Medical Mycology Case Reports 14 (2016) 12–16

Contents lists available at ScienceDirect

Medical Mycology Case Reports

journal homepage: www.elsevier.com/locate/mmcr

Chronic Paracoccidioidomycosis with adrenal involvement mimicking tuberculosis – A case report from Austria

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ARTICLE INFO

Keywords:
Paracoccidioidomycosis
Paracoccidioides brasiliensis
Endemic systemic mycosis
Bilateral adrenal enlargement
Tuberculosis

ABSTRACT

Paracoccidioidomycosis is a systemic fungal infection caused by *Paracoccidioides brasiliensis* and endemic in certain areas of Central and South America. We report a case of a 62-year-old-man with a complex history of tuberculosis and imaging findings of a cerebral lesion and bilateral adrenal enlargement. Biopsy of adrenal gland revealed *Paracoccidioides brasiliensis*. This case highlights the importance of travel history for diagnosis of paracoccidioidomycosis in non-endemic areas and emphasizes the clinical and histopathological similarities with tuberculosis.

1. Introduction

Paracoccidioidomycosis is a systemic fungal infection caused by the thermally dimorphic fungus *Paracoccidioides brasiliensis* [1]. This disease is endemic in certain South and Central American countries with the highest prevalence observed in Brazil (approximately 80%) [2]. People who work in agriculture and live in rural areas are at a particularly high risk for infection [1]. Due to its specific geographical distribution, paracoccidioidomycosis is only observed in patients who have lived or travelled in endemic regions [3]. An increase in migration and travel activities might contribute to a higher prevalence of paracoccidioidomycosis and other systemic mycoses also in Europe.

The thermally dimorphic fungus *Paracoccidioides brasiliensis* grows as a filamentous fungus at 20–26 °C and as yeast at 37 °C [2]. Diagnosis is based on the direct identification of the fungus with microscopy, culture or histology from clinical specimen [2]. In addition, molecular biological techniques such as polymerase chain reaction (PCR) demonstrate high sensitivity suitable for diagnosis and monitoring of treatment [4,5]. Serological tests are used for evaluation of treatment response and disease recurrence [6].

Paracoccidioidomycosis clinically appears in two different forms: an acute/subacute juvenile form and a chronic adult form [2]. More than 90% of cases are chronic forms predominantly affecting men 30–60 years old and are characterized by slow progression over months or even years. This form can occur either as unifocal if only the lungs are affected (approximately 25%) or multifocal with extrapulmonary dissemination to oral or nasal mucosa, skin, lymph nodes or adrenal glands. Less frequently, involvement of the eyes, central nervous system (CNS), bones, vascular system and genital lesions may occur [2].

The fungus has been detected in soil, but the natural habitat is unknown. Human to human transmission has not been described, yet [7]. Similar to other systemic mycoses, *Paracoccidioides brasiliensis* enters the host via the respiratory tract and is usually inhaled during agriculture-related activities. Depending on the patient's immune status, it may stay inactive or spread by lymphatic and haematogenous dissemination to various secondary sites [1,2]. The choice of treatment with azole derivatives, amphotericin B and sulfonamides depends on the severity of the disease [8].

Diagnosis of imported paracoccidioidomycosis in non-endemic countries is challenging [9]. First, the latency period between inoculation of the pathogen and manifestation of overt symptoms may be very

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http://dx.doi.org/10.1016/j.mmcr.2016.12.002
Received 14 November 2016; Received in revised form 30 November 2016; Accepted 1 December 2016
Available online 02 December 2016

long [2]. Second, physicians in non-endemic countries have limited clinical experience with endemic systemic mycosis. Third, clinical and histopathological presentation of this fungal infection resembles several other infectious and non-infectious diseases.

We report on a rare case of paracoccidioidomycosis in Europe that was initially misdiagnosed and treated as tuberculosis.

Aim of this case report is to strengthen awareness for imported endemic systemic mycosis - in particular paracoccidioidomycosis - and emphasize the similarities to tuberculosis and importance of travel history.

2. Case

A 62-year-old man was transferred from a community hospital to our department due to suspected diagnosis of reactivated tuberculosis of the lungs and adrenal glands in February 2015 (day 0). He reported left-sided chest and abdominal pain, weight loss of 12 kg during the last 3 weeks as well as night sweats and cough. The punctum maximum of the abdominal pain was located at the left costal margin and aggravated at inspiration.

Past medical history revealed several episodes of tuberculosis with involvement of the lungs, testes and adrenal glands (Fig. 1). The patient reported that tuberculosis was diagnosed for the first time at the age of 7 years, followed by reactivations in the lungs with dissemination to the testes at the age of 14 and 21. Therefore, the patient had received tuberculostatic therapy, repeatedly. In 2010, he underwent CT-guided biopsy of a suspicious pulmonary nodule in the right lower lobe and left adrenal gland due to considerable enlargement of adrenal glands. Based on the histopathological finding of epithelioid cell granuloma with central necrosis, the diagnosis of tuberculosis of lungs and adrenal glands was made. At that time, sputum smear, PCR and culture for acid fast bacilli were negative. Due to increasing size of the adrenal glands the patient underwent a second biopsy in the same hospital in 2012.

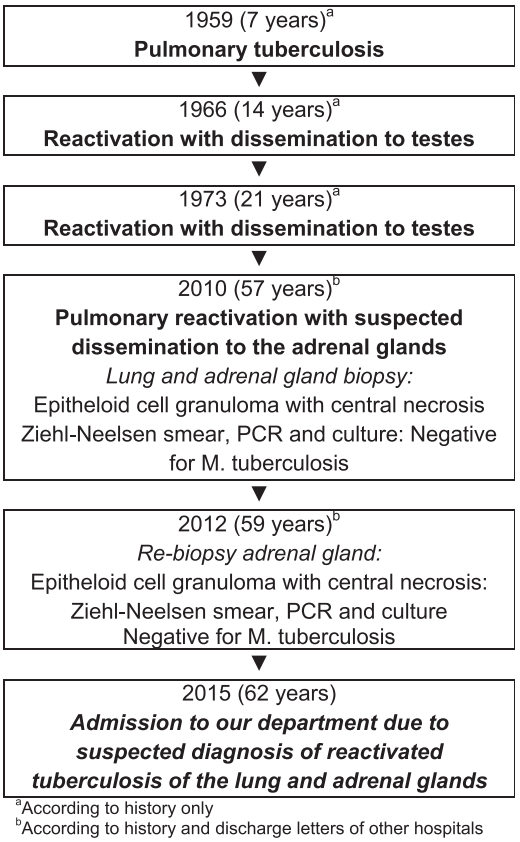

Fig. 1. Timeline of patient's tuberculosis.

Histopathological finding were similar to previous biopsy and again considered to be tuberculosis.

From the year 1997 until 2001 he made yearly visits – each for several weeks - to a village in Regio de Pasco (Peru), a rural area located next to the rainforest of the Amazonas. He lived there in a house with a garden for approximately three years (2002–2004) and helped to construct a hospital. He did no agricultural or field work. During his stay in Peru he had no injury or disease worth mentioning. Except for two days in Arica (Chile) he did not visit any other South or Central American regions or countries. In addition, he reported that one day he recognized bats in the ceiling of his house and inhaled their excrements during cleaning.

In addition to tuberculosis our patient had a past medical history of chronic bronchitis, Billroth II surgery due to peptic ulcer disease, cholecystectomy and prostate cancer treated with radiation therapy approximately 10 years ago. The patient was a retired patient transport service driver in an Austrian hospital. Family history revealed a tuberculosis infection of his father. He was a current smoker with a history of 45 pack years, reported occasional alcohol consumption and no known allergies. He was on no chronic medication.

Upon admission, the patient appeared in a good general condition with normal body temperature and a blood pressure of 120/70 mmHg. Auscultation and percussion of lungs and heart were unremarkable. The abdomen was soft and showed periumbilical tenderness without resistance. Peripheral edema was not observed. Basic neurological examination and skin were unremarkable. No enlarged lymph nodes were found.

Electrocardiogram showed normal sinus rhythm with 78 beats per minute and no pathological findings. There was a mild eosinophilia (6%) and monocytosis (16%), but total white cell count (8.1 G/l), hemoglobin (13.9 g/dl), and platelet count (366 G/l) were within normal limits. Levels of serum creatinine, and blood urea nitrogen (BUN) were normal. The concentration of serum gamma glutamyltransferase (GGT, 193 U/l), alkaline phosphatase (224 U/l), and C-reactive protein (9.0 mg/dl), plasma fibrinogen (560 mg/dl), and erythrocyte sedimentation rate (ESR, 54/81 mm) were elevated. Serum albumin (3.4 g/dl) and sodium (135 mmol/l) were slightly decreased while other electrolytes were normal. Myocardial biomarkers such as high sensitive Troponin-T (hs-TnT), creatine kinase (CK) and muscle-brain type creatine kinase (CK-MB) were within normal range.

Computed tomography (CT) showed postspecific pulmonary lesions. Compared to previous examinations, abdominal CT (day +0) revealed an increasing inhomogeneous enlargement of the adrenal glands (4.0×6.3 cm) (Fig. 2). Additionally, several enlarged retroperitoneal and mesenterial lymph nodes were found. Subsequently

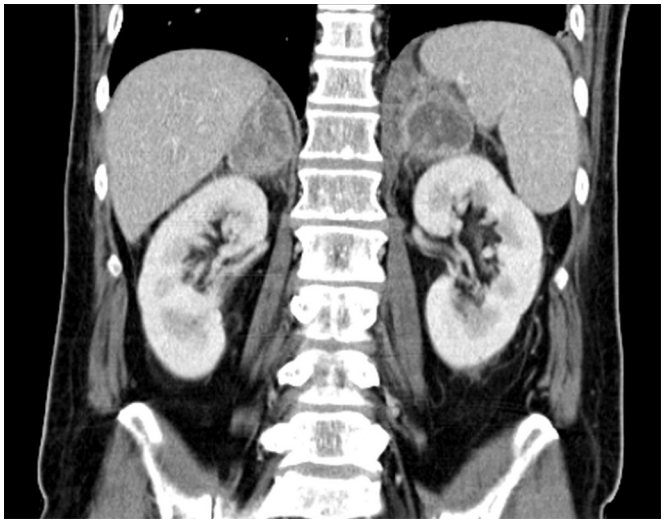

Fig. 2. Abdominal CT scan showing considerable enlargement of adrenal glands.