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Case report

Pulmonary nocardiosis in Chronic Obstructive Pulmonary Disease: A new clinical challenge

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ABSTRACT

Pulmonary nocardiosis (PN) is a rare but severe disease caused by *Nocardia* spp. Despite the traditional description as opportunistic infection, case reports and case series of pulmonary nocardiosis have recently been reported in immunocompetent patients too, in particular among people with chronic pulmonary diseases such as advanced Chronic Obstructive Pulmonary Disease (COPD).

PN is characterized by non-specific symptoms and radiological findings; bacteriological culture can be difficult. For the reasons above, diagnosis of PN is challenging, sometimes resulting in a misdiagnosis of tuberculosis.

We report an interesting case of PN in a 75-year-old male with COPD. He complained a 3-months history of fatigue, evening rise in body temperature, night sweats, unexplained weight loss of 5 kg, worsening dyspnea, cough and mucopurulent sputum. The chest X-ray showed multiple nodules with cavitations bilaterally in the apical and subclavian regions. *Nocardia cyriacigeorgica* with 100% identity was identified in three sputum samples.

Since the patient has never undergone a systemic and/or inhaled steroid therapy, and has no respiratory failure and comorbidities entailing immunodepression, it is conceivable that, in this immunocompetent patient, the COPD could represent an isolated risk factor for PN.

Risk factors, clinical presentations, radiographic findings, differential diagnosis and review of the literature of PN cases in COPD, pointing out the similarities and differences, are also described.

1. Introduction

Pulmonary nocardiosis (PN) is a rare but severe opportunistic infectious disease caused by *Nocardia* spp. The microorganism was first isolated by Edmond Nocard in 1888 from cattle with bovine farcy [1]; Eppinger reported the first human case of nocardiosis in 1890 [2]. The bacteria is commonly found in long standing dust, soil and stagnant water. Aerosol route is the main portal of entry into the body; direct inoculation as result of trauma or intravenous drug assumption or, more rarely, ingestion of contaminated food have also been described [3]. Human-to-human transmission has not been documented [4,5].

The prevalence of PN is not known. Traditionally, PN has been described in immunocompromised patients, with human immunodeficiency virus (HIV) infection, alcohol abuse, diabetes mellitus, organ transplantation and lymphoreticular neoplasm as the most frequently associated conditions [4,5]; lung transplant patients have the highest frequency of PN among recipients of solid organs [6]. Iatrogenic immunosuppression is a further risk factor, with long-term steroid, chemotherapeutic immunosuppressive and anti TNF-α agents as the most commonly associated drugs [4–8]; in particular, chronic steroid therapy has been highlighted in 36% [8],

Abbreviations: Chronic Obstructive Pulmonary Disease, COPD; Human Immunodeficiency Virus, HIV; High Resolution Computed Tomography, HRCT; Pulmonary Nocardiosis, PN; Tuberculosis, TB; trimethoprim-sulfamethoxazole, TMP-SMX.

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62.2% [9] and 64% [4] PN patients in three reviews. Intravenous drug abuse has also been described [10].

Commonly, PN presents as a subacute or chronic disease, with a marked tendency towards remissions and exacerbations. It is characterized by non-specific symptoms such as low fever, night sweats, weight loss, cough, expectoration, dyspnea and chest pain; radiological findings include areas of consolidation, nodules and cavitations which are not pathognomonic [4]. Bacteriological culture can be problematic too. Therefore the clinical and imaging presentation can be very similar to tuberculosis (TB) which represents one of the differential diagnosis [11,12]. Mortality is very high, ranging from 14 to 40% and increasing to 60–100% in patients with dissemination to the central nervous system [5,13]. Life-saving treatments are widely available: trimethoprim-sulfamethoxazole (TMP-SMX) is often used alone, but combination therapy is recommended and should continue until clinical patient improvement occurs and Nocardia species identification and antimicrobial drug susceptibility information can be confirmed; single-drug therapy may suffice thereafter [14].

In recent years, nocardiosis has been described among immunocompetent patients, both as isolated cases and case series, in lungs and other sites [15–20]. They can represent from 33% to 56% of total cases [21,22]. In particular, among patients with chronic respiratory diseases, Chronic Obstructive Pulmonary Disease (COPD) and bronchiectasis have been found as predisposing factors [23–39]. Despite reports in literature are limited, COPD is considered the third most common risk factor, surpassed only by chronic steroid treatment and solid organ transplantation [4,33,40–42].

Moreover, COPD life expectancy can be strongly affected by PN: a mortality rate of 17% within the first month and 33% within the first year from diagnosis of PN have been reported [42]. In comparison, the mortality rate for acute exacerbation of COPD is 8% during hospital stay and 23% after 1 year of follow-up [43].

Here we present a case of PN mimicking TB in a patient with undiagnosed COPD.

2. Case presentation

A 75-year-old white male, weighing 65 kg, presented to our center with complaints of a 3-months history of fatigue, evening rise in body temperature, night sweats, unexplained weight loss of 5 kg, worsening dyspnea, cough and mucopurulent sputum. He was a current smoker (30 pack/years) and worked in a stone quarry up to 12 years before; he had a history of chronic catarrhal bronchitis, benign prostatic hypertrophy and an intestinal polypectomy. He denied performing spirometry and taking systemic or inhaled corticosteroids; a chest x-ray of 3 years before showed rarefaction of bronchovascular tree.

On examination, he was afebrile and reduced vesicular murmur and widespread rhonchi were heard on auscultation of the chest. Remainder of the physical examination was unremarkable.

Blood tests showed neutrophilic leukocytosis (white blood cells 16500/mL, 70% neutrophils), mild anemia (hemoglobin 11,4 g/dl), moderate increase in serum inflammatory markers (erythrocyte sedimentation rate 72 mm/h, C-reactive protein 20 mg/l). Plasma immunoglobulin, liver and renal function were in the normal range and HIV antibody testing was negative.

A spirometry test was performed, revealing a severe obstructive ventilation defect, post b2 agonist Forced Vital Capacity of 72% and Forced Expiratory Volume in one second of 46% predicted. The chest X-ray showed, bilaterally in the apical and subclavian regions, sclerosis and multiple nodules with cavitations (Fig. 1). The chest high resolution computed tomography (HRCT) was reported as following: “Multiple nodular opacities are recognized in the upper lobes, in the apical segments of the lower lobes and in subpleural location; small and regular central cavitations are there in some of these lesions. Multiple focal points of “tree in bud” and bronchiectasis, with prevalent cystic type, in both lung apices are also present. No significant mediastinal lymphadenopathy. These findings are consistent with chronic TB” (Fig. 2).

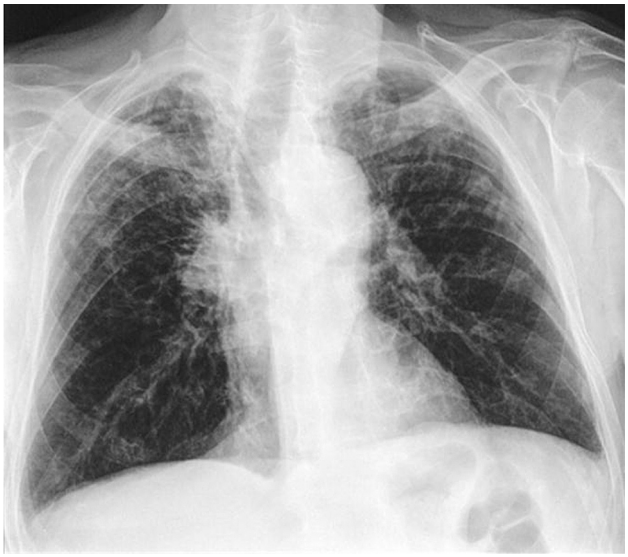

Fig. 1. Chest X-ray showing sclerosis and multiple nodules with cavitations in upper and medium lung zones bilaterally.

Three sputum samples on three different days were collected and submitted for the search of *Mycobacteria* spp. Specimen were digested and decontaminated according to Kubica procedure; sputum smears for acid-fast bacilli examination using Kinyoun staining and culture on solid (Löwenstein–Jensen) and liquid medium (Mycobacteria Growth Indicator Tube) were then prepared. The microscopic examination showed filamentous, slim, branched (mycelium and hyphae), blue-to-fuchsia colored (acid-alcohol variable) elements (Fig. 3). *Nocardia* spp. was suspected and confirmed by Gram staining (not shown) and blood agar culture (Fig. 4). Culture on Löwenstein–Jensen medium is showed in Fig. 5. All the previous exams were negative for *M. tuberculosis*.

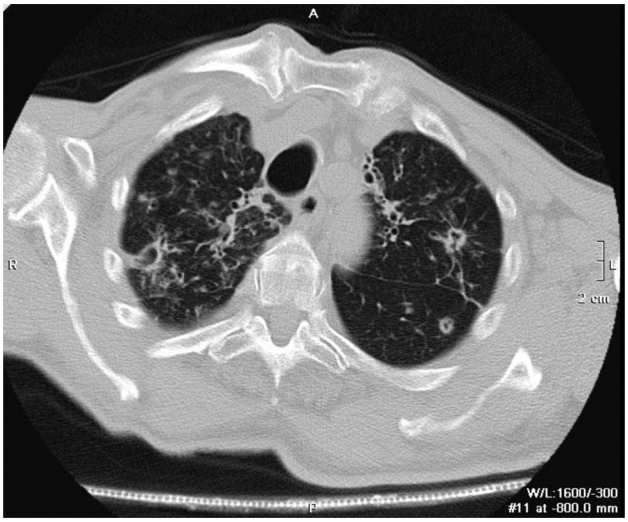

Fig. 2. Chest HRCT scan showing multiple nodular lesions with cavitations in upper lung zone bilaterally.