Reactivation of coccidioidomycosis in a fit American visitor

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Abstract
The case history is presented of an American visitor, known to have had primary coccidioidomycosis previously, who became very unwell during a visit to the UK. Despite consideration of reactivation of coccidioidomycosis from the outset, other pathogens were identified while Coccidioides immitis was not initially, leading to a delay in treatment.

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Coccidioidomycosis is a fungal infection endemic in the south western United States, Mexico, and Central and South America. Infection by the organism Coccidioides immitis usually produces a mild ‘flu-like illness or no symptoms at all, and previous exposure to C immitis may be detected by serological and skin testing.

Case report
A 48 year old Caucasian man had developed a ‘flu-like illness followed by dyspnoea and a productive cough shortly after arriving in the UK for a Christmas holiday. He had lived all his life in California and was working as a park ranger, but denied contact with animals. He was a life long non-smoker and had no risk factors for human immunodeficiency virus (HIV). He presented to the referring hospital and was found to have signs of bilateral pneumonia. There was a neutrophil leucocytosis (total white cell count (WCC) 11.2 × 10⁹/L), arterial blood gases on air revealed hypoxaemia (pH 7.54, PaO₂ 6.8 kPa, PaCO₂ 2.9 kPa, SaO₂ 91%), and the chest radiograph showed consolidation in the left mid and lower zones and the right lower zone. Two years previously he had had “valley fever”, a self-limiting infection caused by C immitis which had manifested as a ‘flu-like illness and an abnormal chest radiograph. As is usual in valley fever, skin tests had become positive and the illness had resolved without treatment.

The patient had been admitted to the referring hospital and intravenous cefuroxime and erythromycin were administered. Culture of purulent sputum revealed a heavy growth of group A β haemolytic streptococcus (GBHS) and the influenza A titre was raised and fell three weeks later (1 in 128 to 1 in 40). The working diagnosis was severe streptococcal pneumonia secondary to influenza, and this was supported subsequently by raised streptolysin O (300) and DNAse titres (800) which subsequently fell to 100 and 300, respectively. The referring team considered reactivation of coccidioidomycosis but sputum sent to Bristol Public Health Laboratory Service failed to grow C immitis and serological tests were also negative. Despite this, and a negative HIV test, amphotericin B was started 10 days after admission because the patient failed to improve.
On the 15th day he was transferred. On arrival, oxygen saturation on air was 86%, WCC 17.6 (neutrophils 13.6, eosinophils 0.4 × 10⁹/l), and C reactive protein 233 mg/l. The chest radiograph showed more extensive consolidation with extension to the right middle lobe (fig 1). Fibroptic bronchoscopy was performed and two transbronchial biopsy and bronchoalveolar lavage (BAL) specimens were taken from the right lower lobe. Microscopic examination of the BAL fluid revealed a large number of white cells, predominantly neutrophils, but no organisms, and histological examination of the biopsy specimen showed chronic pneumonia without granulomas or spherules on silver stain. The patient continued to deteriorate. Six days later C immitis was grown from both the BAL fluid and admission sputum samples. Repeat serological tests sent at the time of transfer returned strongly positive for C immitis (1:640 by complement fixation). Amphotericin B (1 mg/kg) was recommenced. Over the next two weeks bilateral pleural effusions developed and microscopic examination of this bloodstained exudate showed occasional fungi but no growth on culture. Such high serological titres predict dissemination¹ but cerebrospinal fluid examination was normal and a bone scan was negative. Over the subsequent three weeks his clinical condition improved and C immitis complement fixation titre fell to 1:80. Amphotericin B was given until a total dose of 1 g was reached and oral fluconazole 400 mg a day was substituted. HIV serology remained negative.

Discussion
This case raises several interesting points. Firstly, the diagnosis of coccidioidomycosis was not easy to confirm despite being considered throughout and, secondly, none of the usual causes of reactivation were present.

A recent review of coccidioidomycosis states that difficulty in making the diagnosis usually arises from failure to consider the organism.¹ In this case coccidioidomycosis was considered from the outset and evidence of other infections did not deter either team from an active search for C immitis. He was documented to have had primary coccidioidomycosis two years previously which had resolved completely. Recurrent coccidioidomycosis arises by one of two mechanisms: reactivation of the primary infection in individuals who become immunocompromised—for example, by HIV, malignancy, immunosuppressive drugs, diabetes and alcoholism—or by repeat exogenous infection in those exposed to high levels of the organism, typically laboratory workers handling the organism.² None of these risk factors was identified.

We believe that the initial stages of pneumonia were caused by GABHS. Although it is possible that GABHS came from the pharynx, he did not complain of sore throat, the culture was a heavy pure growth and the ASO/DNAse titres support infection. GABHS pneumonia is an unusual and severe bacterial pneumonia and influenza is known to predispose to it, especially in children.³ The patient also developed extensive pulmonary coccidioidomycosis. It is possible that he had ‘flu complicated by GABHS pneumonia and that, in the context of this severe pulmonary infection, reactivation of coccidioidomycosis occurred. This would explain why culture of C immitis was negative initially. We know of no other case of bacterial infection per se leading to reactivation and surmise that GABHS pneumonia was sufficiently immunosuppressing to have caused reactivation coccidioidomycosis.