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BRIEF REPORT

Anne Vandôme
Georges Philippe Pageaux
Michael Bismuth
Jean Michel Fabre
Jacques Domergue
Colette Perez
Marc Makeieff
Georges Mourad
Dominique Larrey

Nocardiosis revealed by thyroid abcess in a liver – kidney transplant recipient

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A. Vandôme · G. P. Pageaux · M. Bismuth
J. M. Fabre · J. Domergue · D. Larrey
Fédération Médicochirurgicale,
Hôpital Saint Eloi, 34295 Montpellier
cedex 5, France

C. Perez
Laboratoire de Bactériologie,
Hôpital Arnaud de Villeneuve,
34295 Montpellier cedex 5, France

M. Makeieff
Service d'Otorhinolaryngologie A,
Hôpital Gui de Chauliac,
34295 Montpellier cedex 5, France

G. Mourad
Service de Néphrologie,
Hôpital Lapeyronie,
34295 Montpellier cedex 5, France

G. P. Pageaux (✉)
Fédération Médico-chirurgicale
des Maladies de l'Appareil Digestif,
Hôpital Saint Eloi, 80 rue Augustin Fliche,
34295 Montpellier cédex 5, France
Tel.: + 33-46733-7061
Fax: + 46752-3897
e-mail : gp-pageaux@chu-montpellier.fr

Abstract Nocardiosis is a life-threatening infection, particularly among immunocompromised patients, which usually affects lungs, skin and central nervous system. We report a case of disseminated nocardiosis revealed by suppurative thyroiditis in a liver-kidney transplant recipient with poor nutritional status at the time of infection. *Nocardia Asteroides* was isolated from fine-needle aspiration material of the thyroid abscess. Clinical manifestations resolved after surgical drainage of the thyroid abscess, prolonged antibiotherapy and diminution of immunosuppressive regimen. Clinicians should be aware of this entity, as *Nocardia Asteroides* may need more than 5 days of culture to be isolated.

Keywords Nocardiosis · Liver transplantation · Thyroid abcess

Introduction

Organ transplantation and immunosuppressive therapy are associated with a high incidence of infections, even if they have decreased since the use of cyclosporine and tacrolimus as a clinical routine. Nocardiosis is a rare but potentially life-threatening opportunistic infection caused by an aerobic branching gram-positive rod. Its usual clinical presentation includes pulmonary, cutaneous or neurological manifestations [10]. We report an atypical presentation of disseminated nocardiosis revealed by acute thyroiditis in a liver-kidney transplant recipient.

Case report

A 58-year-old man underwent liver and cadaveric kidney transplantation for polycystic disease after 2 years of hemodialysis. The immunosuppressive regimen associated azathioprine, prednisone and antithymocyte globulin (ATG) for 8 days when ATG was replaced by tacrolimus. No rejection episode occurred, but the nutritional status was poor, with a body mass index estimated to 16.

On day 28 the patient developed fever. Evaluation revealed pericardic effusion with cytology indicative of viral etiology (Epstein Barr virus?), and pleural effusion with increased neutrophils on cytology but negative cultures. Cytomegalovirus infection, tuberculosis, and post-transplant lymphoproliferative disorder were eliminated. At that time, the tacrolimus blood trough level was 8.1 ng/ml, and he was under azathioprin, 50 mg/day, and prednisone, 20 mg/day. After 8 days of imipenem and vancomycin, the fever disappeared but pericardic and pleural effusions persisted. He was discharged on day 45.

On day 60, he was admitted with fever, painful swelling of the anterior region of the neck and dysphagia. Tacrolimus blood trough level was 6 ng/ml, and he was under prednisone at 15 mg/day. Examination revealed a satellite adenopathy and right pleural effusion. There was no skin lesion. Cultures of blood and urine were sterile. Pleural effusion was sterile with normal cytology. Thyroid function tests were normal. Chest X-ray showed nothing but the right pleural effusion. Pericardic effusion was diminished on ultrasound study compared with examination made on day 30. Ultrasound examination of the neck showed a heterogenous nodule of the left lobe of the thyroid and satellite adenopathies. Ultrasound-guided fine-needle aspiration brought purulent material. Direct examination of Gram-stains showed many gram-positive, branching, filamentous rods, permitting the identification of *Nocardia* organisms, and no organisms other than *Nocardia* grew after cultures. The species *Nocardia Asteroides* was determined by the National Reference Center for Mycosis and Antifungal Agents (P. Boiron, Institut Pasteur, Paris, France). Cerebral tomodensitometry was normal. Despite imipenem and amikacin intravenous therapy, pain and dysphagia persisted, and the patient underwent surgical drainage of the thyroid abscess on day 70. On day 68, renal ultrasonic study showed a nodule on the renal graft suggestive of infectious localization.

On day 81, chest tomodensitometry revealed right pleural effusion with suspicion of pleural empyema. There were only neutrophils on cytology. Immunosuppressive therapy was gradually tapered: prednisone from 15 mg-10 mg/day and tacrolimus from 6 mg-3 mg/day with blood trough level of 5,2 ng/ml. Liver enzyme tests and renal function remained normal. Clinical and radiological manifestations resolved with amoxicillin-clavulanic acid maintained for 7 weeks, and Trimethoprim / Sulfamethoxazole (TMP/SMX) was maintained for 24 weeks.

Discussion

It has been estimated that 500–1000 new cases of nocardial infection occur annually in the United States, 13 % of them among organ transplant recipients [2], and 150–250 new cases occur in France each year; 70,5 % of them being opportunistic, whatever the cause of immunodepression [4]. In fact, organ transplant recipients represent a particularly exposed population to nocardiosis. The reported incidence of nocardiosis among renal transplant recipients varies from 0–20 % with a means of 2,8 % [1, 10]. Forbes et al. found an incidence of 3,7 % among liver transplant recipients[6]. The incidence of nocardiosis among renal and cardiac transplant recipients dropped threefold after cyclosporine was used routinely for immunosuppression [1, 5]. Host defense against *Nocardia* enables us to understand why transplant recipients are at risk. *In-vitro* studies showed that neutrophils inhibit the growth of *Nocardia* but do not kill the rods. Animal studies have revealed that cellular immunity, mediated by T-cells and activated macrophages, promotes the clearance and prevents dissemination of *Nocardia* from the lungs. Thus, cellular immune dysfunction is the major risk factor for nocardiosis [10].

The onset of infection occurs mainly in the first year after transplantation, when immunosuppressive therapy is most intensive [5, 10]. In our patient, nocardiosis started between the first and second month after transplantation, when immunosuppressive therapy was maximal. His poor nutritional status at this time was an additional factor of immunodepression. The lungs are the main portal of entry of nocardial infection, and pulmonary disease is the most common manifestation (85–90 % in transplant recipients) without pathognomonic syndrome [5, 10]. Skin and subcutaneous lesions may be due to primary inoculation or secondary localization from the lungs. For our patient, the primary site of infection may have been the lungs, even if pleural effusion culture was sterile and cytology was normal at the moment of diagnosis, as a chest computed tomography showed right pleural empyema. Cultures of *Nocardia* require 5–21 days for growth and most routine cultures are discarded at 3 days [5]. Besides, nocardiosis is a sub-acute or chronic disease. We suggest that the fever and pleural effusion our patient presented on day 28 might have been the initial manifestation of nocardiosis, incompletely resolved after 8 days of imipenem therapy. This highlights the interest of prolonged cultures of clinical specimens, especially for immunodeficient patients. Dissemination from the lungs and the skin occur in 30–50 % of the transplant recipients [1, 5]. The main organs involved in dissemination are the central nervous system (20–38 %), the skin, the kidneys, the lymph nodes and the liver. Other rare localizations are the spleen, the eyes, the mediastinum, the joints and the bones [5].

Suppurative thyroiditis is extremely rare because of the anatomic isolation of the gland, its rich system of drainage, and the presomptive antibacterial effect of the high iodine concentration [3]. Most of the infectious diseases of the thyroid are of bacterial origin, (68 %) but opportunistic agents have been identified: *Candida, Aspergillus, Coccidioides, Pneumocystis Carinii, Cytomegalovirus*, especially among immunocompromised patients [9]. Only one other case of nocardial suppurative thyroiditis has been reported in a further immunocom-

promised patient, a 20-year-old woman with systemic lupus erythematosus treated for 2 years with high doses of prednisone and cyclophosphamide. There was no pulmonary syndrome contemporary of the thyroiditis but a preceding episode of fever and radiological pulmonary infiltrates on the chest X-ray, 6 weeks before, attributed to Cytomegalovirus infection [7]. Ultrasonic-guided fine-needle aspiration of the thyroid enables the diagnosis, which must not be delayed, since prognosis depends on prompt recognition and treatment. In our patient, we can presume that the initial pleural effusion was related to nocardiosis, and that the thyroid abcess was due to the time lag between infection of the lung and the final diagnosis.

Trimethoprim/Sulfamethoxazole (TMP/SMX) is considered the therapy of choice for nocardiosis because of *in vitro* synergistic activity of TMP and SMX against *Nocardia*, excellent penetration of organs including the CNS, and because of the comfort of oral intake. However, the risk of nephrotoxic interaction between TMP/SMX and anti-calcineurin immunosuppressive drugs may limit its utilization for transplant recipients. Alternative therapies include Ampicillin, Amoxicillin-clavulanic acid, Imipenem, Ceftriaxone, Cefotaxime, Amikacin and Minocycline [1, 6, 8, 10]. Antimicrobial therapy is often pursued for a prolonged period because of the risk of relapse, but its optimal duration is not yet well defined. For the majority of authors, therapy lasts for at least 6 months for immunocompromised patients [1]. When suppurative thyroid clinical manifestations persist despite adapted antimicrobial therapy, surgical excision and drainage are recommended, as was the case with our patient. The management of immunosuppressive therapy in transplant recipients is controversial. Arduino et al. [1] chose to maintain the same therapy (except for one patient with overwhelming disease), Wilson et al. [10] suggested an adjustment on an individual basis and we did likewise. The nutritional status of the patient is also an important point to consider, as it also is a risk factor of immunosuppression. We suggest that poor nutritional status calls for an individual adjustment of the immunosuppressive therapy.

In conclusion, we report an atypical presentation of disseminated nocardiosis revealed by a thyroid localization in a liver-kidney transplant recipient without evidence of pulmonary or skin involvement at the moment of diagnosis. The poor nutritional status of our patient may have been an additional risk factor of immunodepression.

References

1. Arduino RC, Johnson PC, Miranda AG (1993) Nocardiosis in renal transplant recipients undergoing immunosuppression with Cyclosporine. Clin Infect Dis 16: 505–512
2. Beaman BL, Burnside J, Edwards B, Causey W (1976) Nocardial infections in the United States, 1972–1974. J Infect Dis 134: 286–289
3. Berger SA, Zonszein J, Villamena P, Mittman N (1983) Infectious diseases of the thyroid gland. Rev Infect Dis 5: 108–122
4. Boiron P, Provost F, Chevrier G, Dupont B (1992) Review of nocardial infections in France 1987 to 1990. Eur J Clin Microbiol Infect Dis 11: 709–714
5. Chapman SW, Wilson JP (1990) Nocardiosis in transplant recipients. Semin Respir Infect 5: 74–79
6. Forbes GM, Harvey FAH, Philpott-Howard JN, O'Grady JG, Jensen RD, Sahathevan M, Casewell MW, Williams (1990) Nocardiosis in liver transplantation: variation in presentation, diagnosis and therapy. J Infect 20: 11–19
7. Lewin SR, Street AC, Snider J (1993) Suppurative thyroiditis due to *Nocardia Asteroides*. J Infect 26: 339–340
8. McNeil MM, Brown JM, Hutwagner LC, Schiff TA (1995) Evaluation of therapy for *Nocardia Asteroides* complex infection. Infect Dis Clin Pract 4: 287–292
9. Solary E, Rifle G, Chalopin JM, Rifle-Mediavilla C, Rebibou JM, Camerlynck P, Justrabo E, Cuisenier B, Caillot D, Mousson C (1987) Disseminated aspergillosis revealed by thyroiditis in a renal allograft recipient. Transplantation 44: 839–840
10. Wilson JP, Turner HR, Kirchner KA, Chapman SW (1989) Nocardial infections in renal transplant recipients. Medicine 68: 38–57