for permission to publish this report and for helpful advice and criticism. My thanks are also due to Dr. George McDonald, who carried out the iliac crest biopsy.

I. L. EVANS, M.B., CH.B., M.R.C.P.GLASG., M.R.C.P.ED.,
Late Medical Registrar, Royal Infirmary, Glasgow C.4.

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Mithramycin Treatment of Malignant Hypercalcaemia

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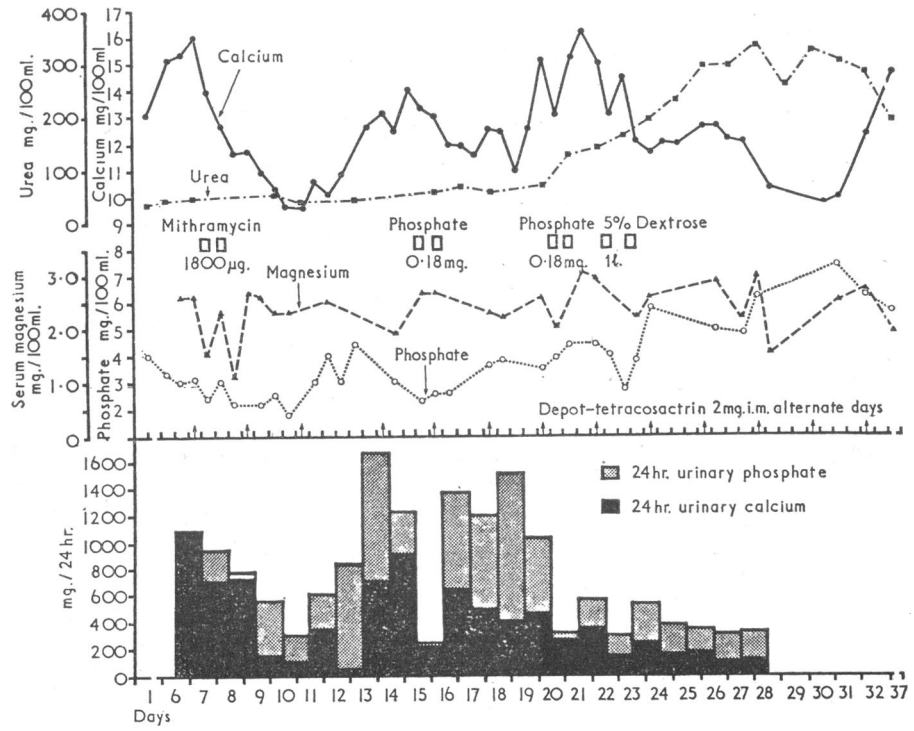
Mithramycin is an antibiotic with anti-tumour activity similar to actinomycin D. Hypocalcaemia has been reported following its use (Brown and Kennedy, 1965), and it has been suggested that it should be given in the emergency treatment of hypercalcaemia, particularly when associated with malignant disease (Parsons *et al.*, 1967 ; Baum, 1967). We report the findings in a patient with malignant hypercalcaemia treated in this way.

CASE REPORT

In 1963 a 47-year-old woman underwent a left radical mastectomy, followed by radiotherapy, for a stage 3 anaplastic carcinoma of the breast. In 1965 secondary deposits in the thoracic and lumbar spine and pelvis were treated with bilateral oophorectomy, local radiotherapy, androgens (fluoxymesterone and nandrolone), and prednisolone for eight months. In January 1967 further irradiation of the pelvis and upper femora was necessary. In May 1967 she was readmitted with severe pain in the lower back and legs, having been confined to bed since January and requiring opiates for control of her pain. On this admission her serum calcium was 7.7 mg./100 ml. and serum phosphorus 3.4 mg./100 ml. She was given blood transfusion and prednisolone, 30 mg. daily. As the pain was not relieved prednisolone was replaced after two weeks by intramuscular long-acting synthetic β^{1-24} corticotrophin (depot-tetracosactrin), 1 mg. on alternate days (Besser *et al.*, 1967). The pain rapidly disappeared and within a month she was mobilized and discharged, able to walk without sticks. In September 1967, after four days of nausea, vomiting, and headache, she was found to have hypercalcaemia and was readmitted.

Investigations on Admission.—Serum calcium 13.1 mg./100 ml. ; phosphorus 4.0 mg./100 ml. ; magnesium 2.6 mg./100 ml. ; alkaline phosphatase 8 K.A. units/l. ; bilirubin 0.8 mg./100 ml. ; aspartate aminotransferase 38 units/l. ; proteins and electrophoretic pattern normal ; urea 36 mg./100 ml. ; potassium 4.6 mEq/l. ; sodium 131 mEq/l. ; chloride 85 mEq/l. ; bicarbonate 35 mEq/l. ; haemoglobin 12.1 g./100 ml. ; white cell count 6,000/cu. mm., differential normal ; urinary calcium excretion 1,180 mg./24 hours ; phosphorus 946 mg./24 hours ; creatinine clearance 42 ml./min. ; urine analysis —trace of protein, no glycosuria, bacteriologically sterile.

The dose of depot-tetracosactrin was increased to 2 mg. on alternate days, but nevertheless the serum calcium rose to 16.0 mg./100 ml. Therefore mithramycin was administered. Two doses were given on consecutive days: 25 μg./kg. (1.8 mg.) was infused intravenously over eight hours in 1 litre of 5% dextrose on each day. There was a rapid fall in serum calcium and magnesium and in urinary calcium and phosphate excretion (see Chart), and a smaller fall



Changes in serum calcium, magnesium, phosphate, and urea and in urinary calcium and phosphate excretion in a patient treated with intravenous mithramycin, phosphate, and 5% dextrose.