CORRESPONDENCE: Reader Submitted Case Reports

Edited by Dr Ronald L. Hamilton

JULY 2004: 40-YEAR-OLD MAN WITH HEADACHES AND DYSPNEA

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Clinical description and imaging studies. A 40-year-old man presented with severe frontal headaches, dry cough, impaired balance and dizziness for 6 weeks. On examination he had low-grade pyrexia and investigations revealed mild lymphopenia. Brain CT was normal and chest x-ray showed right hilar adenopathy with bilateral parenchymal infiltrates. A diagnosis of atypical pneumonia was made.

Four weeks later he presented with persistent headache, oscillopsia and unsteadiness of gait. On examination he was alert and orientated with minimal blurring of the disc margins, decreased heel shin testing and an inability to tandem. His CXR was unchanged; a high resolution CT thorax confirmed right hilar abnormalities (Figure 1). Infectious screen was negative. Brain MR post contrast revealed cerebellar enhancement and swelling with moderate tonsillar herniation (Figure 2); findings which precluded the performance of a lumbar puncture. He was commenced on high dose intravenous steroid therapy. Hilar node microscopy showed hyalinization with occasional well-formed epithelioid granulomata. No organisms were identified. A presumptive diagnosis of sarcoidosis was reached.

Despite an initial symptomatic improvement following commencement of steroid therapy, his headache persisted with variable intensity; neurological examination remained stable. Repeat MRI, 11 days later, showed reduced cerebellar enhancement and swelling with no change in the degree of tonsillar herniation. Over the next 24 to 36 hours he deteriorated with evidence of clinical herniation. Despite intravenous antibiotics and mannitol he suffered a respiratory arrest and was intubated. Repeat CT brain demonstrated severe cerebral oedema with evidence of coning. The following day he had fixed and dilated pupils and was declared brain dead after brain stem testing.

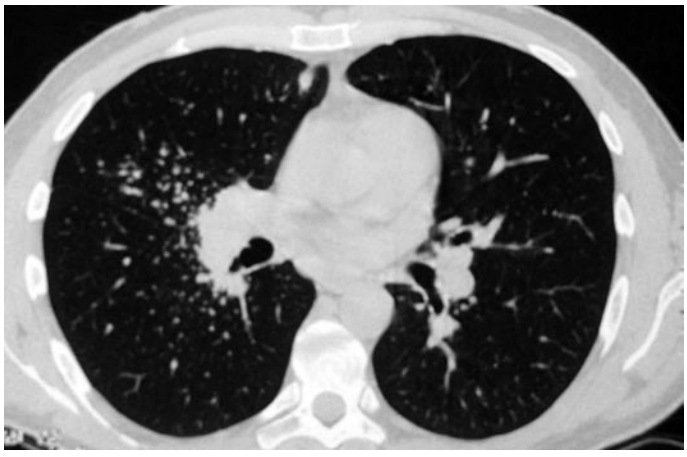

Figure 1.

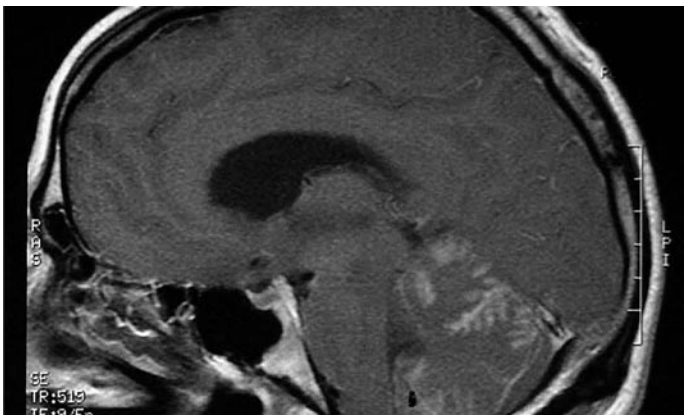

Figure 2.

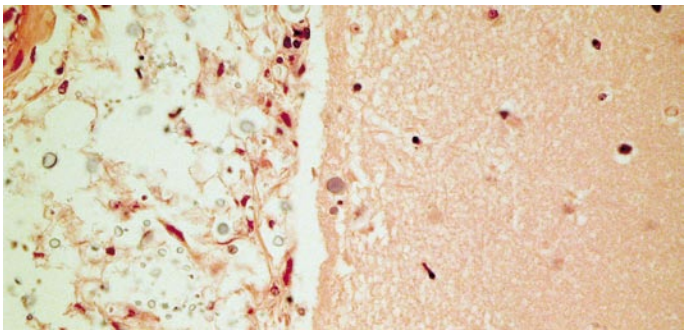

Figure 3.

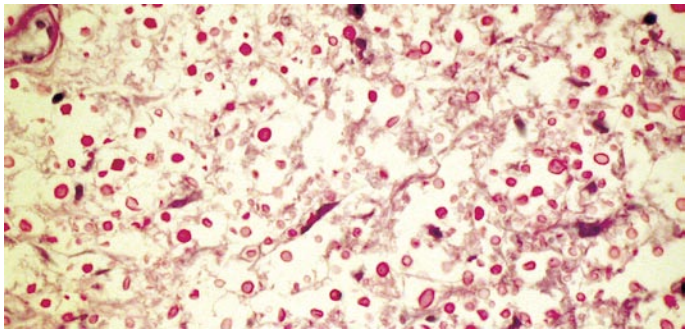

Figure 4.

Post mortem examination. Autopsy examination of the brain revealed cerebral oedema with tonsillar herniation. The leptomeninges appeared dull and opaque with a gelatinous exudate over the surface of the brain, especially at the base. Microscopy revealed numerous organisms (Figure 3) that were highlighted by Grocott and PAS (Figure 4). No acid or alcohol fast bacilli could be demonstrated by Ziehl-Neelsen stain. There was minimal associated inflammatory reaction and no evidence of granuloma formation.

Examination of the thoracic cavity confirmed hilar adenopathy and sectioning the lungs revealed a fibrotic nodular appearance with one single necrotic lesion identified in the midzone of the right upper lobe. Microscopic examination of the hilar nodes revealed hyalinized non-caseating granulomata with no organisms or foreign material identified. Lung parenchyma was fibrotic with occasional non-caseating granulomata and Langerhan giant cells. Organisms were identified only in the necrotic focus. Extra-pulmonary sarcoidosis was not identified.

Diagnosis. Cryptococcal meningitis and focal pneumonitis in a patient with pulmonary sarcoidosis.

Discussion. Cultures of post mortem lung parenchyma and meninges yielded *Cryptococcus neoformans* variety *neoformans*. This patient with stage II sarcoidosis died from cryptococcal meningitis. Sarcoidosis was diagnosed antemortem but cryptococcal meningitis was undiagnosed. His neurological symptoms were attributed to neurosarcoidosis.

Sarcoidosis, a systemic disorder of unknown cause, is characterised by the presence of non-caseating epithelioid granulomata, with Langerhan giant cells, Schaumann and asteroid bodies (6). Because the lungs and thoracic lymph nodes are almost always involved, most patients present with respiratory symptoms. Lung, bone and skin are the commonest sites affected with neurosarcoid occurring in only 5% of cases (8). In this case the patient presented principally with neurological symptoms but had no evidence of neurosarcoid at autopsy. The investigation of the dry cough and the observation of bilateral hilar lymphadenopathy and pulmonary infiltrates led to the diagnosis of sarcoidosis. It is difficult to determine how long this patient had pulmonary sarcoidosis, but based on the extensive fibrosis in the hilar nodes and lung parenchyma it was long standing (3). Cryptococci were not present in hilar nodes or in the granulomatous lung foci making it highly unlikely that the granulomatous reaction in the lungs was due to cryptococcus.

Pulmonary cryptococcosis is an uncommon and generally benign infection (4), but as an opportunistic T-cell mediated mycosis, is an important disease in patients with supressed immune function. The vast majority of patients who present with fulminant cryptococcal infection are immunocompromised as a result of HIV infection, chemo- and/or radio-therapy or corticosteroids. In this case the steroid therapy did not play a role in the development of cryptococcal meningitis as the headaches were the initial and significant observation. There are rare cases of cryptococcal infection in immunocompetent patients and a small proportion of these are described in patients with supervening sarcoidosis (2, 7). Cryptococcus in association with sarcoidosis is thought to occur due to an inversion of the CD4/CD8 ratio, probably because of redistribution of helper T-cells to the lungs and other sites of disease activity. There are 2 varieties of *Cryptococcus neoformans—gattii* and *neoformans* with the latter commonly affecting immunocompromised patients (5).

Patients with *C. neoformans* in the CSF have a high mortality. Despite being seronegative for HIV, our patient was predisposed to opportunistic infection because of the underlying sarcoidosis. He thus presented a diagnostic challenge to the clinicians. The absence of typical symptoms (hemoptysis, chest pain and pleural effusion) usually seen in pulmonary cryptococcus served to confound the diagnosis. Bronchoscopy was non-diagnostic, initial blood cultures were negative and lumbar puncture was not possible due to raised intracranial pressure. The finding of leptomeningeal enhancement on MR, an uncommon finding in cryptococcal meningitis (1), further confused the issue leading to a diagnosis of neurosarcoid. Therefore a strong index of clinical suspicion is necessary to diagnose this exceedingly rare association of cryptococcus complicating sarcoidosis.

In conclusion, we present a 40-year-old, HIV-negative man who presented with the rare association of sarcoidosis and cryptococcal infection. The presence of neurological signs in a patient with pulmonary sarcoid and leptomeningeal enhancement on MR does not necessarily mean that the patient is suffering from neurosarcoid.

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