CASE REPORT

A Rare Case of Pulmonary Nocardiosis in Late Post Renal Transplant Period

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ABSTRACT

Nocardiosis is an uncommon but important infection in solid organ transplant recipients. It is a life-threatening disease in these patients. We report a case of 44- years-old kidney recipient who developed pulmonary nocardiosis that was successfully treated with intravenous imipenem and doxycycline in conjunction with a reduction in immunosuppressive therapy. This case emphasizes the role of new potent immunosuppressants and diabetes in the occurrence of opportunistic infections.In transplant recipients,who present with pulmonary symptoms and do not respond to usual antibiotics, a Nocardial infection should be suspected.

Keywords: Immunosuppressive therapy;Pulmonary nocardiosis; Renal transplantation.

INTRODUCTION

Nocardiosis is a lethal disease in solid organ transplant recipients. Nocardiosis belongs to the order Actinomycetales. It is a weakly acid fast, Gram-positive, branching filamentous aerobic bacteria. The most frequent species associated with infections in humans are Nocardia asteroids, Nocardiabra siliensis, Nocardia farscinica and Nocardia nova.

The usual mode of acquiring infection is through inhalation resulting in a pneumonitis followed by a dissemination of the infection, or can occur through skin trauma. It's three clinical forms include: cutaneous, pulmonary and disseminated. The cutaneous form is related to the transcutaneous inoculation and is common in tropical and warm temperate areas. The most common mode of transmission remains inhalation, resulting in pulmonary localization.

Nocardia is an opportunistic pathogen, causing pulmonary and systemic infections in immunocompromised patients. Patients in an immunocompromised state and having disseminated forms have poor prognosis.

In India, nocardiosis was reported in 1.4% of renal transplant recipients[1], most common species being Nocardia asteroids. Intense immunosuppression is the commonest predisposing factor.

We report herein a rare case of pulmonary nocardiosis developing in late post renal transplant period.

CASE REPORT

A 44 years old male patient, with end stage renal disease secondary to an unknown nephropathy, received renal transplantation in November 2019. The donor was his wife. They had 3 HLA mismatch. He had been treated for Hepatitis C before renal transplantation. He was given induction with Basiliximab and started on triple immunosuppressive therapy of Prednisolone, Tacrolimus and Mycophenolate mofetil. He had delayed graft function with serum creatinine being 4.1 mg/dl on postoperative day 7. Graft biopsy done, was reported as mixed rejection with acute tubular necrosis. He received methylprednisolone pulse therapy, intravenous immunoglobulin, plasmapheresis-4 sessions, 3 doses of anti-thymocyte globulin. Patient was discharged with good and stable renal function (serum creatinine of 1.5 mg/dl) on 15th postoperative day. New onset diabetes mellitus occurred fifteen months later and was managed by oral anti diabetic drugs.

In August 2021 (21 months post renal transplantation), he was admitted to the Nephrology department with complaints of fever, left sided pleuritic

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chest pain, shortness of breath along with cough and expectoration for 15 days.

Clinical examination revealed: body temperature of 39.6°C, respiratory rate of 28 per minute, blood pressure was 80/60 mm Hg, oxygen saturation of 82% on room air and 97% with 6 L/min oxygen support. Lung examination revealed tachypnoea and crepitations along left lung areas.

Laboratory investigations revealed haemoglobin of 14.8 m/dl, a total leucocyte count of 20,100/mm^3, neutrophils 90%, lymphocytes 6% and ESR was 58 mm in the first hour. Random blood sugar was 460 mg/dl. Renal function showed blood urea of 80 mg/dl and serum creatinine of 2.0 mg/dl. Other blood investigations which includes serum electrolytes and liver function tests were normal.

Chest radiograph showed non-homogenous opacity in left upper and lower zone [Figure 1]. CT chest revealed consolidation with internal air bronchogram, ground glass haziness in left upper and lower lobe suggestive of pneumonitis [Figure 2].

Microbiological investigations included sputum Gram stain which showed the presence of slender, Gram-positive, branching filamentous bacilli.

The patient was started on higher antibiotics, insulin infusion for blood sugar control and inotropic support for maintaining blood pressure. Sputum sent for modified Ziehl-Neelsen staining, revealed numerous acid-fast branching filamentous organisms, morphologically consistent with Nocardia species. [Figure 3].

Trimethoprim-sulfamethoxazole at therapeutic dose was added along with intravenous imipenem-based treatment and oraldoxycycline. Moreover, immunosuppressant drugs were temporarily reduced by decreasing dose of tacrolimus by 50% and stopping mycophenolate mofetil. Unfortunately, on treatment, the patient's condition got deteriorated and he succumbed to the illness.

DISCUSSION

Nocardiosis is aninfrequent infection and its diagnosis is difficult.Infection occurs in severely immunocompromised patient with reduced-cellular mediated immunitysuch solid organ transplants,human-immunodeficiency virus infected patients, auto-immunediseases, neoplasia and chronic lung disease.The most common risk factors are corticosteroid therapy and immunosuppression.

An observation by Carnet et al concluded that patients having Tacrolimus based immunosuppression were at increased risk for nocardiosis when compared to those on cyclosporin[2].

Our patient received induction treatment with Basiliximab and was maintained on mycophenolatemofetil, steroids, and Tacrolimus. He also received intravenous immunoglobulin, plasmapheresis, anti-thymocyte globulin for treatment of acute rejection. Moreover, diabetes mellitus is an additional risk factor favouring occurrence of opportunistic infection in our patient.

Nocardial infection is most common in first six months' post-transplant period[3]. Rarely reported after the first year of transplantation[4], but in our case presented after twenty-one month[5] post-transplant.

In pulmonary nocardiosis, the most common clinical presentationis a sub-acute or chronic necrotizing pneumonia. Pulmonary nocardiosis has a quintessential presentation, which includes fever, malaise, cough, anorexia, dyspnea, and chest pain. Our patient also had fever, cough and breathlessness as presenting complaints.

The most important diagnostic tool of pulmonary nocardiosis is Gram staining of sputum. However, no specific clinical or radiological features suggest nocardiosis. Only one third of sputum samples may show Nocardia, so multiple sputum specimens have to be examined.

Case studies showed that about 60-80% of nocardiosis in renal transplant patients is pulmonary nocardiosis and half of them have isolated lung involvement. A solitary pulmonary involvement was present in our patient without clinically apparent dissemination.

The most affected organs include: the lungs, skin, subcutaneous tissue and cerebro-nervous system. Other locations have been described: cardiac, ocular, osteoarticular.

So, for management of pulmonary nocardial infections, the key is to have a high index of suspicion, early diagnosis and adequate treatment. In transplant recipients, who present with pulmonary symptoms and do not respond to usual antibiotics, a Nocardial infection should be suspected.

Radiological patterns of pulmonary nocardiosis include, non-specific findings such as air space consolidation, presence of irregular nodular lesions, which may or may not associated with cavitation. Mediastinal and hilar lymphadenopathy may also be seen. In our patient, multilobar involvement was present with airspace consolidation but cavitation was lacking.

Prophylaxis with cotrimoxazole is recommended in renal transplant patients for pneumocystis carinï and urinary tract infection, and it is believed by some authors to protect from Nocardia infection. However, there is increasing cases of breakthrough infections in patients taking TMP-SMXprophylaxis.

Sulphonamides, mainly cotrimoxazole, are the treatment of choice, although other drugs, such as imipenem, amikacin, linelozid, cefotaxim, clarithromycin, ofloxacin, amoxicillin-clavulanic acid and tetracyc lines derivates are safe and effective.

Usually, six to nine months of antibiotic therapy, in case of localized pulmonary infections are needed and nine to twelve months in case of cerebro nervous system involvement.

Reduction of immunosuppression may be a helpful adjunctive therapy in severe forms of the disease but it is not a mandatory approach.

In pulmonary localization, mortality is about 40% and increases to 64% in disseminated nocardiosis and 100% in the presence of cerebro nervous system involvement5.

CONCLUSION

Transplant physicians should be aware of this rare infection and consider nocardiosis in differential diagnosis of pneumonia even in late post-transplant period, especially when the radiological features are atypicaland in patients who have not responded to the empirical treatment.

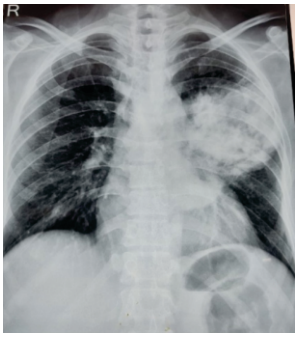

Figure 1. Chest X-ray

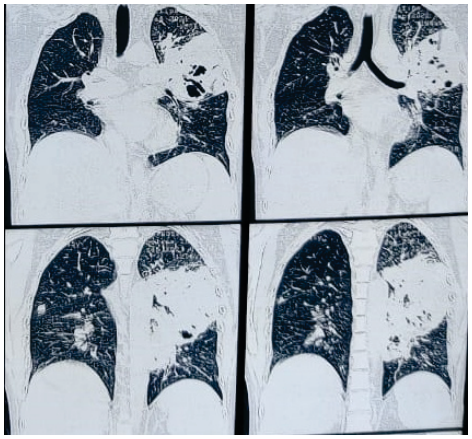

Figure 2. CT chest

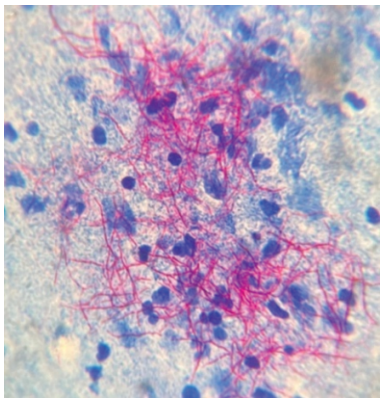

Figure 3. Modified ZiehlNeelsen stain

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