CASE REPORT

Case of coccidioidomycosis in Ireland

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SUMMARY

Coccidioidal infection is a well-recognised cause of pulmonary disease in certain parts of the south-western USA, Central and South America; however, it is rarely encountered elsewhere in the world. We describe the case of a previously healthy man presenting to a Dublin hospital with fever, dry cough and chest pain, following a visit to the western USA. Despite treatment with broad-spectrum antimicrobials, the patient developed progressive bilateral pulmonary infiltrates and a large pleural effusion. After extensive investigations including CT, bronchoscopy and pleural fluid analysis, a diagnosis of pulmonary coccidioidomycosis was made. Following the initiation of appropriate antifungal therapy, the patient made a full recovery. This case was of interest due to the rarity of the disease outside its areas of endemicity and the unusual findings associated with its diagnosis.

BACKGROUND

Coccidioidomycosis is a form of mycosis caused by *Coccidioides immitis* and *Coccidioides posadasii*. It is endemic to particular regions of the south-western USA and Mexico, as well as certain parts of Central and South America, where its incidence has risen dramatically in the last decade.¹

Coccidioidomycosis has rarely been described in Europe. There have been a handful of reports in the UK, Italy, France, the Netherlands and Scandinavia over the last decade or so, some of which have been in immunosuppressed patients or visitors from the USA. One report in the UK referred to an American resident presenting with a nodule mimicking malignancy.²

It is transmitted by inhalation of spores, typically during periods of dry weather, and has an average incubation period of 10–16 days, meaning that travellers to these areas of endemicity may not develop symptoms until they return home.³

The majority of immunocompetent patients who contract coccidioidomycosis will either not develop any symptoms or not seek medical attention. The illness typically presents with non-specific respiratory and constitutional symptoms such as fever, cough, dyspnoea or fatigue. It may also be associated with erythema nodosum or multiforme.⁴ More severe manifestations of the disease, such as respiratory failure, severe sepsis, or disseminated coccidioidomycosis, while common in immunosuppressed populations, are rare in the immunocompetent. In more severe cases, pulmonary infection may manifest as a localised pneumonia, formation of pulmonary nodules (with or without cavitation), pleural effusion or diffuse infiltrates.⁵

CASE PRESENTATION

A 64-year-old man presented to hospital with a 5-day history of cough, shortness of breath and left-sided chest pain, following a trip to the USA 2 weeks earlier. He initially reported visiting the Eastern USA only, and that he had visited a relative in a North Carolina hospital. He was previously healthy, with a background history of benign prostatic hypertrophy only, and was a never smoker. Physical examination revealed coarse crepitations and dullness to percussion at the left base. Initial investigations revealed a markedly elevated C reactive protein of 265 mg/L and a white cell count of $14 \times 10^9/L$. He had mild impairment of his liver function tests (alkaline phosphatase 188 IU/L, γ -glutamyltransferase 211 IU/L). Chest X-ray (figure 1) demonstrated a patchy left basal infiltrate.

The patient was treated with coamoxiclav and clarithromycin; however, he failed to improve over the following days, with persistent shortness of breath and fever. Antimicrobial treatment was changed to vancomycin and meropenem on day 5 of admission, but he continued to deteriorate clinically, with persistent fever and development of type 1 respiratory failure, and progression of bilateral pulmonary infiltrates on chest X-ray.

INVESTIGATIONS

A CT scan performed on day 5 of admission showed left basal consolidation with associated pleural effusion (figure 2).

A bronchoscopy was performed which showed frank pus draining from the apical segment of the left lower lobe. Washings and brushings were taken for microbiological assessment. Repeat chest X-ray on day 10 of admission showed significant deterioration with a new right-sided infiltrate. Subsequent

Figure 1 Chest X-ray showing a patchy infiltrate in the left lower zone.

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Figure 2 CT thorax showing dense left basal consolidation with associated pleural effusion.

CT thorax showed interval development of bilateral nodular infiltrates, with dense left basal consolidation and worsening pleural effusion, with some loculation and areas of low attenuation concerning for empyema (figure 3).

A diagnostic thoracocentesis was performed which was consistent with an exudative pleural effusion but without evidence of empyema.

Bronchial washings, blood cultures and pleural fluid initially failed to culture any pathogen. Urinary pneumococcal and legionella antigens were negative. HIV serology was negative, as were ANCA, ANA, ENA and rheumatoid factor. Immunoglobulin levels were normal, apart from an elevated IgE at 460 IU/mL.

Eventually, on day 9 of admission, a light fungal growth (initially considered to be *Aspergillus*) was noted on cultures (figure 4).

On further questioning, it transpired that the patient had in fact visited Yosemite National Park in California during his trip to the USA.

Figure 3 CT thorax showing bilateral nodular infiltrates, with dense left basal consolidation and worsening pleural effusion, with some loculation and areas of low attenuation concerning for empyema.

Figure 4 Culture plate showing growth of fungal species, later confirmed as *Coccidioides* sp.

DIFFERENTIAL DIAGNOSIS

The patient had features of a complicated pneumonia following a trip to the east and west coasts of the USA. The picture was consistent with an infectious process, but there was a lack of response to broad-spectrum antibiotics. Nosocomial infection was a possibility, as he had visited a relative in a North Carolina hospital on two occasions.

Viral pneumonia was considered. Hantavirus can cause a severe pulmonary syndrome, and there had been an outbreak in Yosemite in 2012.⁶

However, fungal infection seemed probable, given the nodular pattern of the evolving pulmonary infiltrates, and eventually the report of a fungal growth on cultures. In addition to coccidioidomycosis, blastomycosis, which is endemic in the south-eastern USA, was considered. Aspergillosis was also initially suspected, as was cryptococcal infection and pneumocystis, although the patient did not appear to be immunosuppressed, and the CT findings lacked the ground glass infiltrates typical of pneumocystis infection.

OUTCOME AND FOLLOW-UP

Shortly after the addition of amphotericin B to his antimicrobial regimen, the patient's clinical picture began to improve, with resolution of fever and decrease in inflammatory markers. Further analysis of the fungal cultures in the Mycology Reference Laboratory in Bristol, England, confirmed the presence of *Coccidioides* sp (Figure 4), and was further supported by positive *Coccidioides* serology. At this point, antibiotics were stopped, with continued clinical improvement.

His liver function tests gradually returned to normal. His antifungal therapy was changed to intravenous fluconazole, and he was discharged 32 days post admission on a course of oral fluconazole, which was continued for a duration of 6 months. During this time, the patient continued to steadily improve. At 6 months postdischarge, he was feeling completely well. Repeat CT thorax showed significant improvement in the bilateral infiltrates with persistent nodular changes throughout lung fields and some fibrocavitary changes, particularly in the left lower lobe (figure 5).

DISCUSSION

This case was of interest due to the rarity of this condition in Europe and the patient's complicated course. Coccidioidomycosis is rarely encountered in Europe; however, we can expect the

Figure 5 CT thorax at 6 months postdischarge, showing bilateral pulmonary nodules and persistent fibrocavitary disease in the left lower lobe.

frequency of coccidioidal infections to increase in non-endemic areas for a variety of reasons. First, travel to endemic areas is becoming more common. The frequency of coccidioidal infection has also increased dramatically in its endemic areas recently. Its incidence has increased from 5.3 cases per 100 000 population in 1998 to 42.6 cases per 100 000 population in 2011.⁷ While much of this increase is explained by more sensitive serological testing, there has also been a significant rise in the absolute number of cases, which is due to a number of factors such as climate change and increasing susceptibility of populations to the disease through age and immunosuppression. The increasing use of novel immunosuppressants such as tumour necrosis factor- α inhibitors may put patients at particular risk of developing the disease.¹

The case illustrates the importance of an accurate travel history, particularly in patients presenting with unusual infections. Although the patient at first reported having visited the eastern USA, it was not until the diagnosis of an unusual fungal infection became apparent that he was questioned more thoroughly and added that he had also visited the west coast. However, Yosemite Park is not within the high-risk area for coccidioidomycosis.

The diagnosis of coccidioidomycosis, as was the case here, is often delayed. This is largely due to the fact that the condition is not considered in the initial differential, particularly outside endemic areas. Another consideration is the difficulty in obtaining material to culture. In this case, bronchoscopy was required to obtain adequate material. Although *Coccidioides* will grow on routine culture media, they do take longer to isolate (up to 1 week) than would be the case for more common respiratory pathogens.⁸ Serological testing is often used to make a diagnosis in ambulatory patients in whom it is not necessary or practical to obtain clinical specimens.

It is generally accepted that milder forms of the disease do not usually require treatment in immunocompetent patients, but that they should be closely monitored for a period of up to 2 years.^{1 3} However, our patient clearly had a severe infection

requiring systemic antifungal therapy. Azoles are typically first line, with amphotericin kept in reserve for more severe or resistant infections, due to its greater toxicity.¹ Our patient was initially empirically treated with amphotericin, and once the diagnosis was confirmed, he was switched to first intravenous and later oral fluconazole, with sustained clinical response.

Radiographic findings will typically recede after a period of some months; however, in a minority of cases, there can be persistence of pulmonary nodules, thin-walled cavities or more chronic fibrocavitary disease for months to years after primary infection.⁵

Learning points

- ▶ Coccidioidomycosis is an increasingly important cause of respiratory and systemic infections in its areas of endemicity, particularly the south-western USA.
- ▶ It is rarely encountered in European countries; however, given increased travel to these areas and increasing patient susceptibility to the disease, it is important to consider it in the differential diagnosis of patients with a relevant travel history.
- ▶ Milder forms of the disease may not require treatment; however, more severe cases require prolonged courses of antifungals.
- ▶ In certain cases, chronic nodular or fibrocavitary disease may persist for months to years following treatment, and physicians should pay close attention to radiographic changes during follow-up.

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