

# Acute Respiratory Distress Syndrome Caused by Pulmonary Nocardiosis in a Patient With Systemic Lupus Erythematosus

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*Nocardia* is a gram-positive bacillus that infects mainly immunodepressed patients. Its association with lupus erythematosus has been described only occasionally and we have found no reports in the literature of an association between lupus and acute respiratory distress syndrome due to pulmonary nocardiosis. We present such a case and discuss the mechanisms that make this lung infection so virulent as well as its epidemiological and microbiological characteristics, clinical presentation, diagnosis, and treatment.

**Key words:** *Nocardia*. Pulmonary nocardiosis. Systemic lupus erythematosus. Acute respiratory distress syndrome.

Síndrome de distrés respiratorio agudo provocado por nocardiosis pulmonar en un paciente con lupus eritematoso sistémico

*Nocardia* es una bacilo grampositivo que infecta principalmente a pacientes inmunodeprimidos. Su asociación con el lupus eritematoso sistémico se ha descrito pocas veces, y en la bibliografía médica revisada no hemos encontrado ningún caso asociado al síndrome de distrés respiratorio agudo por una nocardiosis pulmonar. A partir de un caso clínico se realiza una descripción de los mecanismos de virulencia de esta bacteria, así como de las características epidemiológicas, microbiológicas, forma de presentación clínica y procedimientos diagnósticos y terapéuticos de esta entidad.

**Palabras clave:** *Nocardia*. Nocardiosis pulmonar. Lupus eritematoso sistémico. Síndrome de distrés respiratorio agudo.

## Introduction

Nocardiosis is an opportunistic infection whose association with systemic lupus erythematosus (SLE) is rare (0.7%-2.8%).<sup>1,2</sup> Only 30 cases have been reported in the literature since 1957,<sup>1-5</sup> and in one of the largest databases of SLE—created in Singapore—only 6 patients out of 786 examined over a 5-year period also had nocardiosis. Three of those 5 had lung involvement.<sup>1</sup>

We report a case of pulmonary nocardiosis that was difficult to manage in a patient with SLE. The patient later developed complicated acute respiratory distress syndrome, which resolved slowly but satisfactorily. We are unaware of any previous publications on this complication of SLE.

## Case Description

The patient was a 34-year-old woman with a history of chorea, retinal vasculitis, repeated miscarriage, hypertension, thrombopenia, and lupus anticoagulant positivity. She had been diagnosed with SLE 3 years earlier and, after a renal biopsy, with lupus kidney. The complicated management of her underlying disease had required prolonged treatment with high doses of corticosteroids (40 mg/day) over the previous 24 months before the present admission.

The patient complained that 1 month earlier she had begun to feel weak. A chest radiograph revealed a nodular image measuring 1□1 cm in the lower right lobe. Ten days before admission to the intensive care unit she developed a productive cough with green sputum, and fever with profuse sweating. Her condition deteriorated, and she developed dyspnea at rest. Physical examination upon admission revealed Cushingoid moon face, abundant acne and hypertrichosis, tachypnea (36 breaths/min) and increased work of breathing, temperature of 37.2°C, blood pressure of 104/50 mm Hg, and heart rate of 126 bpm. Auscultation revealed diminished vesicular sounds at the base of the right lung and crackles at the base of the left. Results of arterial blood gas analysis showed a pH of 7.47, PaCO<sub>2</sub> of 32 mm Hg, PaO<sub>2</sub> of 38 mm Hg, HCO<sub>3</sub><sup>-</sup> of 23.3 mEq/L. The hemogram

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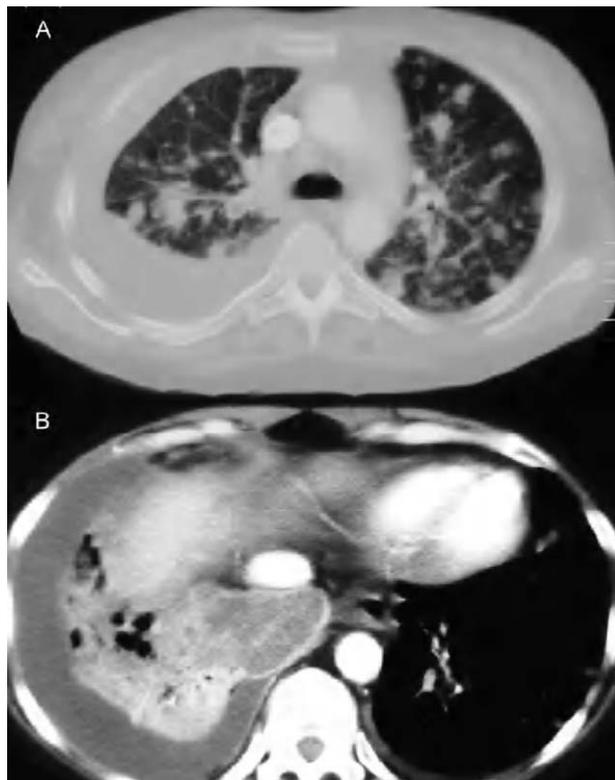
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**Figure 1.** Posteroanterior chest radiograph that shows multiple nodular acinar opacities that are poorly differentiated, in both lung fields. There is a larger nodular lesion in the lower right lobe associated with pleural effusion.

revealed marked leukocytosis ( $36\,000 \times 10^3/\text{mL}$ , 94% polymorphonuclear cells), a hemoglobin concentration of 10.7 g/dL and a platelet count of  $130\,000 \times 10^3/\text{mL}$ . Biochemistry indicated acute kidney failure (creatinine 3.3 mg/dL, urea 150 mg/dL), a C-reactive protein level of 374 mg/L, and albumin concentration of 2.9 mg/L. Other parameters were normal. The chest radiograph revealed multiple nodules in both lung fields and right pleural effusion. Those findings were confirmed by computed tomography (Figures 1 and 2).

An initial attempt at ventilation with continuous positive airway pressure support failed to change the clinical picture or arterial blood gas results indicative of severe respiratory insufficiency (with continuous positive end-expiratory pressure of 5 cm H<sub>2</sub>O and inspired oxygen fraction of 65%, pH was 7.35; PaO<sub>2</sub>, 71 mm Hg; PaCO<sub>2</sub>, 34 mm Hg; HCO<sub>3</sub><sup>-</sup>, 19.6 mEq/L; base excess, -4.5; and the ratio of PaO<sub>2</sub> to inspired oxygen fraction, 110). Therefore orotracheal intubation and mechanical ventilation were ordered. Empirical treatment with imipenem, quinolones, and liposomal amphotericin was started, and the corticosteroid treatment prescribed for the underlying disease was continued. Direct inspection of the blood culture showed gram-positive bacilli. Growth of *Nocardia asteroides* was evident at 7 days. Empyema (pH, 7.0) necessitated placement of a pleural drain along with thrombolytic therapy with intrapleural urokinase. A bronchial aspirate sample began to grow branching acid-fast bacilli suggestive of *Nocardia* species. The antibiogram demonstrated resistance to cotrimoxazole and sensitivity to imipenem; therefore the latter treatment was continued and the antifungal agent was discontinued. A computed tomography brain scan was negative. A bilateral interstitial-alveolar pattern was observed in the thoracic images. That finding, along with arterial blood gas results, indicated acute respiratory distress syndrome after left ventricular heart failure had been ruled out. Therefore, prophylactic mechanical ventilation was maintained for 30 days. A tracheostomy was required for weaning. Finally,



**Figure 2.** Contrast-enhanced computed tomography (CT) scans of the thorax. A: CT slice of the lung through the carina that reveals multiple pulmonary nodules of varying sizes on both sides. B: CT slice of the lower lobes and mediastinum in which extensive heterogeneous consolidation can be seen on the right side with areas of low attenuation and fluid collection consistent with either necrotizing pneumonia or pleural effusion.

tubes were removed and the patient was discharged home in satisfactory condition. No recurrence of *Nocardia* infection was observed over the 18-month follow-up period.

## Discussion

*Nocardia* organisms are found widely distributed in the environment, including in airborne dust particles. Inhalation is the main path by which *Nocardia* pathogens enter the body and therefore the lung is the most commonly affected organ,<sup>2,6</sup> although there is no evidence of human-to-human transmission.<sup>7</sup>

*Nocardia* organisms are pathogenic intracellular bacteria that express their virulence in patients with altered T-lymphocyte mediated immune systems. Such is the case of patients with SLE and those being given high-dose corticosteroid treatment,<sup>8</sup> which appears to be an independent risk factor for nocardiosis.

No radiologic signs characteristic of pulmonary nocardiosis have been identified, although the condition has been described in the presence of single or multiple nodules.<sup>9</sup> Pulmonary masses (often cavitated), reticular-nodular and interstitial infiltrates, and pleural effusions have also been reported.<sup>7</sup> Differential diagnosis sometimes involves consideration of metastatic lung disease.<sup>10</sup> Our patient's radiographs and clinical

condition at first suggested pulmonary tuberculosis or fungal infection, although direct visualization of gram-positive bacilli in the blood culture indicated that the empirical antibiotic treatment should be continued.

The course of pulmonary nocardiosis can be acute or subacute. It may even imitate other chronic processes like tuberculosis, fungal infections or cancer in that symptoms are nonspecific: fever, nocturnal sweating, fatigue, anorexia, weight loss, dyspnea, cough, hemoptysis, and pleuritic chest pain.<sup>7</sup> A tentative diagnosis is made upon direct visualization of branching filamentous bacilli that are gram-positive. The diagnostic yield of cultures increases if they are maintained about 4 weeks given that *Nocardia* bacilli grow slowly.<sup>7</sup> For our patient, diagnostic confirmation from blood culture was received after 7 days, a relatively fast report given that the mean period between presentation of symptoms and bacterial growth in culture was 12 months in a published series of cases.<sup>11</sup> When invasive diagnostic methods are used, cultures are positive in 85% to 90% of cases,<sup>12</sup> whereas the yield of blood cultures is only 25%.<sup>13</sup>

The central nervous system (CNS), which is affected in 20% of cases, is the structure for which this germ has the most affinity. Dissemination to the CNS can be ruled out by a computed tomography brain scan, as it was in our patient. Another characteristic of these pathogens is that infection recurs easily, such that treatment should be prolonged to avoid relapse. Overall mortality due to *N asteroides* infection in SLE is high (35%) and that rate doubles (75%) if the CNS is involved.<sup>2</sup>

The first line of treatment is considered to be trimethoprim-sulfamethoxazole (15 mg/kg/day),<sup>1</sup> because tissue penetration is excellent and because the cost is low; evidence from randomized controlled trials is unavailable, however. Some authors recommend starting treatment with antibiotics with greater potency—such as imipenem and amikacin—in patients with severe disease or in patients who are immunodepressed, based on demonstration of the improved activity of those drugs in vitro or greater synergy in animal models.<sup>14</sup> In the case we report, the sensitivity study showed resistance to cotrimoxazole. We therefore prescribed imipenem, which was not combined with amikacin because of the patient's deteriorated kidney function. Optimal duration of treatment has not been determined, but current recommendations are that it be extended to prevent frequent recurrences. In patients with pulmonary or systemic nocardiosis without CNS involvement, duration of treatment is from 6 to 12 months. However, the minimum period should be 1 year for immunodepressed patients or those in whom the CNS is affected.<sup>7</sup>

Severe sepsis is believed to be the main cause of acute respiratory distress syndrome. Therefore, it is supposed that in a disease context with high mortality such as immunodepression with pulmonary nocardiosis,

many patients who die probably develop acute respiratory distress in the context of multiorgan failure leading to death. Nevertheless, we find only a few references to acute respiratory distress syndrome related to nocardiosis in the literature,<sup>14-16</sup> and none in a context of pulmonary nocardiosis and SLE. To prevent development of the inflammatory reaction that leads to acute respiratory distress syndrome, highly active antibiotic therapy must be applied, particularly in immunodepressed patients, in order to eradicate possible septic foci and thereby try to prevent uncontrolled perpetuation of the infectious process. If the process of acute respiratory distress syndrome has already begun, prophylactic mechanical ventilation with low flow volume and high positive end-expiratory pressure is recommended.<sup>17,18</sup>

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