

Case Report

Pulmonary and cutaneous nocardiosis in a patient treated with corticosteroids*

BRUNO GUEDES BALDI¹, ALFREDO NICODEMOS CRUZ SANTANA², TERESA YAE TAKAGAKI³

ABSTRACT

Nocardiosis is a localized or disseminated infection caused by gram-positive bacteria of the genus *Nocardia*. The infection most commonly affects the lungs, skin and central nervous system. Nocardiosis principally occurs in individuals with cellular immunodeficiency and should be considered in the differential diagnosis when such individuals present respiratory, cutaneous or neurological alterations. Herein, we report a case of pulmonary and cutaneous nocardiosis in a patient receiving oral corticosteroids to treat bronchiolitis obliterans accompanied by organizing pneumonia of unknown origin. After long-term treatment with sulfamethoxazole-trimethoprim, the clinical and radiological profile improved.

Keywords: *Nocardia* infections; Lung diseases; Bronchiolitis obliterans; Adrenal cortex hormones; Case reports [Publication type]

INTRODUCTION

Nocardiosis is an infection that usually occurs in individuals with cellular immunodeficiency. It can be localized or disseminated and most often affects the lungs, skin and central nervous system (CNS).⁽¹⁻⁵⁾ The clinical-radiological presentation is nonspecific. The diagnosis is often delayed because the disease is not included in the differential diagnosis and because of

difficulties in culturing the bacteria.^(2,4)

Herein, we present the case of a patient being treated with systemic corticosteroids who developed pulmonary and cutaneous nocardiosis, with satisfactory evolution after treatment with the combination of sulfamethoxazole and trimethoprim (SMZ-TMP)

* Study carried out in the Pulmonology Department of the Faculdade de Medicina da Universidade de São Paulo (FMUSP, University of São Paulo School of Medicine), Sao Paulo, Brazil

1. Specialist in Internal Medicine and Emergency Medicine. Resident physician in the Pulmonology Department of the Faculdade de Medicina da Universidade de São Paulo (FMUSP, University of São Paulo School of Medicine), Sao Paulo, Brazil

PhD student in the Pulmonology Department of the Faculdade de Medicina da Universidade de São Paulo (FMUSP, University of São Paulo School of Medicine), Sao Paulo, Brazil

PhD in Pulmonology from of the Faculdade de Medicina da Universidade de São Paulo (FMUSP, University of São Paulo School of Medicine), Sao Paulo, Brazil

Correspondence to: Bruno Guedes Baldi. Av. Dr. Enéas de Carvalho Aguiar 255, Sala 7.079 - CEP: 05403-900, São Paulo, SP, Brasil. Tel: 55 11 3069-7202. Email: bruno.guedes2@terra.com.br

Submitted; 6 February 2006. Accepted, after review, 6 March 2006.

CASE REPORT

A 60-year-old white male patient, resident of the city of São Paulo (Brazil) and an insurance salesman, presented with fever for twenty days (approximately 38.5°C), sweats and dyspnea during heavy exertion, as well as tumors in the right cervical region and left arm. The patient had been taking prednisone for three months (20 mg/day at the time of the evaluation) for the treatment of bronchiolitis obliterans with organizing pneumonia of unknown origin. There was clinical and radiological evidence that this condition had been resolved. The patient did not smoke and did not have any accompanying diseases.

The physical examination revealed good general health status. However, in addition to the fever, there were rhonchi in both hemithoraces, and subcutaneous nodules (5 cm in diameter) were observed in the right cervical region and left arm, although without signs of inflammation (Figure 1).

Chest X-ray revealed multiple nodules disseminated throughout both lungs (more prominent on the right side), accompanied by opacification of the right costophrenic sulcus. A computed tomography scan of the chest confirmed the presence of nodules of various sizes, some of which presented cavitation. The laboratory test results were normal, and the serology for human immunodeficiency virus was negative, as were the results of two blood cultures.



Figure 1 - A) Subcutaneous nodule (approximately 5 cm) in the right cervical region; B) Subcutaneous nodule (approximately 5 cm) in the left arm

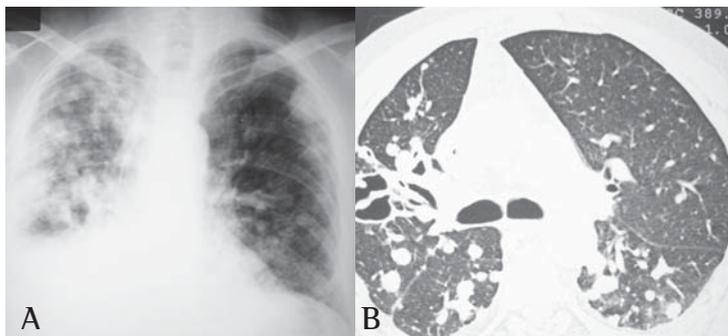


Figure 2 - A) Anteroposterior chest X-ray demonstrating multiple bilateral pulmonary nodules, some of them coalescent, accompanied by opacification in the right lung base; B) Computed tomography scan of the chest demonstrating diffuse nodular lesions, principally on the right side, some presenting cavitation

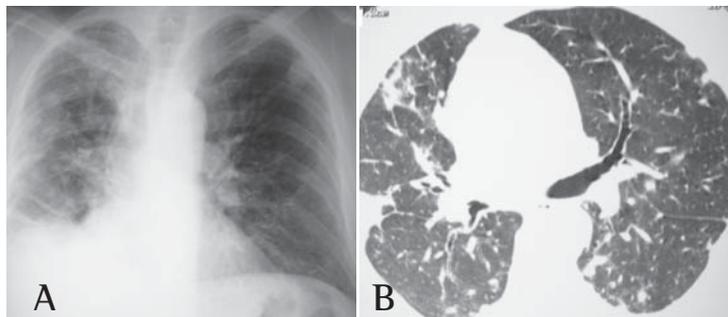


Figure 3 - A) Anteroposterior chest X-ray at 6 months after the initiation of treatment demonstrating reduction in the volume of the nodules but maintenance of the opacity in the right lung base; B) Computed tomography scan of the chest at 6 months after the initiation of treatment demonstrating reduction in the volume of the nodules and absence of cavitations

Fiberoptic bronchoscopy was performed, together with bronchoalveolar lavage and transbronchial biopsy. However, no diagnosis was made. Concomitantly, needle biopsy was performed on the subcutaneous cervical nodule, and the culture of the material tested positive only for *Nocardia asteroides*. After the diagnosis of nocardiosis had been made, the patient was submitted to a computed tomography scan of the brain, which was normal.

Thus, the patient was treated with SMZ-TMP (10 mg/kg/day of TMP) for six months, resulting in complete resolution of the symptoms, involution of the subcutaneous nodules and significant radiological improvement (Figure 3).

DISCUSSION

Nocardiosis is a localized or disseminated infection caused by gram-positive aerobic bacilli of the genus *Nocardia*, which present positivity in Ziehl-Neelsen staining (weakly positive for acid-fast bacilli), and can occur in animals or humans.

These bacilli are typically environmental saprophytes that live in the soil, in decomposing organic matter or in water. The principal species involved are *N. asteroides* (80% to 90% of the cases), *N. farcinica*, *N. nova*, *N. brasiliensis*, *N. otitidiscaviarum* and *N. transvalensis*.

Transmission of the disease usually occurs via inhalation, with deposition in the lungs, which can be disseminated to other sites. However, primary cutaneous infection can result from direct inoculation of the micro-organism, such as that occurring during trauma or surgery. There is no evidence of human-to-human or animal-to-human transmission.

Nocardiosis usually occurs in situations of cellular immunodeficiency, such as in recipients of solid organ or bone marrow transplants, patients with the human immunodeficiency virus and long-term users of corticosteroids, as well as in individuals presenting neoplasms or chronic lung diseases. However, in approximately 10% of the cases, the predisposing condition is not identified. In recent years, an increase in the number of reported cases has been observed, due to the evolution of the diagnostic modalities, the increase of the immunocompromised population and the inclusion of nocardiosis more frequently in the differential diagnosis of the infectious profiles of this group of patients.

The clinical profile is nonspecific, and must be suspected in patients with concomitant respiratory, cutaneous or neurological manifestations. Therefore, it is included in the differential diagnosis of sarcoidosis, actinomycosis and aspergillosis. The lung is the most frequently affected organ, and it must be remembered that nocardia is not part of the normal flora of the respiratory tract, and its identification in respiratory fluid should therefore always be evaluated as the potential causative agent of infection. Evolution can be acute, subacute or chronic, and possible complications include empyema, mediastinitis, pericarditis, necrotizing pneumonia, superior vena cava syndrome and pulmonary fibrosis.

The thoracic radiological presentation is also nonspecific, including nodules or masses (isolated or multiple), with or without cavitation (with cavitation being more common), reticular infiltrates, alveolar consolidation and pleural

effusion. Such alterations are predominately seen in the upper lobes and are often confused with tuberculosis, also due to the fact that nocardia is positive in Ziehl-Neelsen staining. In this situation, the culture is fundamental in the differential diagnosis. Tomography scans of the chest rarely reveal lymph node enlargement.

To differentiate between the localized and disseminated forms, the latter is defined as the bacteria being identified in two or more organs. The most frequently involved sites are the lungs, CNS, skin, kidneys, bones, heart and eyes. In relation to the CNS, the principal form encountered is parenchymatous abscess. Cutaneous involvement can occur in the primary and disseminated forms. *N. brasiliensis* is the most frequently isolated species and can manifest as ulceration, cellulitis or subcutaneous abscess.

For a definitive diagnosis, it is necessary to isolate and identify the organism through the analysis of a biopsy or aspirate from the affected sites or through the evaluation of respiratory fluid. The diagnosis is often delayed due to the difficulty of culturing the bacteria. On direct examination, it is characterized by ramiform gram-positive bacilli and by the positivity in Ziehl-Neelsen staining (weakly positive for acid-fast bacilli). In the culture, growth typically occurs at between two and five days, although incubation must be maintained for at least three weeks to rule out the diagnosis. Thus, it is fundamental to inform the laboratory of the suspicion of nocardiosis, so that the culture will be maintained for 20 or 30 days. Blood culture is rarely possible.

The histopathological evaluation reveals necrosis and abscess, with accumulation of neutrophils, lymphocytes and macrophages, without granuloma formation. There are no serologic tests for the evaluation of the infection. Neither needle aspiration nor cerebral lesion biopsy are necessary in confirmed cases of pulmonary or cutaneous nocardiosis. However, they can be considered in patients with the acquired immunodeficiency syndrome, in whom other infections should be ruled out.

The antibiotic treatment recommended depends on the severity and location of the infection and on the host immunity. There have been no randomized clinical trials demonstrating the best therapeutic regimen for nocardiosis, and

the choice is based on retrospective studies and case reports. For pleuropulmonary infections (with or without cutaneous involvement), as well as for the primary cutaneous form, the regimen of choice is the SMZ-TMP combination (5 to 10 mg/kg/day of TMP). When the infection is disseminated or when there is CNS involvement, it is recommended that, for the first six weeks, higher doses of SMZ-TMP (15 mg/kg/day of TMP) or the combination of imipenem (2 g/day) and amikacin (10 to 15 mg/kg/day) be used, maintaining the SMZ-TMP combination at lower doses (5 to 10 mg/kg/day of TMP) until the end of the treatment period.

The duration of the treatment depends on the location of the lesions and on the host immunity. For cutaneous lesions, the treatment should be maintained for three months, compared with up to six months for the pulmonary and systemic forms (without CNS involvement). In immunocompromised patients and in cases of CNS involvement, the treatment should be maintained for twelve months. Clinical improvement usually occurs between seven and ten days. In patients that are intolerant of or refractory to the SMZ-TMP combination, the combination of imipenem and amikacin can be used, as can monotherapy with ceftriaxone, minocycline, linezolid or the combination of amoxicillin and clavulanate. Antimicrobial susceptibility tests are suggested in refractory patients, patients experiencing recurrence and patients presenting hypersensitivity to the current regimen.

Surgical treatment is indicated for the majority of patients presenting CNS lesions that are refractory to antibiotic therapy, accompanied by extensive cutaneous involvement.

In summary, nocardiosis is an infection that is difficult to diagnose and should be included in the differential diagnosis of patients in which there are respiratory, cutaneous and/or neurological manifestations, principally in individuals with cellular immunodeficiency or chronic lung disease. The diagnosis is usually delayed, due to the lack of specificity of the clinical profile and the difficulty in culturing the bacteria, which in turn delays the initiating of treatment, thereby increasing morbidity and mortality. The treatment should be extended, typically to between six and twelve months, due to a tendency toward recurrence of the infection when it is treated for shorter periods.

REFERENCES

1. Nocardia infections. *Am J Transpl.* 2004;4(Suppl.10):47-50.
2. Narushima M, Suzuki H, Kasai T, Tsuzura Y, Tomita S, Endoh S, et al. Case report: Pulmonary nocardiosis in a patient treated with corticosteroid therapy. *Respirology.* 2002;7(1):87-9.
3. Saubolle MA, Sussland D. Nocardiosis: review of clinical and laboratory experience. *J Clin Microbiol.* 2003;41(10):4497-501.
4. Corti ME, Villafane-Fiotti MF. Nocardiosis: a review. *Int J Infect Dis.* 2003;7(4):243-50.
5. Hui CH, Au VW, Rowland K, Slavotinek JP, Gordon DL. Pulmonary nocardiosis re-visited: experience of 35 patients at diagnosis. *Respir Med.* 2003;97(6):709-7.
6. Lederman ER, Crum NF. A case series and focused review of nocardiosis clinical and microbiologic aspects. *Medicine (Baltimore).* 2004;83(5):300-13.
7. Ribeiro SC, Santana AN, Arriagada GH, Martins JE, Takagaki TY. A novel cause of invasive pulmonary infection in an immunocompetent patient: *Aspergillus candidus*. *J Infect.* 2005;51(4):e195-7.