Mediastinal mass and pericardial tamponade in a renal transplant recipient: A rare case of nocardia infection

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Patient: Female, 30
Final Diagnosis: Nocardiosis
Symptoms: Cardiac tamponade • cough • dyspnea • hoarseness • mediastinal mass • pericardial effusion • short of breath
Medication: —
Clinical Procedure: —
Specialty: Transplantology

Objective: Rare disease
Background: Nocardia infections can complicate solid organ transplantation. The usual clinical presentations include pulmonary infiltrates with or without cavitation and subcutaneous and brain abscesses. We report an unusual case of nocardia infection in a kidney transplant recipient that presented as mediastinal mass and was associated with pericardial tamponade.

Case Report: A 30 year old African American renal transplant recipient presented with cough, hoarseness and shortness of breath nine months after kidney transplantation. She received basiliximab perioperatively and her maintenance immunosuppression included tacrolimus, mycophenolate mofetil and prednisone. Computed tomography (CT) showed a large mediastinal mass with a large pericardial effusion. An echocardiogram revealed collapse of the right ventricle consistent with tamponade. We performed emergent pericardiocentesis to treat the tamponade. A mediastinoscopic biopsy of the mediastinal mass was done to establish a diagnosis. The mediastinal biopsy confirmed the growth of Nocardia. After 2 weeks of imipenem and 6 weeks of linezolid, there was marked radiographic improvement in the size of the mediastinal mass.

Conclusions: We report a rare case of a large mediastinal mass associated with pericardial tamponade from nocardia infection in a renal transplant recipient. An invasive approach may be necessary to obtain tissue diagnosis to direct treatment in these cases. Prompt and appropriate medical therapy leads to marked radiographic improvement.

Key words: nocardia • mediastinal mass • pericardial tamponade • kidney transplantation

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Background

Nocardia infection is an increasingly recognized complication among solid organ transplant recipients. The clinical spectrum of Nocardia is broad. The usual clinical presentation includes pulmonary infiltrates with or without cavitiation and subcutaneous abscesses. The central nervous system may also be involved and brain abscesses are not uncommon. Mediastinal and pericardial involvement are rare. We present a rare case of Nocardia infection presenting as a large mediastinal mass associated with pericardial tamponade in a renal transplant recipient.

Case Report

A 30 year old African American female underwent deceased donor kidney transplant for end stage renal disease due to systemic lupus erythematosus. She received an interleukin-2 receptor blocker, basiliximab, for induction and was on tacrolimus, mycophenolate mofetil and prednisone for maintenance immunosuppression. She is allergic to sulfa based medications and received three doses of monthly pentamidine inhalation for Pneumocystis jirovecii prophylaxis. She completed three months of valganciclovir for Cytomegalovirus (CMV) prophylaxis. She had excellent graft function with nadir serum creatinine 1.1 mg/dl two months post transplant.

Her initial symptoms started four months before her current presentation when she was admitted to another institution for fever, cough and shortness of breath. Her chest radiograph (CXR) showed a left upper lobe infiltrate and she was treated with 14 days of moxifloxacin for community acquired pneumonia. One week after she completed moxifloxacin, she received two weeks of amoxicillin/clavulanate due to persistent symptoms. Sputum and blood cultures were negative for bacterial growth. Three months prior to her current presentation, despite her second course of antibiotic, she had intermittent fever and cough. She was readmitted in the same local hospital where CXR showed persistent left upper lobe infiltrate. The computed tomography (CT) of her chest confirms the infiltrate and also showed small pericardial effusion. She had bronchoscopy and bronchial washing did not reveal bacterial etiology of the pneumonia. She completed three weeks of levofloxacin and had resolution of her symptoms.

Nine months after transplant she presented to our hospital with three weeks of intermittent fever and cough associated with progressive worsening of shortness of breath and hoarse voice. On physical examination, she was febrile and tachycardic. The auscultation revealed distant heart sounds and rales on bilateral lung fields. She had leukocytosis of 55,480/mm³ with left shift and 93% neutrophils. She had acute kidney injury with increase in serum creatinine to 4.3 mg/dl. The chest radiograph showed bilateral pleural effusion, a widened mediastinum and an enlarged cardiac silhouette. She initially received vancomycin, piperacillin-tazobactam and azithromycin for possible bacterial and atypical pneumonia. The CT scan of the chest (Figure 1) revealed a large mediastinal mass and a large pericardial effusion. There was diastolic collapse of the right ventricle on echocardiogram consistent with tamponade (Figure 2). Emergent pericardiocentesis was performed and 640 ml of serosanguinous fluid was drained. The pericardial fluid exhibited no growth of bacteria or acid fast bacilli. The fluid cytology did not reveal malignant cells. Soon after pericardiotomy, the patient’s serum creatinine was noted to gradually decrease back to her baseline of 1.1 mg/dl. The impression was that the patient had renal hypoperfusion from the massive pericardial effusion, causing acute kidney injury, which reversed after a significant amount pericardial fluid was drained.

The mediastinal mass measured 7×5×9 cm in size with mediastinal lymphadenopathy. The differential diagnosis for the mediastinal mass included thymoma, lymphoma, germ cell tumors and infectious etiology including fungal, bacterial and mycobacterial infections. We held mycophenolate mofetil as the differential diagnosis also included post transplant lymphoproliferative disorder (PTLD) and Epstein-Barr virus (EBV). She remained febrile after two days of admission and antibiotics were broadened to cover anaerobes and extended spectrum beta lactamase microbes. Antibiotics were changed from piperacillin-tazobactam to imipenem. The absence of pulmonary infiltrates made atypical infection less likely and azithromycin was discontinued. Fine needle aspirate of the mediastinal mass was obtained via endobronchial ultrasound, but the results were inconclusive. A cervical mediastinoscopy was then performed and biopsies of mediastinal mass were done to obtain a definitive diagnosis. Three wrinkled orange colonies grew in Sabouraud dextrose agar and stained partially on modified acid fast. The microscopic examination showed branching beaded rods suspicious for Nocardia which was confirmed by ribosomal deoxyribonucleic acid (DNA) sequencing. Mycobacterium fortuitum was also isolated by DNA sequencing in sputum cultures. The CT scan of the brain did not reveal any lesions which may be present in other cases of disseminated nocardia infection. Antitubercular medications were not initiated due to the absence of pulmonary infiltrates despite isolation of atypical mycobacterium in sputum. She continued antibiotic therapy with imipenem and linezolid for two weeks until Nocardia susceptibilities showed resistance to imipenem which was then discontinued. The patient remained on linezolid monotherapy, and after six weeks of treatment, the repeat CT scan showed marked decrease in the size of mediastinal mass to 4.7×3.4×5 cm (Figure 1) with resolution of pericardial effusion. Her creatinine improved to baseline of 1.1 mg/dl and she remained on tacrolimus and prednisone for maintenance immunosuppression.
Nocardia is an aerobic actinomycete and is a member of the Nocardiaceae family [1]. With the development of polymerase chain reaction (PCR) enzyme analysis and ribosomal ribonucleic acid (rRNA) sequencing, there are now over 50 species of Nocardia identified. It is a ubiquitous gram positive bacterium with filamentous branching hyphae on direct microscopy [2]. It may infect immunocompromised individuals including transplant recipients, those with HIV infection, malignancy and on long term steroid use [3]. The frequency of infection is higher among those who received heart (3.5%) and lung (2.5%) transplants compared to those with kidney transplants (0.2%) [4].

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Discussion

Nocardia is an aerobic actinomycete and is a member of the Nocardiaceae family [1]. With the development of polymerase chain reaction (PCR) enzyme analysis and ribosomal ribonucleic acid (rRNA) sequencing, there are now over 50 species of Nocardia identified. It is a ubiquitous gram positive bacterium with filamentous branching hyphae on direct microscopy [2]. It may infect immunocompromised individuals including transplant recipients, those with HIV infection, malignancy and on long term steroid use [3]. The frequency of infection is higher among those who received heart (3.5%) and lung (2.5%) transplants compared to those with kidney transplants (0.2%) [4].

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pericardial tamponade. Among solid organ transplant recipients, this is the first reported case of Nocardia presenting as a mediastinal mass. There are several unusual aspects in this case aside from the unusual clinical presentation. The risk factors that have been previously identified for the development of Nocardia among transplant recipients are not present in our patient. She had three episodes of pneumonia, treated with three different antibiotics with resolution of pulmonary infiltrates before presenting with mediastinal mass and pericardial tamponade. Definitive diagnosis for etiology of pneumonia was not elucidated despite bronchoscopy on her prior episodes of pneumonia. She then presented with a large mediastinal mass. She required an invasive approach using mediastinoscopy guided biopsy of mediastinal mass as endoscopic ultrasound guided biopsy was still inconclusive. Isolation of *Mycobacterium fortuitum* in sputum raises the concern for coinfection, which impacts choice of treatment. The hoarseness is thought to be from recurrent laryngeal nerve involvement which has improved after marked decrease in the size of the mediastinal mass. Despite mild compression of trachea on CT scan, surgical intervention was not necessary with clinical and radiographic improvement after prompt antibiotic therapy.

The clinical spectrum of Nocardia infection is broad and may range from localized involvement to disseminated infection. Clinical manifestations in solid organ transplant recipients typically include pulmonary infiltrate and abscesses involving subcutaneous tissue and brain [4–10]. Intrarenal abscess, epididymo-orchitis and atypical zygomycosis has been reported [11–14]. Mediastinal and pericardial involvement are rare. A case of nocardiosis presenting as anterior mediastinal mass in a patient with thymoma and myasthenia gravis was recently reported [15]. The patient had a mediastinal cystic mass, underwent thoracotomy for biopsy and was subsequently diagnosed with malignant thymoma. Abscesses in the mediastinum later developed and isolated Nocardia. Another case of purulent pericarditis from Nocardia has also been reported in a renal transplant recipient [16]. In this case however, the patient had a prior episode of pericardial effusion that required pericardiocentesis. In these cases, one may postulate that Nocardia was an infectious complication of prior surgical procedures with percutaneous seeding, considering the ubiquitous nature of the organism.

The radiographic features of pulmonary nocardiosis have been studied in a large series of 44 patients [17]. Majority of the patients presented with airspace disease and pulmonary nodules. Lung parenchymal masses were noted in 11 of 44 patients without lobar predominance but none had a mediastinal mass.

Risk factors for Nocardia infection among solid organ transplant recipients have been investigated. Greater risk of infection is noted among those with extremes of age, high dose steroids, granulocytopenia and uremia [18]. A history of CMV infection and high levels of calcineurin inhibitors were also identified as independent risk factors [4]. These characteristics were not present in our patient. The risk factors observed are maintenance immunosuppression and possibly not receiving trimethoprim/sulfamethoxazole (TMP/SMX) postoperatively for *Pneumocystis jirovecii* prophylaxis.

There are two potential pathogens isolated in this case, raising a possibility of coinfection. Coinfection of *Mycobacterium fortuitum* with Nocardia is rare and has been reported in lipid pneumonia after aspiration [19]. The absence of pulmonary infiltrates in CT scan argued against the pathogenicity of atypical mycobacterium in the sputum. Therefore, in contrast to the previously reported case of coinfection, antituberculous therapy was not initiated.

Our patient had disseminated Nocardia infection based on the mediastinal mass and pericardial effusion despite negative blood cultures. The previous episodes of pneumonia may be due to undiagnosed pulmonary nocardiosis that partially responded to treatment with fluoroquinolones and amoxicillin/clavulanate. As pulmonary is the most common portal of entry for Nocardia, we postulate that the multiple partially treated episodes of pneumonia later progressed to mediastinal nocardiosis.
Guideline for treatment of Nocardia has not been established. A high index of suspicion and prompt appropriate medical therapy is of utmost importance. Our patient initially had broad spectrum coverage with piperacillin-tazobactam, vancomycin and azithromycin for bacterial and atypical pneumonia but continued to have intermittent fevers. The antibiotics were then switched to imipenem and oral linezolid to cover for anaerobes, gram negative and gram positive bacteria, including Nocardia. She received two weeks of dual therapy until the susceptibility data showed that the Nocardia strain was resistant to imipenem. She continued treatment with linezolid monotherapy, with resolution of symptoms and marked radiographic improvement of mediastinal mass by 6 weeks of therapy.

Conclusions

Nocardia infection is a recognized complication among immunocompromised patients. Transplant recipients who are allergic to sulfonamide and who have not received TMP/SMX for Pneumocystis jirovecii prophylaxis may be at an increased risk for developing the infection. Persistent or recurrent pneumonia should raise the suspicion for pulmonary nocardiosis. Nocardia can rarely present as a mediastinal mass with pericardial effusion, even in the absence of pulmonary infiltrates. In mediastinal nocardiosis, fine needle aspiration via endoscopic ultrasound may not yield definitive diagnosis and mediastinoscopy for biopsy may be necessary. Although dual therapy is initially used to treat Nocardia infection, linezolid can be considered for monotherapy even for those presenting as mediastinal mass.

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