Purulent Pericarditis and Cardiac Tamponade Caused by
Nocardia farcinica in a Nephrotic Syndrome Patient

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Abstract

Nocardiosis is an uncommon infection that occurs primarily in immunocompromised patients. We herein report an extremely rare case of Nocardia farcinica (N. farcinica) pericarditis. A 53-year-old man with nephrotic syndrome that required chronic corticosteroid therapy presented with pleuritic chest pain and cardiac tamponade. Pericardiocentesis revealed purulent pericardial effusion and a bacteriological examination showed the characteristic branching filamentous bacteria identified as N. farcinica. Aggressive surgical drainage and a trimethoprim-sulfamethoxazole based regimen resulted in clinical improvement. To the best of our knowledge, this is the first reported case of N. farcinica pericarditis in Thailand.

Key words: Nocardia spp., pericarditis, purulent, cardiac tamponade, nephrotic syndrome

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Introduction

Nocardiosis is a rarely occurring human infection, but an increasing number of cases are being reported worldwide. Nocardia species are saprophytic aerobic actinomycetes that mainly infect immunosuppressed patients, particularly those that have deficiencies in cell-mediated immunity such as those with malignancy, lymphoma, high-dose corticosteroid use, AIDS or following organ transplantation. Nocardia asteroides (N. asteroides) remains the most common pathogen reported to cause invasive diseases by far (1-3). However, Nocardia farcinica (N. farcinica) is more commonly associated with a life-threatening systemic infection (4). Moreover, N. farcinica characteristically shows microbiological resistance and is generally associated with a higher pathogenicity; hence, the identification of this particular pathogen and differentiation from N. asteroides is of great clinical importance (5, 6). A typical infection may involve virtually any organ; however, but primary pulmonary infection is the predominant mode. The subsequent spread to adjacent structures or to the brain is not uncommon. Patients usually present with a sub-acute course of fever, constitutional symptoms and organ-specific symptoms; however, the clinical course may be shortened in patients who are severely immunosuppressed (1-3).

Nocardia pericarditis, in particular, is an extremely rare disease. Since 1967, only 19 cases of such disease have been reported worldwide and, of these, only two were caused by the N. farcinica species (7, 8). We herein report the third documented case of N. farcinica pericarditis, and its progression into cardiac tamponade.

Case Report

A 53-year-old Thai man with nephrotic syndrome and steroid-induced diabetes presented with a one-week history of pleuritic chest pain and progressive dyspnea. He did not suffer from either fever, chills or coughing. Five months before the current presentation, he developed nephrotic-range proteinuria, and a subsequent renal biopsy led to the diagnosis of minimal change disease. No secondary causes of the nephrotic syndrome could be determined, as there was no evidence of malignancy, antibodies against hepatitis B and C viruses, antibodies against HIV or antinuclear antibodies. His serum levels of C3, C4 and CH50 were normal. He was initially treated with oral prednisolone at a dosage of 60 mg daily for 1 month. Due to persistent proteinuria, the dose of prednisolone was slowly tapered down to 40 mg daily. The accumulated dosage of prednisolone prior to this admission...
was approximately 6.5 g. He was diagnosed with steroid-induced diabetes 1 month prior to the current presentation and received metformin along with dietary modification. He was a smoker and a social drinker.

Upon admission the patient was tachypneic and tachycardic (150 bpm). He was afebrile and his blood pressure was 108/76 mmHg. There was no pericardial rub present. His lungs were clear upon auscultation. He had leukocytosis with a white blood cell (WBC) count of 23,390/μL with 93% neutrophils and a total lymphocyte count of 1,570/μL. His fasting blood sugar was 104 mg/dL and his glycosylated hemoglobin was 7.9%. His serum albumin level was 2.7 mg/dL, and his creatinine clearance was 52 mL/min. A urinalysis revealed 3+ proteinuria, and the urine protein-to-creatinine ratio was 1.1.

An electrocardiogram [ECG (Fig. 1)] showed sinus tachycardia with the diffuse ST segment elevation that is suggestive of pericarditis. A chest roentgenogram disclosed cardiomegaly and no pulmonary infiltrates. Chest computerized tomography revealed the presence of pericardial fluid at 2.8 centimeters in maximal thickness, as well as atelectasis and interlobular septal thickening at both basal lungs (Fig. 2).

Emergency echocardiography revealed a moderate sized pericardial effusion and the evidence of tamponade physiology. Emergency pericardiocentesis yielded 500 mL of purulent pericardial fluid containing 59,000 WBC/mm³ (93% polymorphonuclear cells). Gram staining and modified acid fast staining revealed numerous filamentous, beaded, branching bacilli (Fig. 3A, B); therefore, the patient was started empirically on a combination of intravenous trimethoprim-sulfamethoxazole, amikacin, imipenem and linezolid but only intermediate or resistant to clarithromycin, doxycycline, minocycline, ciprofloxacin and ceftriaxone. The bacteriological cultures from the pericardial tissue, sputum and blood cultures were negative. The serological test results were once again negative for HIV. No additional laboratory investigations regarding immunoglobulin levels, complement components and CD4+ T lymphocyte count were performed.

Postoperatively, the patient gradually recovered and received a three-week course of intravenous antibiotic therapy. Oral trimethoprim-sulfamethoxazole was then initiated for a planned 1-year course in order to prevent relapse. During the hospital admission, prednisolone at a dosage of 15 mg daily was prescribed, and adequate glycemic control was achieved. The patient was well at his 6-month follow-up, and still requiring prednisolone at a dosage of 5 mg daily. The laboratory data at that time revealed trace proteinuria, a urine protein-to-creatinine ratio of 0.2 and a serum albumin level of 3.8 mg/dL.

Discussion

Nocardiosis is a rare opportunistic disease that affects mainly patients with deficient cell-mediated immunity. The most common manifestation of nocardiosis in both immunocompetent and immunocompromised patients is pulmonary infection. The subsequent spread to adjacent structures or to the brain is not uncommon (3). N. asteroides remains by far the most common pathogen reported to cause invasive diseases; however, N. farcinica is more often associated with life-threatening systemic infections (4). Moreover, N. farcinica characteristically shows microbiological resistance and is likely associated with a higher pathogenicity; hence, the identification of this particular pathogen and the differentiation from N. asteroides is of great clinical impor-
tance (2, 5, 6). In 2005, Poonwan et al. reported *N. farcinica* as the most commonly isolated species from patients in Thailand, as identified by 16S ribosomal DNA sequencing (9).

*Nocardia* pericarditis, in particular, is an extremely rare manifestation of a *Nocardia* infection. An extensive review of 26 patients with purulent pericarditis from various causes demonstrated an overall 77% mortality (10). This review included only one patient with *Nocardia* pericarditis. Since 1967, only 19 cases of such disease have been reported worldwide and, of these, only two were due to *N. farcinica* [Table (7, 8)]. Frequently, purulent pericarditis patients develop cardiac tamponade or subsequent pericardial constriction. In a literature review by Poland et al. (11), six patients with purulent pericarditis due to *N. asteroides* were identified. All of these patients had a preexisting pulmonary focus of infection with *Nocardia*. Only three out of the six patients survived, and it was those patients that underwent surgical pericardectomy with subsequent appropriate antibiotic therapy. The Poland et al. review emphasizes the importance of the combination of surgical drainage with the appropriate empiric antibiotic selection in treating *Nocardia* pericarditis.

To date, there are no standardized guidelines for the treatment of nocardiosis, so most infectious authorities advocate empiric coverage with two or three intravenous agents such as trimethoprim-sulfamethoxazole, imipenem/cilastatin or amikacin while awaiting the results of the susceptibility testing (1, 2, 12, 13). *N. farcinica* isolates are generally sensitive to amikacin, linezolid and imipenem, but are frequently resistant to third-generation cephalosporins, clarithromycin, ciprofloxacin, gentamicin and tobramycin (14, 15). The resistance of *N. farcinica* to trimethoprim-sulfamethoxazole varies geographically, with a reported resistance of up to 91% in the US (15). Our patient was treated empirically with trimethoprim-sulfamethoxazole and imipenem/cilastatin, and the susceptibility data later confirmed the sensitivity to both agents. An initial antibiotic therapy should be given intravenously for at least 3-6 weeks until the patient shows clinical improvement. The recommended total duration of antimicrobial treatment in disseminated nocardiosis, especially in immunocompromised patients, is at least one year (1).

In patients receiving prolonged high-dose systemic corticosteroid therapy, the role of trimethoprim-sulfamethoxazole prophylaxis has been well established for *Pneumocystis carinii* pneumonia (16). Trimethoprim-sulfamethoxazole has been shown to be protective against a clinical infection with *Nocardia* in solid-organ transplant recipients (17, 18). However, other reports have demonstrated infection with *Nocardia* despite trimethoprim-sulfamethoxazole prophylaxis (7, 19). If, at the end of therapy for *Nocardia* infection, the patient requires continued immunosuppressive therapy, prophylaxis against *Pneumocystis* with trimethoprim-sulfamethoxazole should be given (16). However, the standard regimen of trimethoprim-sulfamethoxazole prophylaxis against *Nocardia* infections has not yet been definitely determined (19, 20).

To our knowledge, this is the first reported case of *N. farcinica* pericarditis in Thailand. This is noteworthy for being such an uncommon site of infection by an equally uncommon pathogen. He was likely infected due to his immunosuppressed state as well as the ubiquitous nature of the organism. This patient received chronic corticosteroid therapy that suppressed cellular immunity. Nephrotic syndrome patients may experience the urinary loss of complement com-

**Figure 2.** Computerized tomography of the chest revealing pericardial fluid of 2.8 centimeters at maximal thickness, as well as atelectasis and interlobular septal thickening at both basal lungs.

**Figure 3.** A: Gram stain of the purulent pericardial effusion showing gram-positive beaded, branching, filaments (original magnification ×1,000). B: Modified acid fast stain of the purulent pericardial effusion showing red-stained branching filaments of *Nocardia* spp. against a blue background (original magnification ×1,000).
components and immunoglobulins which may result in an impaired opsonization of encapsulated organisms such as Streptococcus pneumoniae and Escherichia coli (21). Hence, the most common infections attributable to nephrotic syndrome are invasive bacterial infections, especially cellulitis, peritonitis and sepsis (22). Nephrotic syndrome itself is not a strong risk factor for Nocardia infections. The suspected mode of transmission in this patient is through the respiratory tract, which is the most common portal of entry having contiguous spread to the pericardium. The rapid and accurate identification of Nocardia isolates to the species level was vital for a definitive diagnosis. We believe that the combination of an appropriate antibiotic therapy and aggressive surgical drainage through pericardiectomy played an important part in the favorable outcome of the dire condition of this patient.

Nocardia pericarditis is a rare condition with a high morbidity and mortality. The prompt identification of the Nocardia isolates is essential for an accurate diagnosis and effective treatment. The combination of an appropriate antibiotic therapy and an aggressive surgical pericardial drainage is crucial in the treatment of Nocardia pericarditis.

The authors state that they have no Conflict of Interest (COI).

Authors’ Contribution

SN and WT were involved in the data collection, the literature review and the writing of the manuscript. OT was involved in the data collection and in the interpretation of the data. RS was involved in the data collection and in editing the manuscript. All authors have read and approved the final manuscript.

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