thromboplastin or other substances from the amniotic sac into the maternal circulation, resulting in the continuous consumption of fibrinogen. The increased incidence of amniotic fluid embolism with intrauterine death of the fetus may be due to the increased friability of the membranes, which are therefore more likely to split or tear, thus creating favourable conditions for amniotic fluid infusion during labour and delivery.

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MEDICAL MEMORANDA

Intracranial Tuberculosis Resembling Hand-Schüller-Christian Disease

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Tuberculosis is common among non-European immigrants to this country and often presents in unfamiliar ways (Wiseman and Mahmood, 1967). We report a case of intracranial tuberculosis in a Pakistani youth in whom diagnosis was delayed by the resemblance to Hand-Schüller-Christian disease.

Case Report

A youth aged 18 who had been in England for two years presented with a lump on the scalp, protrusion of the right eye, and thirst. He had a mild fever but was not seriously ill. There were soft subcutaneous masses about 3 cm in diameter over the right parietal bone and zygomatic arch, and a smaller mass in the right cheek. The right eye was proptosed 8 mm but there were no neurological signs. E.S.R. was 63 mm in the first hour, blood eosinophils 650/mm³. Mantoux reaction was positive with 1 unit of purified protein derivative, but he may have had previous B.C.G. vaccination. Urinary concentration tests excluded diabetes insipidus.

The chest x-ray film showed an ill-defined opacity towards the left apex but was otherwise clear. In the lateral skull film there was an irregular translucency with surrounding sclerosis (Fig. A). Plain films and tomography of the right orbit showed that the superior orbital fissure was enlarged with an indefinite margin and sclerosis of the lesser and greater wings of the sphenoid bone. A right carotid arteriogram (Figs. B, C, and D) showed a large avascular extracerebral space-occupying lesion in the parietal and temporal regions.

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Biopsy of parietal and cheek lesions yielded non-caseating exuberant granulomatous tissue judged to be consistent with the clinical diagnosis of Hand-Schüller-Christian disease; no acid-fast bacilli were seen. After beginning local radiotherapy (because of increasing proptosis) the right temple swelling became fluctuant and needle aspiration showed pus in which occasional acid-fast bacilli were seen. Cultures from this and the cheek lesion eventually yielded a scanty growth of *Mycobacterium tuberculosis*.

Treatment with streptomycin, isoniazid, and rifampicin produced rapid improvement. After three months he was back at work, the subcutaneous lesions had healed, the proptosis was only 4 mm, and E.S.R. was normal. Chest x-ray examination showed no change, but the skull lesions showed signs of healing.

Comment

Isolation of the organism from two of the lesions and the rapid response to specific therapy indicate that this patient was suffering from tuberculosis. Though mimicking the classical triad of Hand-Schüller-Christian disease, he did not have diabetes insipidus (thirst perhaps being related to fever), exophthalmos was unilateral, and the osteolytic skull lesions were not typically punched out (Lichtenstein, 1964). However, variants of Histiocytosis X are common, eosinophilia occurs (Oberman, 1961), and an intracranial mass has been described (Elian *et al.*, 1969).

Tuberculosis of the bones of the skull vault is unusual (Barton, 1961). A focus of infection in the lung or elsewhere is not always found (Strauss, 1933), and Shaw and Basu (1970) have drawn attention to apparently primary subcutaneous cold abscesses. Tuberculosis meningitis and intracranial tuberculomata may present in atypical ways (Kocen and Parsons, 1970) but a large intracranial extracerebral collection, as shown by arteriography in the present case, is very unusual. This patient was fortunate not to develop meningitis, especially after radiotherapy. But spread of tuberculosis from the skull vault to involve the meninges and brain is rare (Strauss, 1933; Meng and Wu, 1942).

In contrast to the present case several patients with Hand-Schüller-Christian disease have been recorded in whom the initial erroneous diagnosis was tuberculosis (Abbasy *et al.*,

FIG. A—Lateral skull showing translucent defect with surrounding sclerosis in right parietal region. FIGS. B, C, and D—Right carotid angiogram showing large avascular extracerebral space-occupying lesion in parietal and temporal regions.

1958). Indeed, Hand (1893) believed his original patient, a boy aged 3 with skull defects and polyuria, to be suffering from tuberculosis.

This report re-emphasizes the importance of considering tuberculosis in immigrants presenting with unusual inflammatory and skeletal lesions.

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Methyldopa and Associated Thrombocytopenia

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Methyldopa has long been successfully used for the control of hypertension. Among the complications of continued treatment with this drug is a positive direct antiglobulin test with or without haemolytic anaemia (Worledge *et al.*, 1966). Reversible leucopenia (Hallwright, 1961; Clark, 1967; Greene and Spence, 1967) and thrombocytopenia (Benraad and Schoenaker, 1965; ten Pas *et al.*, 1966) have been reported as rare findings, but in none of the cases, so far as we are aware, have tests for platelet antibodies been recorded.

Case Report

A 64-year-old Caucasian woman was admitted to hospital in August 1969, having been found unconscious at home. On admission the only significant finding was a left-sided hemiparesis, diagnosed as a cerebrovascular accident. The blood pressure was 160/90. Six years previously she had been admitted with a subarachnoid haemorrhage and angiography had shown aneurysms of the right middle cerebral and anterior communicating arteries. She had a raised blood pressure at that time.

Investigations.—Haemoglobin 14.4 g/100 ml; total white cell count 9,000/mm³ with a normal differential count; blood urea 52 mg/100 ml; C.S.F. normal. She made an uneventful recovery and after two weeks was discharged on methyldopa 250 mg thrice daily.

Two months later she presented with a purpuric rash on her lower limbs and multiple bruises; no other physical signs were found. She was afebrile. Blood pressure was 160/90 and she was still on methyldopa.

Investigations.—Haemoglobin 12.5 g/100 ml; total white cell count 5,000/mm³ with a normal differential count; platelet count 1,000/mm³; reticulocytes 1.2%; serum bilirubin 0.5 mg/100 ml. Tests for antinuclear factor and lupus erythematosus cells were negative. The peripheral blood film showed a few microcytic red cells, but no definite spherocytes. Bone marrow was mildly hypercellular with an increase in the number of megakaryocytes, showing deficient platelet budding. The direct antiglobulin test on the red cells with broad-spectrum and anti-gamma G antihuman globulin sera were both positive. Tests with specific anti-complement reagents were negative. The serum contained an

antibody reacting with all of a comprehensive panel of genotyped red cells by enzyme techniques only. Investigation for platelet and leucocyte antibodies—Platelets: saline agglutination test at 4°, 20°, 37° C was negative, complement fixation test at 37° C was positive, and Coombs consumption test at 20° C gave an equivocal result. Leucocytes: saline agglutination test at 4°, 20°, 37° C was negative and complement fixation test at 37° C was positive.

Methyldopa therapy was discontinued for 24 hours and the platelet count rose to 94,000/mm³ in this period (see Chart). When the drug was tried again the platelet count at the end of four days was 23,000/mm³ and remained at this level for two more days, when methyldopa was finally discontinued. Two days after withdrawal of the drug the platelet count was 63,000/mm³, and five days later reached normal levels. Platelet and leucocyte antibody investigations repeated after the patient was off methyldopa for four weeks were all negative, but the direct antiglobulin test on the red cells remained positive.

Comment

This patient showed a positive direct antiglobulin test together with severe thrombocytopenia while on methyldopa therapy. The significant finding was a positive complement fixation test for platelet and leucocyte antibodies which became negative when she was taken off the drug.

As red cell autoantibodies are so often encountered in long-term methyldopa treatment, it is worth while extending the serological investigation of such cases to cover leucocyte and platelet antibodies. The discovery of non-specific platelet antibody in a patient on this drug may herald the onset of acute thrombocytopenia.

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