Toxoplasma pneumonitis: fatal presentation of disseminated toxoplasmosis in a patient with AIDS

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ABSTRACT: Toxoplasma gondii infection is an uncommon cause of pneumonitis in patients with acquired immune deficiency syndrome (AIDS). We report a case of fatal pulmonary toxoplasmosis, which clinically resembled Pneumocystis carinii pneumonia (PCP). Conventional diagnostic methods for toxoplasmosis lack sensitivity. Bronchoscopy and histological evaluation of transbronchial biopsy specimens failed to identify the infecting organism. At autopsy there was evidence of disseminated infection.

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Focal necrotizing encephalitis is the commonest clinical manifestation of Toxoplasma gondii infection in patients with the acquired immune deficiency syndrome (AIDS) [1]. Clinically apparent extra central nervous system involvement is rare [2-4]. We describe a case of Toxoplasma pneumonitis in a patient with AIDS rapidly leading to respiratory failure and death.

Case report

A 24 yr old Caucasian male was admitted with anorexia, pyrexia, dry cough and progressive dyspnoea on exertion. He was an ex-intravenous drug user and had been diagnosed human immune deficiency virus (HIV) seropositive in 1987. In 1988, he developed pulmonary and extrapulmonary tuberculosis. Following a 9 month course of anti-tuberculous therapy, he was maintained on isoniazid prophylaxis. However, his condition continued to deteriorate and he died 5 days after admission.

Laboratory investigations (range in brackets): haemoglobin 108 g·l⁻¹ (130-180 g·l⁻¹), total white cell count 1.8x10⁹ (4-11); CD4 count 0.0x10⁹·l⁻¹; platelets 279x10⁹ (150-400). Lactate dehydrogenase (LDH) 1,632 IU·l⁻¹ (100-350). Arterial blood gas estimation demonstrated hypoxia with arterial oxygen tension (Pao₂) 9.9 kPa (11-15), arterial carbon dioxide tension (Paco₂) 3.7 kPa (4.6-6). The latex agglutination test for Toxoplasma was 1/128, immunoglobulin M (IgM) enzyme-linked immunosorbent assay (ELISA) for Toxoplasma was negative. The Sabin-Feldman dye test was not done. Culture of sputum specimen isolated Haemophilus influenza. Ziehl Neelsen (ZN) stains of sputum, urine and faeces were negative.

Initial chest X-ray showed a fine reticulonodular pattern and a patchy infiltrate of the right midzone. Computerized tomographic (CT) contrast studies of the brain showed marked cerebral atrophy but no evidence of a focal lesion. Intravenous amoxycillin was commenced. Due to failure of clinical response, a bronchoscopy was performed 48 h after admission. Cytological and microbiological examination of bronchoalveolar lavage (BAL) washings and touch preparations of lung tissue were negative for Pneumocystis carinii and Mycobacterium tuberculosis. The transbronchial biopsy specimen showed nonspecific interstitial pneumonitis. No microorganisms were identified with special stains. Over the following 72 h the patient developed progressive respiratory failure. Serial chest X-rays (fig. 1) demonstrated the appearance of bilateral mid and lower zone infiltrates. LDH rose to 5,028 IU·l⁻¹. The patient was commenced empirically on intravenous pentamidine, cefotaxime and full antituberculous therapy. However, his condition continued to deteriorate and he died 5 days after admission.
At autopsy there were bilateral pleural effusions. The lungs (R=970 gm, L=900 gm) had a rubbery consistency and showed accentuated lobulation and purple-tan discolouration. There were fibrinous adhesions over both apices. Microscopically, the alveolar septae were markedly congested and there were small foci of intra-alveolar haemorrhage. In addition there were multiple foci of acute bronchopneumonia and organizing pneumonia (fig. 2). The alveolar exudate contained small numbers of polymorphs and histiocytes. On high magnification, typical *Toxoplasma gondii* cysts and tachyzoites were identified in all sections of lung examined (fig. 3). *Toxoplasma gondii* was also present in sections of pancreas, oesophagus, stomach, adrenal glands, myocardium and bone marrow, and in two discrete areas of necrosis in the occipital cortex. The organisms were stained immunocytochemically by a polyclonal anti-toxoplasma antibody, (ICN ImmunoBiologicals, Costa Mesa, Ca., USA) using the peroxidase antiperoxidase method, and had the characteristic ultrastructural features of *Toxoplasma gondii*. There was no evidence of viral infection. Stains for other pathogens including *Pneumocystis carinii* were negative. Finally, retrospective immunocytochemical staining of the transbronchial biopsy specimen for toxoplasma was negative, confirming the (false) negative transbronchial biopsy results.

**Discussion**

Toxoplasma encephalitis is the most frequent opportunistic infection of the central nervous system in AIDS [6]. Despite the high incidence of respiratory complications in AIDS [7], *Toxoplasma gondii* appears to be an unusual pulmonary pathogen. The exact incidence and significance of pulmonary toxoplasmosis is unclear [5]. In one review, of over 440 patients with pulmonary complications of AIDS, there was only one case of pulmonary toxoplasmosis [7]. However, a prospective study of BAL fluid examination in HIV-positive patients, found prevalence rates for pulmonary toxoplasmosis as high as 5% [8]. How often pulmonary toxoplasmosis is clinically manifest is unknown, but the condition may be underdiagnosed.

The diagnosis of *Toxoplasma pneumoniae* may prove difficult. The clinical and radiological features are nonspecific [9] and may resemble PCP. Serological studies lack both sensitivity and specificity and are of limited value [10].

Definitive diagnosis of toxoplasmosis requires either histological demonstration of the organism or isolation by culture. However, inadequacy of conventional staining techniques and small specimens may cause false negative results [5, 10, 11]. Transbronchial biopsy and BAL examination are effective methods for the diagnosis of pulmonary opportunistic infections, particularly PCP, in patients with AIDS. However, where infection is minimal or focal, histopathological and cytological evaluation of bronchoscopy specimens in patients with AIDS have a low diagnostic yield [12].
Failure to identify *Toxoplasma gondii* in our patient was probably due to sampling error, because the organisms, although very numerous in some sections, were not diffusely distributed in the lungs at autopsy.

*Toxoplasma gondii* can be detected on haematoxylin and eosin stained specimens, although in one study of cerebral toxoplasmosis, the organism was not seen in over 50% of positive cases [10]. Newer techniques may prove more useful. Peroxidase antiperoxidase staining techniques are more sensitive and specific, although background staining may be a significant problem in interpretation and once again sampling is a major limiting factor. Electron microscopy can be used to demonstrate the characteristic ultrastructure of toxoplasma tachyzoites in tissue specimens [13]. More recently, Derouin *et al.* [14] have reported sensitive tissue culture techniques which can provide evidence of pulmonary infection within two days.

Disseminated toxoplasmosis is identified in less than 8% of AIDS patients at postmortem examination [11, 16]. Symptoms associated with Toxoplasma pneumonitis rarely predominate as in the present case, most patients present with symptoms associated with Toxoplasma encephalitis. In patients with symptomatic pulmonary toxoplasmosis [1], however, the mortality is high [2, 5]. Due to inadequacy of conventional staining techniques, small size of transbronchial tissue specimens and focal infection, BAL and lung biopsy evaluation may fail to identify *Toxoplasma gondii*. Thus, pulmonary toxoplasmosis is likely to be underdiagnosed. In the absence of other microorganisms, particularly *Pneumocystis carinii*, the diagnosis should be considered. Greater clinical awareness and improved diagnostic techniques complemented by open lung biopsy in cases where transbronchial biopsy and lavage fail to yield evidence of PCP infection, should help clarify the true incidence of pulmonary toxoplasmosis and reduce the mortality from a potentially treatable condition.

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**References**