MEDICAL MEMORANDA

Disseminated Intravascular Coagulation with Thymoma-associated Cushing's Syndrome

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Increased concentrations of certain clotting factors have been noted (Ozsoylu *et al.*, 1962) and the possibility of a hypercoagulable state occurring in Cushing's syndrome was supported by Parkhimovich (1969) who reported a high incidence of thromboembolic phenomena frequently associated with disturbances of the coagulation-fibrinolytic mechanisms. Cortisone administration depresses the reticuloendothelial system (Heller, 1955) and cushingoid patients show an increased susceptibility to infection. Many bacteria, including Gram-positive organisms, can give rise to coagulation abnormalities which are believed to reflect intravascular coagulation (Goldenfarb *et al.*, 1970). It is also pertinent that cortisone can be substituted for the priming dose of bacterial toxin in eliciting the Shwartzman reaction (Thomas and Good, 1952).

We report a case of Cushing's syndrome with disseminated intravascular coagulation.

Case Report

A 23-year-old woman presented with a seven-month history of progressive hirsutism, amenorrhoea, and excessive leg bruising and swelling. She had severe acne, scattered bruises, and periorbital and leg oedema. Her blood pressure was 140/90 mm Hg.

Investigation showed a normal urine, and electrolyte estimations showed a pronounced hypokalaemic alkalosis (serum potassium 2 to 3·3 mEq/l.). Her platelet count was consistently depressed, being as low as 40,000/mm³. The haemoglobin was 10 g/100 ml and white cell count 7,500/mm³. Plasma cortisol levels were raised both at 9 a.m. and midnight varying between 26 and 36 μg/100 ml. The urinary ketosteroids and hydroxycorticosteroids were consistently raised, the highest levels recorded being 60 mg/24 hr and 109 mg/24 hr respectively. Chest *x*-ray appearances were normal.

While being considered for adrenalectomy she developed glycosuria with a fasting blood sugar of 143 mg/100 ml, and subsequently a severe staphylococcal chest infection with pleural effusion and associated bacteraemia. Serum fibrin degradation products were found to be raised at 80 μg/ml (normal 0 to 20 μg/ml) and urinary fibrin degradation products of 10 μg/ml (normal less than 1·25 μg/ml). The euglobulin clot lysis time was prolonged at 4½ hr (normal 1 to 2½ hr) and plasminogen was normal at 3 units (normal 2·0 to 4·0 units). Multiple pleural aspirates were cytologically negative for malignant cells. There was no response to antibiotic therapy and death occurred two weeks after the onset of her chest infection. The total duration of her illness was 10 months.

At necropsy an area of softening 3 cm in diameter was present in the right occipital lobe of the cerebrum. There was a firm circumscribed mass 3 cm in diameter attached to the anterior surface of the pericardium. The lungs showed extensive consolidation in association with bilateral straw-coloured effusions. The adrenals each weighed 20 g.

Sections of brain showed infarction and perivascular ring haemorrhages with fibrin thrombi in small vessels. The pituitary showed no evidence of ischaemic necrosis while the basophils showed Crooke's hyaline change. In the lungs thick hyaline, fibrinous membranes lined the alveolar walls in association with an infiltrate of predominantly mononuclear cells with fibrin masses in a few small blood vessels. The myocardium showed intravascular platelet thrombi and overlying mural thrombus.

The anterior-mediastinal mass was a thymoma composed predominantly of masses of fairly uniform ovoid cells which showed transition to spindle-shaped whorls in some areas. Fibrous trabeculae, scattered cystic spaces, focal calcification, areas of necrosis, and intravascular fibrin thrombi were present (fig. 1). Mitotic figures and lymphocytic cells were scanty.

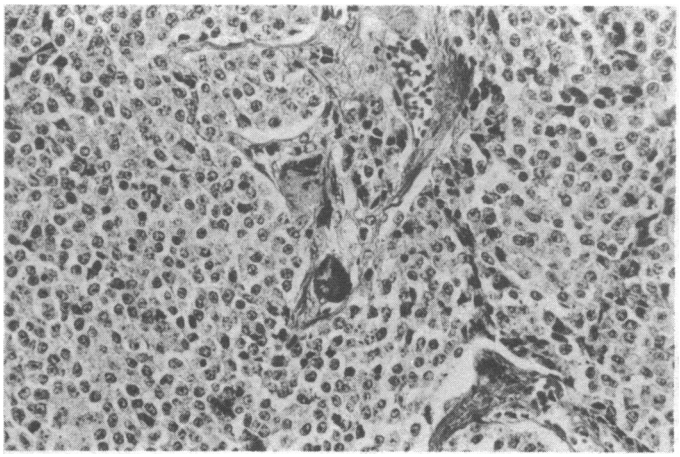

FIG. 1—Thymoma composed of ovoid epithelial cells with a thrombus in a small blood vessel. (Phosphotungstic acid haematoxylin. ×220).

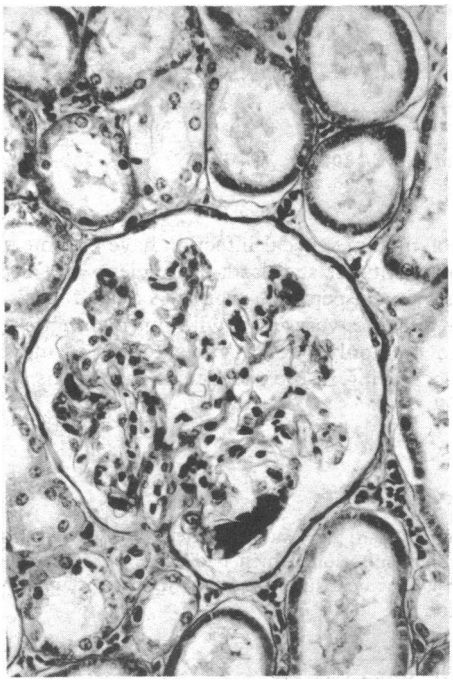

FIG. 2—Glomerulus showing intracapillary fibrin deposits. (Phosphotungstic acid haematoxylin. ×220).

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The liver showed focal necrosis with intrasinusoidal fibrin, and the spleen showed recent infarction and associated fibrin. The kidneys contained fibrin deposits in the capillary loops of some glomeruli but no hypertensive vascular changes (fig 2). The adrenals showed thickened cortices composed of a mixture of extremely hypertrophied compact and clear cells. Large islands of clear cells and focal necrosis in association with intrasinusoidal fibrin were present in some areas (fig. 3). The vertebrae showed a cellular marrow and evidence of microfracture.

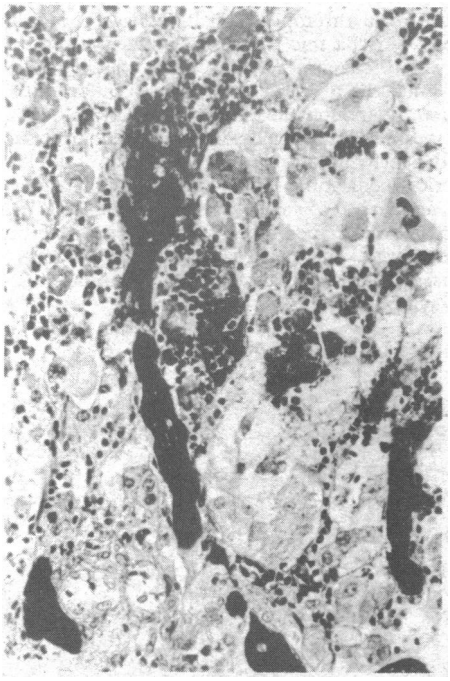

FIG. 3—Adrenal cortex showing cellular hypertrophy and intrasinusoidal fibrin. (Phosphotungstic acid and haematoxylin. ×220).

Comment

The haematological parameters in association with scattered microthrombi at necropsy are strong evidence for the occurrence of disseminated intravascular coagulation in this case.

Release of tissue thromboplastin from necrotic tumour has been implicated in the induction of a hypercoagulable state (Amundsen *et al.*, 1963) but the small size of the tumour and absence of invasion strongly militates against this being a significant mechanism in this patient.

We think that the cushingoid state played a pivotal part in engendering disseminated intravascular coagulation in this case and are unaware of any previous case reports describing this association. The danger of such a state being engendered and increasing the morbidity and mortality of Cushing's syndrome seems to be great in view of the tendency to high levels of clotting factors, depressed reticuloendothelial system, increased susceptibility to infection, and in some cases associated tumours.

We are indebted to Professor D. S. Munro for permission to report this case.

References

Amundsen, M. A., Spittell, J. A., jun., Thompson, J. H., jun., and Owen C. A., jun. (1963). *Annals of Internal Medicine*, **58**, 608.
Goldenfarb, P. B., Zucker, S., Corrigan, J. J., jun., and Cathey, M. H. (1970). *British Journal of Haematology*, **18**, 643.
Heller, J. H. (1955). *Endocrinology*, **56**, 80.
Ozsoylu, S., Strauss, H. S., and Diamond, L. K. (1962). *Nature*, **195**, 1214.
Parkhimovich, R. M. (1969). *Problemy Endokrinologii i Gormonoterapii*, **15**, 43.
Thomas, L., and Good, R. A. (1952). *Journal of Experimental Medicine*, **95**, 409.

Meningococcal Pericarditis without Meningitis

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Epidemics of meningococcal infection have become uncommon with improvements in standards of hygiene and reduction of overcrowding in susceptible groups. Isolated cases continue to be seen but are very rare without meningitis. We have been able to find only one previous report of meningococcal pericarditis occurring in the absence of meningitis (Orgain and Poston, 1939).

Case Report

A 17-year-old Welsh girl was admitted with sharp central chest pain, worse on inspiration, which had come on suddenly two hours previously. Past medical history and symptomatic inquiry produced no explanation.

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On examination she was pale, distressed, and short of breath but not cyanosed. Her temperature was 38·5°C, pulse rate 120/min and regular, blood pressure 140/85 mm Hg, and the jugular venous pressure was not raised. No abnormality was found on auscultation of the heart. The haemoglobin was 9·6 g/100 ml, E.S.R. 5 mm in one hour (Westergren), white blood count 15,700/mm³ (80% neutrophils). A chest radiograph showed nothing abnormal. An E.C.G. showed minimal S-T rise in leads I, aVL, V5, and V6. Later that day she developed neck stiffness, but lumbar puncture produced normal, sterile cerebrospinal fluid.

Fourteen hours after admission her blood pressure dropped to 70/40 mm Hg, jugular venous pressure was raised 5 cm, pulse rate was 140/min, and a pericardial rub was heard at the left lower sternal edge. She was still in considerable pain. An E.C.G. showed further S-T rise now involving leads I, II, aVL, aVF, and V1 to V6 (fig. 1). With the raising of the foot of the bed, the

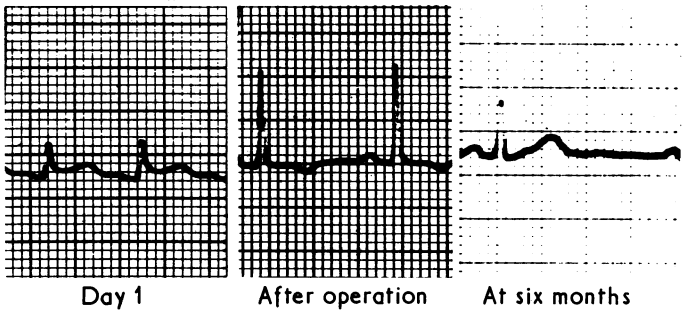

FIG. 1—E.C.G. lead I on the first day, after operation, and six months later.