

# Pulmonary coccidioidomycosis: import illness and the importance of travel history

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## ABSTRACT

A 35-year-old man presented at the outpatient department of pulmonary diseases with fever, rhinitis and coughing. He had recently been on holiday in California. Except for a body temperature of 39.7°C there were no other abnormal findings at the physical examination. Chest X-ray showed a consolidation in the left upper lobe. Under antibiotic treatment his clinical condition deteriorated. Coccidioidomycosis was the suspected diagnosis and confirmed by the results of CT scanning and culture of bronchoalveolar lavage fluid. Treatment with itraconazole resulted in lasting improvement. The case stipulates the importance of travel history.

## KEYWORDS

Coccidioidomycosis, pneumonia, import illness, itraconazole

## INTRODUCTION

Coccidioidomycosis was first recognised in 1892 as a progressive disfiguring skin disease with organ complications and since 1937 as the cause of an acute respiratory syndrome called valley fever.<sup>1</sup> The fungus *Coccidioides immitis* is endemic in certain areas of Northern and Southern America. Of the estimated 100,000 infections per year in the United States, 50 to 60% are subclinical.<sup>2,3</sup> When diagnosed, the most common clinical presentation is acute or subacute pneumonic illness. Extrapulmonary disease may develop, affecting any possible organ, usually within a year after the initial infection. In case of impaired immunity, for example by cancer, HIV infection or immunosuppressive therapy, the infection may appear months to years after the primary infection.<sup>2,4</sup> The low number of imported cases of coccidio-

### *What was known on this topic?*

Coccidioidomycosis is a fungal infection caused by *Coccidioides immitis*, leading to pulmonary and systemic symptoms and occasionally even disseminated disease.

### *What does this case add?*

An advice to consider the diagnosis of coccidioidomycosis in patients with symptoms of a respiratory tract infection who have recently visited the southwest region of the USA, an endemic area.

idomycosis in the Netherlands makes recognition of the infection difficult, and emphasises the importance of travel history.<sup>4,5</sup>

## CASE REPORT

A 35-year-old man presented with flu-like symptoms. He had just spent a three-week holiday in California. The patient's medical history was unremarkable. He was not taking any medications and he did not smoke, drink alcohol or use any illicit drugs. He had a known penicillin allergy.

Before presentation he was treated with azithromycin, which he could not tolerate, followed by cotrimoxazole without any clinical improvement.

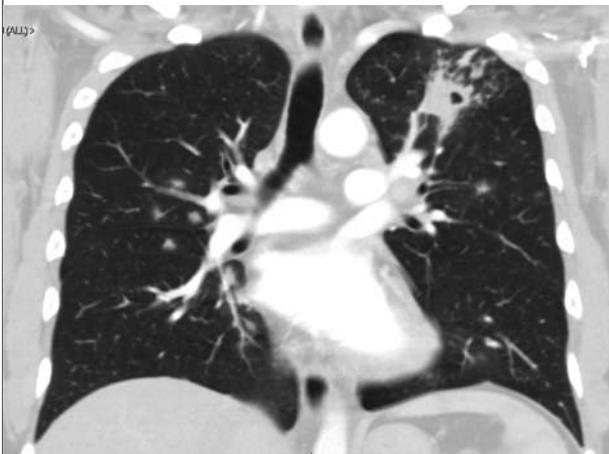
Apart from a fever of 39.7°C, physical examination revealed no abnormalities. Laboratory findings showed an elevated erythrocyte sedimentation rate (49 mm in the first hour) and C-reactive protein (80 mg/l; normal <5 mg/l). No further abnormalities were noted. Chest X-ray showed

**Figure 1.** Chest X-ray showing a consolidation in the left upper lobe (232 x 241 mm)



a consolidation in the left upper lobe (figure 1). Under the diagnosis of pneumonia caused by *Streptococcus pneumoniae* or an atypical pathogen, he was treated with moxifloxacin. Nevertheless symptoms persisted and the patient was hospitalised for further diagnostics and treatment. A new chest X-ray showed subtle infiltrative lesions in the right lung as well. Intravenous Cefuroxime was added. Because of positive *Chlamydia* serology, moxifloxacin was changed for doxycycline, but only after a diagnostic bronchoscopy with bronchoalveolar lavage (BAL) was done. A tuberculin skin test was negative. Because of persisting fever, prednisone was prescribed and the patient could be discharged on doxycycline and

**Figure 2.** CT scan showing bilateral nodular pulmonary infiltrates (309 x 237 mm)



Note the cavity in the left upper lobe.

prednisone. However, due to persisting dyspnoea, CT scanning of the thorax was performed, which showed multiple cavitations and fluffy nodules in both lungs (figure 2). Meanwhile, serology for HIV, antinuclear factor and antineutrophil cytoplasmic antigen was negative, as were auramine tests and PCR for tuberculosis, *Chlamydia* and *Mycoplasma* in the BAL fluid. However, the culture for fungi showed growth, and together with the results of the CT scan, coccidioidomycosis was suspected. Treatment with itraconazole was initiated. Later on, *Coccidioides* serology proved to be positive and the cultured fungus was determined as *Coccidioides immitis*. The patient gradually improved under continued treatment with itraconazole.

## DISCUSSION

*Coccidioides* species are endemic in certain areas of the southwest of the USA, including the deserts of California, Northern Mexico and several areas in South America. In the Netherlands infections are very rare and mainly found among travellers.<sup>1,5</sup>

Coccidioidomycosis is caused by the dimorphic fungus species *Coccidioides immitis* or *C. posadasii*. The incidence of coccidioidomycosis is increasing, from 21 cases/100,000 in 1997 to 91 cases/100,000 in 2006.<sup>6</sup> Factors that are likely responsible for this increasing incidence include a greater number of persons moving into endemic areas, a growing population with immunosuppression, new constructions in previously undeveloped desert areas and more awareness of this infection among physicians.<sup>1</sup> In the Netherlands roughly ten serologically proven cases are seen each year (Jacques Meis, personal communication).

*Coccidioides* species grow in the soil of the desert. The lifecycle consists of a mycelial and a spherule phase. The mycelial phase is a mold in the soil growing in hyphae. While maturing, arthroconidia are formed. These arthroconidia may be inhaled and transformed into multinucleated spherical structures. These spherules form internal endospores, which can be released, forming new spherules. If infected material is returned to the soil or if sputum is cultured in the laboratory, mycelia are formed, completing the cycle.<sup>1,2,7</sup>

The incubation period is 7 to 21 days. Approximately 60% of infections occur subclinically. Symptomatic patients may present with symptoms such as coughing, chest pain, fever and fatigue.<sup>1,2,4</sup> Clinically there may be either a subacute process with respiratory and systemic symptoms lasting weeks to months, or an acute process manifesting as a pneumonia. Other symptoms may include arthralgias, and cutaneous manifestations such as erythema nodosum and erythema multiforme.<sup>1,2,4</sup> In the majority of patients clinical symptoms regress spontaneously after several weeks. Occasionally patients have persisting pulmonary lesions in the form of residual nodules or cavities.<sup>1</sup> Disseminated

coccidioidomycosis is estimated to occur in less than 5% of symptomatic patients.<sup>1,2,4</sup> Dissemination may occur months to several years after the primary infection and notably affects skin, lymph nodes and bones. Meningeal disease is less common but also the most feared complication.<sup>1</sup>

Coccidioidomycosis can be diagnosed by a culture from any body fluid, by identifying coccidioidal spherules in cytological smear or biopsy specimen, or by a positive serological test.<sup>1</sup> Serological assays may be compromised in patients with decreased immune response.<sup>4</sup>

In most patients who present with early infectious disease, it will resolve without specific antifungal therapy.<sup>1,3</sup> Nevertheless, management should routinely include repeated patient encounters for one to two years, either to document resolution or to identify pulmonary or extrapulmonary complications.<sup>3</sup> Patients with an immunocompromised status or those who develop progressive pulmonary disease or disseminated disease require antifungal treatment.<sup>1,3</sup> Commonly prescribed therapies include ketoconazole, fluconazole, itraconazole and amphotericin B. The duration of treatment ranges from three to six months, but this may be longer, especially in immunocompromised patients. In case of meningitis, treatment should be continued indefinitely.<sup>3</sup>

## CONCLUSION

In a patient with symptoms of an upper or lower respiratory tract infection and a recent visit to the southwest region

of the USA, coccidioidomycosis should be considered. Although usually self-limiting, treatment is indicated in progressive or disseminated disease.

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