NOCARDIOSIS AND KIDNEY TRANSPLANTATION:
CASE REPORT IN A RECENTLY TRANSPLANTED PATIENT

Relato de caso de Nocardiose em transplante renal recente

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ABSTRACT
The patient is a 47-year-old white woman who was on hemodialysis from 1999 to 2002, when she received a cadaveric renal transplant (deceased donor). The immediate postoperative immunosuppression consisted of oral tacrolimus, prednisone and mycofenolato mofetil (MMF), and her medications at that time of her admission were tacrolimus (5mg/12h), MMF (1000mg/12-12h), and prednisone (10mg/day). After 8 weeks, the patient went to the hospital and she was admitted presenting fever (37.9°C), cough, malaise and vomiting. The chest radiography revealed a mass in the left superior lobe, which was initially treated with levofloxacin associated to ceftriaxone. There was partial improvement of the cough and total remission of the fever. The patient was discharged after 3 weeks of treatment in stable condition, with negative blood and bronchial cultures. After ten days, she returned to the hospital with relapsed symptoms and a subcutaneous purulent collection was detected in her left leg, and the culture of the drained material evidenced a filamentous microorganism, identified as Nocardia sp, later specified as Nocardia asteroides. Treatment with sulfametoxazole-trimetroprim 800mg t.i.d was initiated, and after five days, the patient was pyretic and treatment was kept for six months.

Keywords: Kidney Transplantation; Complication; Infection; Nocardia Infections; Immunosupression; Tacrolimus.
neck with no adenopathy and extremities without edema. Allograft in the right lower quadrant of her abdomen was nontender. At the date of the admittance in the laboratory, it was presented as follows: leukocytosis, without anemia or diminished platelet counting, serum lactate dehydrogenase 1173 U/l, creatinine 1.6 mg/dL and BUN 230 mg/dL, glucose 184 mg/dL. Chest radiography revealed a left superior lobe mass, which was initially treated with levofloxacin associated to ceftriaxone after collection of blood culture samples (Fig 1). A flexible bronchoscopy was performed; no gross endobronchial masses but purulent secretion were seen. Brushing and washing were sent to citopathology and microbiology. After antibiotic treatment, the cough was partially solved, the fever disappeared and as the creatinine still increased, she underwent an allograft biopsy that revealed acute tubular necrosis associated to tacrolimus toxicity. She was discharged in stable condition after 3 weeks of treatment, with negative blood and bronchial cultures. Ten days later, she returned to the hospital with relapsed symptoms and persistent radiograph image, that time revealing a pulmonary cavity (Fig 2), confirmed by chest CT scan (Fig 3). Another series of blood and bronchial cultures were performed and remained negative. After one week, a subcutaneous purulent collection was detected in the left leg and the culture of the draining material evidenced a filamentous microorganism, identified as Nocardia sp, later specified as Nocardia asteroides. Treatment with sulfametoxazole-
Nocardiosis is a localized or disseminated infection caused by soil-borne aerobic, gram-positive, variably acid-fast, filamentous bacteria. Nocardia species are actinomycetes found in soil, including sand, domestic dust and even swimming pools. Infections caused by Nocardia sp can be present in a variety of clinical forms, including skin lesions, pulmonary lesions, cerebral abscess and ocular lesions occurring isolated or combined.

In the case here reported, the first pulmonary infection could be associated to pulmonary, cutaneous, and disseminated disease. Another cause of persistent negative cultures, specially in bronchial brushings, is the growth of other microorganisms than Nocardia, which hide the appearance of Nocardia colonies. Routine microbiological tests can identify other species such as N. brasiliensis and Nocardia. otitidiscaviarium. Recently, development of more specific tests turned possible the differentiation of two subgroups of N. asteroides, which are considered distinct species: N. farcinica and N. nova.

In the case here reported, the first pulmonary infection could be related to Nocardia sp, but as previously reported, culture samples containing Nocardia species can be prematurely discharged, since they have a slow growth rate. A nodule of persistent negative cultures, specially in bronchial brushings, is the growth of other microorganisms than Nocardia, which hide the appearance of Nocardia colonies.

A pulmonary nocardiosis has an incidence of 2 to 5% in kidney transplant patients, and it can present acute, sub acute and chronic forms, as nodules, cavities, and alveolar infiltration, including resembling a typical bacterial pneumonia with or without pleural effusion. Our patient initially had pulmonary presentation and good response to the used antibiotics turned correct the diagnostic of usual pneumonia.

Additional risk factors for nocardiosis in renal transplant patients include the amount of rejections, age <10 or >40 years, high-dose versus low-dose of prednisozone, cadaveric versus living related kidney transplant, granulocytopenia, and uremia. Our patient had 4 of these risk factors: she was over 40 years, received a cadaveric renal transplant, and she was on an increased immunosuppressive regimen.

Recently, despite the prophylaxis with sulfamethoxazole-trimetroprim, incidence of Nocardia infections in transplant patients seems to be increasing.

Some reports suggest that more aggressive immunosuppression regimens, mainly the combination of tacrolimus and MMF are responsible by the increasing incidence of the disease. Although the exact mechanism is not known, it has been demonstrated that tacrolimus interacts with MMF to produce increasing levels of mycophenolic acid, the active metabolite of MMF. Patient was receiving tacrolimus and MMF, and such combination must be considered a factor in the development of her nocardial infection. The disease has variable incidence, and it decreased after the prophylaxis with sulfamethoxazole-trimetroprim was routinely initiated, although in some related cases, trimethoprim-sulfamethoxazole given as prophylaxis against Pneumonyssis carinii pneumonia and/or urinary tract infection was not effective for nocardia in patients on tacrolimus regimen.

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RESUMO

Introdução: Paciente de 47 anos, branca, mantida em terapia renal substitutiva de 1999 até 2002, quando recebeu transplante renal de doador cadáver. A terapia imunossupressora inicial constava de tacrolimus, prednisona e micofenolato mofetil (MMF). No momento da internação, as doses utilizadas eram respectivamente: 5mg 12/12h de tacrolimus, 1000mg 12/12h de MMF, 10mg/dia de prednisona e 40mg/dia de furosemida. Após oito semanas, a paciente procurou o hospital e foi internada com quadro de febre (37,9ºC), tosse, malestar e vômitos. Foi solicitado RX de tórax, que revelou uma massa no lobo superior esquerdo, inicialmente tratado com levofloxacin associada a ceftriaxone. Houve melhora parcial do quadro de tosse, com remissão total da febre. A paciente recebeu alta após três semanas de tratamento em boas condições, com todas as culturas negativas. Passados dez dias, a paciente retornou ao hospital com os mesmos sintomas anteriores, tendo sido encontrada coleção purulenta subcutânea na perna esquerda, que foi drenada, e o material coletado foi enviado para exame. Foi evidenciado um microorganismo filamentoso identificado como Nocardia sp, posteriormente especificado como Nocardia asteroides. Foi iniciado tratamento com sulfamethoxazol-trimetroprim 800mg 12/12h, e após cinco dias, a paciente já se mostrava afebril e o tratamento foi mantido por seis meses.

Descritores: Transplante Renal; Infecção; Nocardiose; Imunossupressão, Tacrolimus.
REFERENCES