Frequent Exacerbation of Pulmonary Nocardiosis during Maintenance Antibiotic Therapies in a Hematopoietic Stem Cell Transplant Recipient

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Abstract

We describe a rare case of recurrent pulmonary nocardiosis (PN) in a hematopoietic stem cell transplant recipient. The patient developed Nocardia farcinica infection while receiving corticosteroid and cyclosporine for the treatment of bronchiolitis obliterans, probably due to chronic graft-versus-host disease (cGVHD). The patient responded well to the initial treatment with meropenem, but PN recurred 3 times during oral maintenance therapies using different antibiotics, which were chosen on the basis of the results of in vitro susceptibility testing against N farcinica. Minocycline, amoxicillin/clavulanate, and levofloxacin were not effective as oral maintenance therapies. Frequent exacerbation of PN was considered to have resulted from the low blood concentration of these antibiotics, and decreased gastrointestinal absorption, probably due to cGVHD, might have been the underlying problem.

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Key words: Pulmonary nocardiosis; Hematopoietic stem cell transplantation; Chronic graft-versus-host disease

1. Introduction

Although encouraging statistics have now been reported for survival after hematopoietic stem cell transplantation (HSCT), pulmonary complications occur in up to half of patients after HSCT and represent major causes of morbidity and mortality [1,2]. Infectious processes are a major source of such pulmonary complications, but nocardiosis is rarely seen in HSCT recipients, compared with other organ-transplant recipients, probably because of the routine administration of trimethoprim-sulfamethoxazole (TMP/SMX) for prophylaxis against Pneumocystis pneumonia in the HSCT setting [3].

Nocardia is an aerobic filamentous, branching, non–spore forming, Gram-positive rod, and infection with this microorganism is characterized by a primarily respiratory focus and potential hematologic dissemination, mainly to the brain and skin, with serious sequelae [4]. The most common pathogenic species is the N asteroides complex [5]. The mainstay of treatment for nocardiosis is a sulfonamide-containing regimen, and TMP/SMX is currently regarded as the drug of choice [5,6]. Other antibiotics, including amikacin, imipenem, minocycline (MINO), doxycycline, cefotaxim, and ceftriaxone, can be used on the basis of in vitro susceptibility data, particularly in cases where TMP/SMX is contraindicated; however, no convincing data support alternative uses of these antibiotics.

We describe a case of pulmonary nocardiosis (PN) with multiple recurrent episodes during oral maintenance treatments with MINO, amoxicillin/clavulanate, or levofloxacin (LVFX).

2. Case Report

A 17-year-old boy with acute biphenotypic leukemia received an allogeneic peripheral blood stem cell transplant (PBSCT) from his HLA-identical sister during his first remission in March 2005. Tosulloxacin (TFLX) and fluconazole were orally administered 14 days before PBSCT. TMP/SMX (240 mg TMP and 1200 mg SMX 3 times/week) was also used to prevent Pneumocystis pneumonia.
The conditioning regimen comprised cytarabine (8 g/m²) and cyclophosphamide (120 mg/kg) followed by 1200 cGy total body irradiation, and 2.58 × 10⁷/kg granulocyte colony-stimulating factor–mobilized CD34⁺ cells were transplanted. Cyclosporine (CyA) and short-term methotrexate were used for prophylaxis of graft-versus-host disease (GVHD). On day 6, the patient developed acute (stage II) GVHD of the skin, which improved following treatment with methylprednisolone (60 mg/day). This result permitted prednisolone (PSL) tapering. We were able to discontinue PSL treatment without a flare-up of acute GVHD on day 168, and CyA treatment was continued at a low dose (50 mg/day). However, the patient developed extensive chronic-type GVHD (cGVHD) of the mouth, skin, and liver on day 220. Treatment was therefore resumed with PSL (60 mg/day) and CyA (100 mg/day). Although the skin GVHD responded well to these treatments, the liver dysfunction progressed, so we withheld TMP/SMX and TFLX treatments because of the possibility of drug-induced liver damage (Figure 1). On day 352, during PSL tapering at a dosage of 20 mg/day, the patient noticed exertional dyspnea. Subsequent testing of pulmonary function and a chest computed tomography (CT) evaluation revealed possible bronchiolitis obliterans (BO), probably due to cGVHD. PSL and CyA treatments were therefore continued without further dosage reduction. The prophylactic administration of fluconazole was continued.

On day 412, the patient was emergently admitted to the hospital with fever and progressive dyspnea. Chest radiography and CT examinations (Figure 2A) verified a huge cavity of up to 40 mm in diameter with ground-glass opacities in the right upper lobe (S¹). On the basis of the clinical and radiologic examinations, we started empirical therapy with intravenous meropenem (MEPM) at 2 g twice daily. N farcinica (formerly N asteroides with a type V drug-susceptibility pattern [6]) was again isolated from a bronchial-lavage sample of the left B¹. Screening of the whole body, including the brain and skin, revealed no signs of dissemination of the infection to other organs. Pulmonary exacerbation was thus highly suspected. The laboratory data obtained at this time were as follows: leukocyte count, 10,400/µL (differential counts: 0.5% myelocytes, 0% bands, 91% segmented neutrophils, 0% eosinophils, 3% monocytes, and 5.5% lymphocytes); hemoglobin, 13.1 g/dL; platelet count, 24.5 × 10⁹/µL; serum immunoglobulin G, 394 mg/dL; and C-reactive protein, 3.9 mg/dL.

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