Pulmonary Nocardiosis in a Kidney Transplant Recipient: A Case Report and Review of the Literature


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Abstract

Nocardiosis is a life-threatening disease in solid organ transplant recipients. It is an uncommon but important infection for these patients. We report a case of 37-year-old kidney recipient who developed pulmonary nocardiosis that was successfully treated with intravenous imipenem and tetracyclines in conjunction with a reduction in immunosuppressive therapy. Four years later, graft function remains stable with complete regression of radiological abnormalities and absence of relapses. This case emphasizes the role of new potent immunosuppressants and antibiotics in the occurrence of opportunistic infections. Nocardiosis should be suspected in the presence of pulmonary symptoms with unusual radiological presentation.

Keywords: Pulmonary nocardiosis; Renal transplantation; Immunosuppression

Introduction

Nocardia is a ubiquitous aerobic actinomycete responsible for local or disseminated infection. The most frequent species associated with infections in humans are nocardia asteroids, nocardia brasiliensis, nocardia farcinica, and nocardia nova [1]. Nocardiosis is an opportunistic infection, occurring in up to 60% in deeply immunocompromised patients [2]. Clinical symptoms are non-specific, depending on location [3]. Prognosis remains poor, especially in immunocompromised patients and disseminated forms with cerebro-nervous system involvement [4].

We report herein a case of pulmonary nocardiosis in a kidney transplant recipient that was successfully treated by imipenem and tetracycline.

Case

A 37-year-old man, with end stage renal disease secondary to an unknown nephropathy, received kidney transplantation on April 2005. The donor was his sister aged 34 years old. They had 3 HLA mismatch. The immunosuppression consisted of thymoglobulin induction (5 mg/kg), tacrolimus, prednisone, and mycophenolate mofetil. The recipient was discharged on the 15th postoperative day with a good renal function (serum creatinine of 32 mg/dL, oxygen saturation of 97%).

Four years later, there is no relapse and his transplant function is in a good state.

Discussion

Nocardiosis is a rare infection and difficult to diagnose. It is caused by a gram-positive filamentous and strictly aerobic bacteria of the order Actinomycetales called ‘nocardia’. Nocardia is frequently isolated from soils, dust, sand and stagnant water [5,6].

Infection occurs in severely immunocompromised patient with reduced-cellular mediated immunity such solid organ transplants, human-immunodeficiency virus infected patients, auto-immune diseases, neoplasia and chronic lung disease [2,7]. The most common symptoms include fever, cough, anorexia, weight loss, fatigue, night sweats, and skin lesions. The disease is often disseminated and involves multiple organ systems such as the central nervous system, the lungs, the skin, and the musculoskeletal system [8].

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References


[8] Usual presentation of the classical clinical presentation of nocardiosis with unusual radiological presentation.
risk factors are corticosteroid therapy and immunosuppression [7]. The overall incidence of nocardial infections in different immunosuppressed patients ranges between 0.4% and 3.6% [2,8]. In renal transplant recipients, this incidence ranges between 0.7 and 2.6% [4,2].

Newer potent immunosuppressive agents are main risk factors. So, long term corticoid treatment, MMF-tacrolimus association and use of depleting antibodies are risk factors for developing nocardiosis. In a recent matched case-control study of 35 solid organ transplant recipients with nocardiosis, risk factors that were identified are: receipt of high dose steroids, cytomegalovirus disease and a high median calcineurin inhibitor level in the preceding 30 days ( > 15µg/ml for tacrolimus and >300 ng/ml for cyclosporine) [1].

Carnet et al observed only two cases of nocardiosis in 933 recipients transplanted between 1985 and 2002 and receiving Tacrolimus. Their data suggest that heavy immunosuppression, and tacrolimus-based immunosuppression are risk factors of nocardial infection [9].

Two other cases of pulmonary nocardiosis have been reported, respectively by Bilgarnia et al. and Flohr et al. [10,11]. The two recipients are sensitized with elevated panel reactive antibody, have re-transplantation and underwent preconditioning using plasmapheresis and rituximab. The maintenance immunosuppressive regimen for the two patients was mycophenolate mofetil, tacrolimus, and steroids.

Our patient received induction treatment with thymoglobulin and was maintained on mycophenolate mofetil, steroids, and Tacrolimus. This association is deemed to be highly immunosuppressive. Moreover, diabetes mellitus is an additional risk factor favouring occurrence of opportunistic infection in our patient.

The infection is usually acquired through inhalation which results in a pneumonitis and eventually a dissemination of the infection, or through skin trauma [12]. There are three clinical forms: 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.

The most frequent clinical presentation is a sub acute or chronic necrotizing pneumonia [12]. Pulmonary nocardiosis typically presents features made of dyspnoea, cough, chest pain, with no specific symptoms of fever, malaise and anorexia [13]. Radiological features are characterized by the presence of irregular nodular lesions, which may progress to cavitation.

They may also appear as diffuse pneumonic infiltrates or consolidate with pleural effusions [13]. We can find also alveolar syndromes, interstitial or reticulonodular infiltrates and even aspects of miliary and frequently excavated nodules or masses [3,14]. The main complication of this mode of transmission is haematogenous spread, resulting in a disseminated form of nocardiosis, defined by an involvement of two organs [14].

The organs most affected are the lungs, skin, subcutaneous tissue and cerebro nervous system. Other locations have been described: cardiac, ocular, osteoarticular [8].

Prophylaxis with cotrimoxazole is recommended in renal transplant

Figure 1: Chest X-ray revealed a 5 cm para hilar nodular lesion with irregular contours.

Figure 2: Thoracic CT scan revealed a large pseudo nodular lesion of the lower left field, extensive alveolar condensation with bronchogram in the left upper field surrounded by micro nodular lesions.

Figure 3: Resolution of the nodule on chest X-ray after six months therapy.
patients for pneumocystis carinii 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-SMX prophylaxis [1,2,8]. In fact, 14.2% of nocardial infections occur in patients while on cotrimoxazole prophylaxis [2].

Treatment relies on systemic antibiotic therapy. This latter should be adapted to the severity of the clinical picture, the different localization of the infection but also to the species.

Sulphonamides, mainly cotrimoxazole, are the treatment of choice [3,14], although other molecules have proven their effectiveness, such as imipenem, amikacin, linezolid, cefotaxim, clarithromycin, oloxacarin and amoxicillin-clavulanic acid [15,16]. Linezolid, an oxazolidinone antibiotic which is gaining more attention, can be successfully used as an alternative to intravenous rout as well as primary therapy for nocardial infections at a dose of 600 mg twice a day. However, this drug is not recommended for long-term therapy because of its serious side effects such as myelosupression, optic nerve damage and lactic acidosis [8,17,18,19].

In the case of our patient, cefotaxim used as initial empiric therapy was ineffective. Thus, the sensitivity analysis of isolated germ to antibiotics confirms its resistance to this molecule and to TMP-SMX. Treatment with imipenem relayed by tetracyclines was effective and well tolerated. Tetracyclines derivates are safe and effective. They may be considered as an alternative treatment for nocardia infections in transplanted patients. Leitersdorf et al treated ten transplanted patients (solid organ transplants and bone marrow transplants) with either doxycycline or minocycline. Nine out of the ten patients recover and one non compliant patient died of disseminated nocardiosis [20].

Duration of antibiotic therapy has not been well established and varies according to the authors, with a minimum of six months. Usually six to nine months in case of localized pulmonary are needed and nine to twelve months in case of cerebro nervous system involvement [9].

Surgery (drainage or removal) may be useful in cases of brain abscesses or tissue collections unresponsive to antibiotic therapy [8,14]. Reduction of immunosuppression may be a helpful adjunctive therapy in severe forms of the disease but it is not a mandatory approach [8]. In our case, we choose to lighten the immunosuppressive therapy without stopping it, which was effective in controlling the infection.

Mortality remains high particularly in patients with disseminated nocardiosis. In pulmonary localization, mortality is about 40% and increases to 64% in disseminated nocardiosis and 100% in the presence of cerebro nervous system involvement [7].

Conclusion

Transplant physicians should be aware of this rare infection and consider nocardiosis in differential diagnosis of pneumonia especially with patients who have not responded to empiric treatment and when radiological features are atypical. Microbiological isolation is crucial for diagnosis, therefore bronchoalveolar lavage should be considered in patients with atypical pneumonia on radiological examination or with unusual clinical course under empirical treatment.

References


