Toxoplasma encephalitis complicating Hodgkin's disease

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SYNOPSIS A case of *Toxoplasma encephalitis* is described in a patient who had received much immunosuppressive therapy for Hodgkin's disease. Such cases have been reported in immune suppressed patients outside the United Kingdom, but a search of the literature has not revealed any previous reports from this country. Since *Toxoplasma gondii* is a frequent pathogen and states of immune suppression are becoming more common, further cases can be expected. Recognition of the clinical and pathological features is important because the condition can be treated.

Patients with malignant disease often have an immune paresis due to the disease itself or to treatment with cytotoxic drugs, corticosteroids or radiotherapy. They are consequently prone to opportunistic infections which may be particularly severe or occur at unusual sites. *Toxoplasma encephalitis* complicating malignant disease is an example of this phenomenon, and a case is described in a patient suffering from Hodgkin's disease and resident in Chichester, Sussex. A search of the literature has not revealed any previous cases occurring in the United Kingdom.

Case Report

A woman aged 44 years presented at another hospital in 1961 with generalized pruritus and was found to have bilateral cervical, axillary, and mediastinal lymphadenopathy. Biopsy of a cervical node was performed and histology showed sinus catarrh only. In spite of the negative histology it was decided to treat her as though she had Hodgkin's disease, and she received two doses of intravenous mustine followed by megavoltage radiotherapy to the mediastinum, neck, and axilla.

In 1966, a recurrent lymph node was excised from the right axilla and showed the histological features of Hodgkin's disease of mixed cellularity (fig 1). Chemotherapy was given for recurrent adenopathy from this time until November 1971. It comprised

weekly vinblastine intravenously for 23 weeks followed by daily oral procarbazine for 43 months and then one course of combination chemotherapy with mustine, vinblastine, procarbazine, and prednisone in August 1971. Following this course the patient was clinically free from disease but prednisone, 20 mg daily, was continued because of pancytopenia. Splenectomy was performed in September 1971 in order to try to improve the haematological tolerance of chemotherapy. The spleen weighed 98 g and no infiltration with Hodgkin's disease was found in it.

In November 1971 the patient was admitted to the Department of Medicine at St Richard's Hospital, Chichester with fever (37.8°C, 100°F), drowsiness, moderate intellectual impairment, incontinence of urine, and a right hemiparesis. Tendon jerks were normal and plantar responses were flexor. The symptoms had developed slowly during the previous two weeks.

Cerebrospinal fluid pressure was 170 mm, the spinal fluid protein was 180 mg/dl, and there were 10 lymphocytes/mm³. No organisms were seen and cultures for bacteria and fungi were negative. An electroencephalogram showed a diffuse abnormality suggestive of encephalopathy.

The patient remained pyrexial and became more drowsy. The hemiparesis increased in density and the right plantar response became extensor. A second specimen of cerebrospinal fluid 10 days after admission differed from the first only by showing a protein content of 350 mg/dl. The diagnosis of *Toxoplasma encephalitis* was not made during life and the patient died six weeks after the onset of symptoms.

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Fig 1 High-power view of the lymph node biopsy of 1966, showing numerous Sternberg-Reed cells. Haematoxylin and eosin $\times 585$.

Fig 2 Oil immersion view of a *Toxoplasma* pseudocyst in the tissue surrounding an area of necrosis in the cerebral hemisphere. Giemsa $\times 1170$

At necropsy several fairly well circumscribed, rounded lesions (10-40 mm in diameter) were found scattered indiscriminately in the white matter, cortex, and basal ganglia of both cerebral hemispheres. The lesions consisted of pale yellowish, friable, crumbling tissue. Microscopy revealed the presence of numerous *Toxoplasma* cysts and free trophozoites in and around necrotic areas in the cerebral hemispheres (fig 2). There was no evidence of infection with *Toxoplasma gondii* outside the central nervous system nor of residual Hodgkin's disease in any part of the body.

Comment

A benign lymphadenopathy is the most common manifestation of infection with *T. gondii* in patients with normal immune function (Feldman, 1968). Involvement of the brain is extremely uncommon in the adult, although it does occur in the foetus. A necrotizing *Toxoplasma* encephalitis can be seen, however, in patients with malignant diseases; this was first described by Arias Stella (see Frenkel, 1956-7). Vietzke *et al* (1968) and Carey *et al* (1973) reported further cases and reviewed the literature. The light and electron microscopic appearances were studied by Ghatak *et al* (1970). Similar cases have occurred in patients receiving immunosuppressive therapy for non-malignant conditions (Reynolds *et al*, 1966; Cohen, 1970; Dubin *et al*, 1971).

Infection with *T. gondii* is common in England; for instance, more than 40% of women over 40 years of age living in South London have *Toxoplasma* dye test titres positive at 1/16 or more (Fleck, 1969). It is therefore surprising that *Toxoplasma* encephalitis has not been reported as a complication of malignancy in the United Kingdom. While this is an uncommon condition, it is important to make the diagnosis because treatment with sulphadiazine and pyrimethamine may be successful (Vietzke *et al*, 1968). Folinic acid can be used to prevent the myelosuppressive effect of pyrimethamine without impairing its therapeutic action (see TenPas and Abraham (1965) for review). Suspicion may be aroused by the clinical picture and a rising *Toxoplasma* dye test titre. The diagnosis has been confirmed in some cases by biopsy of the cerebral lesions and the discovery of the organisms on microscopy or after inoculation of biopsy material into mice (Vietzke *et al*, 1968).

It was not possible to obtain the original lymph

node biopsied in 1961 for review. It is interesting to speculate whether the sinus catarrh reported at that time was due to *Toxoplasma* lymphadenitis and whether the fatal encephalitis was caused by *Toxoplasmas* which had gained access to the body at that time and lain dormant until the development of a severe immune paresis.

There had been prolonged immune suppression due to Hodgkin's disease, cytotoxic drugs, corticosteroids, and radiotherapy in the patient described here. It is becoming increasingly common to see cases that are similar in this respect now that patients with malignant disease may live for long periods. More opportunistic infections with that ubiquitous organism, *T. gondii*, may therefore be seen in the United Kingdom.

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