Tuberculous meningitis in the developed world: a lurking menace

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INTRODUCTION

Early diagnosis of tuberculous meningitis is vital to prevent serious consequences or death. The bacille Calmette–Guérin (BCG) vaccine does not offer complete protection, so tuberculosis may still affect vaccinated individuals, and not all developed countries routinely vaccinate young individuals. This article presents a case of a previously healthy, unvaccinated Caucasian adult, originally from Western Europe and with no known risk factors, who developed tuberculous meningitis.

DISCUSSION

Clinicians need a high level of awareness for tuberculous infection in patients with clinical features of meningitis. Missed or delayed diagnosis is associated with a high morbidity and mortality. This is emphasized by the near certainty of death from tuberculous meningitis before the use of antituberculous chemotherapy (Thwaites et al, 2000).

The end of the 20th century has seen a resurgence of tuberculosis infections in the developed world, partly as a result of human immunodeficiency virus (HIV) infection, drug-resistant tuberculosis, and migration from countries where tuberculosis is common (Garg, 1999; Thwaites et al, 2000). The annual incidence in England and Wales in 2001 was 12.4 per 100 000 population (3907 pulmonary notifications, 2665 non-pulmonary notifications), with the London area having the greatest number of notifications (37.8 per 100 000 population) (Health Protection Agency, 2004). The CNS is estimated to be involved in approximately 10% of tuberculosis infections (Garg, 1999). In areas of low prevalence, most cases are in adults, for whom HIV infection is the major risk factor (Thwaites et al, 2000).

In the UK, on the basis of Heaf test results, children aged approximately 10–14 years receive the BCG vaccine. As with pulmonary tuberculosis, the BCG vaccine offers protection against tuberculous meningitis. However, the extent of this protection is not fully known. Studies show a partial protective effect of the vaccine (Thwaites et al, 2000), with one meta-analysis calculating a protective effect against tuberculous meningitis of 64%, compared to 50% for pulmonary tuberculosis (Brewer, 2000). Protection declines over time so that no significant protection is provided against tuberculosis after 10 years (Sterne et al, 1998).

Not all developed countries have had the same vaccination programme as in the UK. In the Netherlands, children have not been routinely vaccinated with BCG for the past 30 years (V Kuyvenhoven, Coordinator National Support Unit, Holland, personal communication, 2002).

The initial clinical features are usually non-specific for several weeks.

CASE REPORT

A 37-year-old Caucasian woman presented with headache, neck stiffness, confusion and vomiting. She had no history of respiratory symptoms, nor had there been any recent foreign travel or known contact with persons with tuberculosis. She was pyrexial (38°C) with signs of meningism. A month earlier she had developed a flu-like illness and remained generally unwell with fever, fatigue, anorexia and weight loss, before her condition acutely deteriorated. A computed tomography scan of her brain showed extensive low attenuation areas in the white matter of the parietal and occipital lobes bilaterally. CSF analysis, after a lumbar puncture, showed a raised white cell count of 144/μl, with a preponderance of lymphocytes (72% lymphocytes, 28% polymorphs). Protein levels were elevated (1.27 g/litre) and glucose levels low (0.6 mmol/litre). No bacteria were seen on Gram stain analysis. On further questioning, she had emigrated to the UK from Holland in 1991 and had never received a bacille Calmette–Guérin (BCG) vaccination. Magnetic resonance imaging (MRI) showed severe basal meningitis, extensive parenchymal abnormalities with enhancing multifocal areas consistent with tuberculomas. Further CSF analysis and polymerase chain reaction techniques confirmed the diagnosis of *Mycobacterium tuberculosis* meningitis with pulmonary involvement. Treatment included rifampicin, pyrazinamide, isoniazid, ethambutol and dexamethasone. Human immunodeficiency virus and cytomegalovirus tests were negative.

She developed severe cardiac and respiratory failure, but following treatment she gradually improved, such that by day 14 she was off all intensive care support. Neurological examination showed mild left leg weakness and diplopia. Investigation into this patient's contacts showed that a fellow office worker in England had contracted tuberculosis from his wife who had worked in an Aboriginal colony in Australia.

During the following 3 months her problems included a fluctuating right-sided hemiparesis, expressive dysphasia and focal motor seizures. Repeat MRI showed left middle cerebral artery stenosis as a result of surrounding basal meningeal inflammation, a left basal ganglia infarct and a left transverse sinus thrombosis. Treatment included dexamethasone, warfarin, cyclosporin and thalidomide. Ten months after her admission there had been a marked improvement in coordination, speech and right-sided strength. Warfarin had been discontinued. Unfortunately, her condition deteriorated as a result of a large intraventricular haemorrhage with hydrocephalus, followed later by encephalitis and multiple cerebral infarctions. Despite intensive management she died 4 weeks later.

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These include malaise, fever, myalgia, vomiting and headache in adults. Later the clinical features worsen with continuous headache, meningism and low-grade pyrexia occurring in many patients.

Uncommonly, the presenting features are cranial nerve palsies (20–30%), seizures and hemiplegia (Garg, 1999; Thwaites et al, 2000). One study found that in 55% of cases, symptoms were present for less that 2 weeks, but could be present for up to 9 months. The study also showed that the diagnosis was considered in only 36% of cases, with 6% being treated immediately (Thwaites et al, 2000). If the diagnosis has not been made and treatment commenced then the disease progresses with increasing cerebral injury, leading to confusion, stupor and coma. Decerebrate or decorticate rigidity occurs before death.

Factors that predispose to a poorer prognosis include hydrocephalus, infarcts, tuberculomas, vasculitis, extrameningeal tuberculosis, extremes of age and underlying chronic diseases. However, by far the most important factor is the stage at which treatment is commenced (Garg, 1999; Thwaites et al, 2000).

Tuberculous infections, like tuberculous meningitis, are becoming more common in the developed world. The diagnosis of tuberculous meningitis must be considered in all patients who show clinical features suggestive of the disease, even those perceived as at low risk. Early diagnosis and prompt treatment of tuberculous meningitis is vital to prevent serious consequences or death. **HM**

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