that it be used to investigate other patients with agranulocytosis after exposure to possibly toxic drugs, particularly where more than one drug might be responsible. In the present case cultures were carried out after haematological recovery had occurred. Whether the technique can be used in the acute phase of marrow suppression will depend on the number of colony-forming cells present in the marrow.

Further studies of the patient at a longer interval after recovery, and of her family, are planned, and will be reported subsequently.

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MEDICAL MEMORANDA

Lymphosarcoma Presenting as Löffler's Syndrome

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A case of Löffler's syndrome presenting with respiratory symptoms and a high eosinophilia is reported. Full investigation, including bone marrow biopsy, was carried out with negative results. Four months later further physical signs developed which led to a diagnosis of lymphosarcoma being established by lymph node and bone marrow biopsy. This is a rare finding, and in two extensive reviews of lymphoid tumours Löffler's syndrome was not reported as the presenting clinical picture in lymphosarcoma.

Case Report

A previously healthy 4-year-old boy was admitted to the Royal Manchester Children's Hospital in December 1971. Two weeks before admission he had been treated for a dental abscess with lincomycin. This was discontinued after three days because he developed an urticarial rash. He then had two teeth extracted under general anaesthesia with tetracycline (Achromycin) cover. Two days before admission he was noted to be lethargic and to be sleeping more than usual. Later that day his respiration rate increased and he became flushed. These symptoms persisted until admission, by which time he had developed a dry cough and had vomited three times.

His birth and neonatal history were normal. Both parents and his 8-year-old sibling were well. He had never been abroad, and the family did not have any pets.

On examination he had a temperature of 38.5°C, and his tongue was coated. One small mobile lymph node was palpable in his left inguinal region. There was no other overt lymphadenopathy. He was dyspnoeic with a respiratory rate of 60-70/min but the chest was normal on percussion and auscultation. The cardio-

vascular, alimentary, and central nervous systems were quite normal, in particular the liver and spleen could not be palpated.

On admission radiograph of the chest showed the presence of multiple diffuse nodular opacities throughout both lung fields (see fig.). Other investigations were: haemoglobin 10.2 g/100 ml, total white cell count 35,000/mm³, differential count, eosinophils 71%, neutrophils 11%, lymphocytes 18%.

Chest radiograph showing multiple diffuse nodular opacities throughout lung fields.

His clinical condition rapidly deteriorated with increasing dyspnoea and cyanosis. His liver became palpable, and he complained of epigastric discomfort. The liver was smooth and non-tender with a firm consistency. He was, therefore, nursed in an oxygen tent and given corticosteroid therapy. He improved on this treatment, the epigastric pain eased, and his respiratory symptoms became less severe. The liver gradually diminished in size over a two-week period.

The following tests were carried out shortly after his admission and while he was receiving steroid therapy: E.S.R. 40 mm in the first hour. Liver function tests, the blood urea, serum electrolytes, serum calcium, and serum phosphate were all within normal limits. Cultures of blood, urine, stool, nasal and throat swabs did not show any pathogenic organism. No acid-fast bacilli, worms, or ova were found in gastric washings or in repeated stool specimens. Protein electrophoresis showed an increase in α_2 globulin: serum

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immunoglobulins were within normal limits. Hydatid and toxocara complement fixation tests were negative. Bone marrow examination showed a lymphocytosis and eosinophilia with depression of other cell lines. There was no evidence of malignancy and no increase in blast cells. A liver scan showed a uniformly enlarged liver with no evidence of abscess, tumour, or cyst formation. His total white cell count gradually fell and his eosinophil count after reaching 90% of 28,000 white cells also diminished. The morphology of the eosinophils was noted to be more varied than usual but most of the cells were mature forms.

After 20 days in hospital he was sent home on prednisone 30 mg daily, which was to be reduced gradually over a four-week period. At the end of this time his total white cell count was 3,900/mm³ with a differential of eosinophils 5%, neutrophils 50%, lymphocytes 37%, monocytes 5%. Platelet count, haemoglobin, and E.S.R. were normal.

Two months after stopping his steroid therapy he was readmitted as an emergency. During the previous two weeks he had had swelling of both parotid and submandibular regions. A diagnosis of mumps had been made but the boy returned to the hospital because gross hepatosplenomegaly had been noticed.

Examination on admission showed a temperature of 37° C. Large, firm lymph nodes were palpable in the cervical, inguinal, and axillary regions. The liver and spleen were palpable 7 cm below the costal margin. There were petechial haemorrhages present around the neck, and a subconjunctival haemorrhage was present.

A full blood count showed a haemoglobin of 7.4 mg/100 ml, 16,000 platelets/mm³, total white cell count 7,500/mm³, differential count eosinophils 18%, neutrophils 28%, lymphocytes 54%, and monocytes 8%; no blast cells were seen. A lymph node biopsy showed replacement of the normal architecture with lymphomatous tissue, which was thought to be a diffuse lymphoblastic lymphosarcoma. A small degree of pleomorphism was present, there was a moderate degree of mitosis, and there were occasional scattered macrophages. The reticulin pattern was preserved and no Reed-Sternberg cells were seen.

The bone marrow was cellular, consisting mostly of immature cells of the lymphoid series. There were only occasional red cell and no eosinophil precursors present. Liver function tests and total serum proteins were normal but there was a well defined α_1 band on protein electrophoresis.

A diagnosis of lymphosarcoma with bone marrow involvement was made and therapy was started with prednisone 40 mg/m², vincristine 1.5 mg/m², and asparaginase 10,000 units/m². He responded well to this and a bone marrow biopsy six weeks after starting therapy showed a total remission of the condition. He was in good health and the hepatosplenomegaly and lymphadenopathy had resolved completely. Therapy was maintained using prednisone and cyclophosphamide in daily dosage with vincristine given at six-weekly intervals. He remained in complete remission for six months, at the end of which he developed symptoms and signs of central nervous system involvement with lymphoblasts in the cerebrospinal fluid.

Comment

Löffler's syndrome is defined as eosinophilia with pulmonary infiltration. It may be found in several disorders but lymphosarcoma causing this syndrome appears to be unusual.

It is not within the scope of this report to discuss the mechanism of eosinophilia at any length. Wetherley-Mein (1970) classified the various causes of eosinophilia into the following groups according to the evidence of an immunological basis, with examples. (1) Mechanism certainly immunological; asthma, hay fever, urticaria, drug sensitization. (2) Mechanism possibly immunological; some parasites, eczema, polyarteritis nodosa. (3) Mechanism unknown; dermatitis herpetiformis, tumours, congenital eosinophilia. (4) Autonomous proliferation; eosinophilic leukaemia.

Eosinophilic leukaemia is thought by many not to exist, or certainly to be rarer than reported (Bousser, 1957; Rickles and Miller, 1972).

Various tumours can cause eosinophilia, especially malignant tumours. Of the lymphoid tumours, Hodgkin's disease is associated with an eosinophilia in about 15% of cases (Gall and Mallory, 1942). Eosinophilia is unusual in lymphosarcoma and was never prominent in a series of 1,269 cases reviewed by Rosenberg *et al.* (1961).

The first reported case of malignant disease with eosinophilia was by Reinbach (1893). He described the case of a 31-year-old woman with a large tumour of the neck. His clinical diagnosis, substantiated by histology of tumour aspirate, was lymphosarcoma. At presentation she had a leucocytosis of 120,000 cells/mm³ of which 48% were eosinophils and 48% polymorphonuclear leukocytes. There are various aspects of the case, however, which might throw reasonable doubt on Reinbach's diagnosis: Professor Ponfick reviewed the histology and thought that the tumour was more probably a carcinoma.

Henderson and Meña (1969) described a case of lymphosarcoma presenting with very high eosinophilia. No pulmonary infiltration is described but there was eosinophilic pleurisy and pericarditis. The eosinophil count reached a peak of 70% of the total white cell count.

Lymphosarcoma is a tumour which is rarely accompanied by a significant eosinophilia. In two extensive reviews of lymphoid tumours, lymphosarcoma never presented as Löffler's syndrome (Gall and Mallory, 1942; Rosenberg *et al.*, 1961), and an eosinophilia as high as 90% of the total white cell count is unusual.

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