Lesson of the Week

Intracranial infection due to *Mycobacterium bovis* in Hodgkin's disease

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Multiple intracranial lesions in patients with Hodgkin's disease may be caused by intracranial spread of the disease,¹ secondary neoplasms, progressive multifocal leucoencephalopathy, or opportunistic infections, including tuberculosis,² fungal infections, and toxoplasmosis. We describe a patient with Hodgkin's disease and multiple intracranial lesions, which after extensive investigations proved to be *Mycobacterium bovis* tuberculomas.

Case report

In 1977 a 29 year old secretary at a dairy farm presented with lumps in her right axilla, fevers, and back pain provoked by drinking alcohol. Her sister had lymphocyte predominant Hodgkin's disease. Examination disclosed right cervical and axillary lymphadenopathy. Lymph node biopsy showed nodular sclerosing Hodgkin's disease and she was staged IIb. She received mantle radiotherapy and during the next year inverted Y radiotherapy and chemotherapy for recurrence of abdominal and cervical lymphadenopathy.

In January 1982 fevers, lethargy, and back pain with alcohol returned and she suffered five episodes of hemiparesis and hemianaesthesia, which resembled transient ischaemic attacks. Attacks affected either side, included the face, resolved within 12 hours, and had no epileptic features. In April she was admitted with left sided weakness, which persisted. She was feverish, had no lymphadenopathy, and was euphoric with bilateral papilloedema and a mild left hemiparesis. Blood count, liver function values, Wassermann reaction, tests for autoantibodies, serum immunoglobulin concentrations, chest x ray appearances, and an electroencephalogram were normal. Sedimentation rate was 30 mm in first hour. Abdominal radiography showed probable lymph node calcification. Tests for toxoplasma, brucella, legionella, monospot and viral titres, fungal precipitins, and blood cultures were negative. Result of the Mantoux test was negative (she had not received BCG). Polyomavirus particles were absent in the urine. Bone marrow and abdominal ultrasound showed no evidence of recurrence of Hodgkin's disease. Cerebrospinal fluid contained 1×10^6 lymphocytes/l; the cytological picture, sugar ratio, and pressure were normal; protein concentration was 650 mg/l; and results of cultures and microscopy for tuberculosis, fungi, and listeria were negative. Computed tomography (CT) showed numerous small enhancing lesions of uncertain aetiology in both cerebral and cerebellar hemispheres (figure). Repeat CT scans during her illness showed the evolution of other, similar lesions and enlargement of pre-existing ones; a lesion in the right caudate nucleus resolved before treatment.

In May she developed cervical lymphadenopathy and a pleural effusion. A provisional diagnosis of Hodgkin's disease with intracranial spread appeared to be substantiated by a favourable systemic

The development of multiple intracranial lesions in a patient with Hodgkin's disease requires a comprehensive search for unusual opportunistic infections, including *Mycobacterium bovis*, and may warrant cerebral biopsy

response, with resolution of the lymphadenopathy and effusion, after chemotherapy and cranial irradiation. Her neurological deficit and signs remained unchanged, however, and there were no further episodic phenomena. In September she developed marrow suppression and was given steroids.

CT scans with contrast showing small enhancing lesions in both cerebellar hemispheres and right caudate nucleus.

In October she was readmitted with gradually progressive confusion, dysarthria, and generalised weakness. Examination showed mild epigastric tenderness but no evidence of Hodgkin's disease. She was confused with papilloedema, dysarthria, and a spastic tetraparesis. Repeat routine investigations and tests for opportunistic infections gave negative results. Sedimentation rate was 60 mm in first hour. Cerebrospinal fluid remained normal except for a protein concentration of 950 mg/l. CT showed further, similar intracranial lesions.

Cerebral biopsy was performed and yielded non-caseating meningeal granulomas containing acid and alcohol fast bacilli. Polyomavirus particles were not seen on electron microscopy. Diffuse nodular shadowing developed subsequently in the chest x ray film; acid and alcohol fast bacilli were observed and (classical European type) *M bovis* cultured from transbronchial biopsy specimens. Despite quadruple antituberculous treatment she died six weeks later.

Necropsy findings—Bilateral pulmonary emboli were the immediate cause of death. There was no recurrence of Hodgkin's

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disease. There was evidence of a widely disseminated miliary tuberculous infection. In the abdomen there were many enlarged mesenteric lymph nodes, some calcified. Both lungs contained patchy apical consolidation. The leptomeninges were thickened around the brain stem, and on section there were multiple firm grey white masses in the cerebral and cerebellar hemispheres and midbrain. These lesions proved to be tuberculomas on microscopical examination. Caseating granulomas containing acid and alcohol fast bacilli were also seen in the kidneys, liver, and lymph nodes.

Comment

The incidence of tuberculosis found at necropsy in Hodgkin's disease has fallen substantially² with the virtual eradication of infected milk in Western countries. Classical European *M bovis* is now responsible for only 1.3% of all recorded cases of tuberculosis in south east England.³ Hence despite the prevalence of opportunistic infections in Hodgkin's disease, recently reported cases of classical European *M bovis* causing intracranial infection are rare; occasional cases of meningitis have been reported,⁴ but so far as we can ascertain ours is the first recent case of intracranial tuberculomas to be reported. Our patient had drunk raw milk as a child, and calcified abdominal lymph nodes suggested that a previous tuberculous infection had reactivated.

Opportunistic infections are notoriously difficult to diagnose in immunosuppressed or immune deficient patients; in our patient the Mantoux test result remained negative, there was no cellular response in the cerebrospinal fluid, and repeated microscopy and results of cultures for tuberculosis were initially negative. It may be difficult to establish the cause of intracranial lesions in Hodgkin's disease; this was evident in

our patient with intracranial tuberculomas, who may also have developed systemic recurrence of Hodgkin's disease during her illness. CT scan appearances are not sufficiently dissimilar to differentiate reliably between tuberculomas⁵ and intracerebral Hodgkin's disease.¹

The development of intracranial lesions of unknown cause in a patient with Hodgkin's disease should suggest the possibility of a potentially treatable opportunistic infection. If other biopsies are inappropriate early cerebral biopsy should be considered and may be diagnostic in various opportunistic infections including progressive multifocal leucoencephalopathy (by finding polyoma JC virus particles on electron microscopy) and tuberculosis.

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References

- ¹ Cuttner J, Meyer R, Huang YP. Intracerebral involvement in Hodgkin's disease. *Cancer* 1979;**43**:1497-506.
- ² Arden MJ, Rottino A. Hodgkin's disease complicated by tuberculosis. *Am Rev Respir Dis* 1966;**93**:810-5.
- ³ Collins CH, Yates MD. A study of bovine strains of mycobacterium tuberculosis isolated from humans in south-east England 1977-1979. *Tubercle* 1981;**62**:113-6.
- ⁴ Jones PG, Silva J. Mycobacterium bovis meningitis. *JAMA* 1982;**247**:2270-1.
- ⁵ Loizou LA, Anderson M. Intracranial tuberculomas: correlation of computerised tomography with clinico-pathological findings. *Q J Med* 1982;**201**:104-14.

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Communicable Diseases

Disease associated with milk and dairy products: 1982

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Information on communicable disease associated with milk and dairy products in England and Wales has been presented for the years 1951 to 1980¹ and for 1981.² This report presents comparable data for 1982. There were 19 outbreaks, with at least 1012 cases reported during the year: 18 were attributed to raw milk and one to contaminated pasteurised milk; 15 were due to salmonellas and four to campylobacters. There were three deaths, all associated with salmonella infections. This compares with 23 outbreaks and three sporadic single case incidents totalling 399 cases in 1981 (table).

Salmonella food poisoning

The 15 reported outbreaks of milkborne salmonellosis in 1982 comprised at least 412 cases, compared with 14 outbreaks and 81 cases in 1981. All the outbreaks were due to raw milk. *Salmonella typhimurium* was the causative organism in 14 and *S montevideo* in one, compared with 10 *S typhimurium* outbreaks and four due to other salmonellas in 1981. There were six other outbreaks in which milk or milk powder were suspected as the vehicle of infection, but these were excluded from this analysis

because insufficient epidemiological or microbiological evidence was available to confirm this suspicion.³

In 1982 four of the 15 outbreaks were on farms with between two and eight cases in each. The 11 community outbreaks averaged 36 cases each. The largest outbreak affected 77 out of 161 consumers of raw milk from one producer retailer. Another of 68 cases was due to consumption of raw farm bottled milk; three patients were admitted to hospital and one died. Two outbreaks due to *S typhimurium* were reported after heavy snowfalls in Wales had interrupted milk pasteurisation; 92

Disease associated with milk and dairy products in England and Wales in 1981 and 1982

	1981		1982	
	Incidents	Cases	Incidents	Cases
Salmonella food poisoning	14	81	15	412
Staphylococcal food poisoning	2	26	—	—
Campylobacter infection	7	213	4	600
<i>Clostridium perfringens</i> food poisoning	1	77	—	—
<i>Corynebacterium ulcerans</i> infection	2	2	—	—
Total	26	399	19	1012