Non-Tuberculous Mycobacterial Infection Localized in Small Intestine Developing after Allogeneic Bone Marrow Transplantation

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Abstract

A 33-year-old man with myelodysplastic/myeloproliferative disease underwent allogeneic bone marrow transplantation. Around day 80 post-transplant, he complained of abdominal pain and diarrhea. Colonoscopy and esophagogastroduodenoscopy findings were unremarkable. Double-balloon enteroscopy revealed atrophic villi and mild erosions localized in the small intestine. Histological examination revealed marked proliferation of histiocytes with numerous acid-fast bacilli in their cytoplasm. The specific polymerase chain reaction for Mycobacterium tuberculosis was negative, and a diagnosis of intestinal non-tuberculous mycobacteria (NTM) was made. Physicians should recognize that NTM infection is one of the gastrointestinal infectious complications in immunocompromised patients such as bone marrow transplant recipients, and could localize in the small intestine.

Key words: non-tuberculous mycobacteria, small intestine, allogeneic hematopoietic stem cell transplantation, double-balloon enteroscopy

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Introduction

Non-tuberculous mycobacteria (NTM) have been reported to cause pneumonia, lymphadenitis, skin and soft tissue infection, and central venous catheter infection (1). Disseminated NTM infection has been reported in non-human immunodeficiency virus-associated immunocompromised hosts (2). NTM infection after hematopoietic stem cell transplantation (HSCT) is quite rare (3, 4), and intestinal NTM infection is even rarer; only one case has been reported after HSCT (5). Here, we present a case of intestinal NTM infection which developed after allogeneic HSCT. Furthermore, we briefly review the reported cases of intestinal NTM infection developing after HSCT and solid organ transplantation.

Case Report

A 33-year-old man with unclassified myelodysplastic/myeloproliferative disease underwent allogeneic bone marrow transplantation from a human leukocyte antigen-matched unrelated donor after being conditioned with total body irradiation (12 Gy) and high-dose cytarabine (2,400 mg/m²). Tacrolimus and short-course methotrexate were given for prophylaxis of graft-versus-host disease (GVHD). His post-transplant course was complicated with acute and chronic GVHD (extensive-type) solely involving the skin, both of which were successively treated with long-term prednisolone. Initial dose of prednisolone was 1 mg/kg for 2 weeks, and the dose was slowly tapered to 0.5 mg/kg over 2 months. Since day 80 post-transplant, when he had been treated with prednisolone for acute GVHD, he repeatedly
complained of severe abdominal pain and diarrhea with high-grade fever. His white blood cell count was 1.9×10^9/L with 71% of neutrophils and 26% of lymphocytes, and serum immunoglobulin G was 635 mg/dL. No significant renal or hepatic dysfunction was observed. Standard bacterial and fungal cultures of blood and stool detected no causative pathogens. Colonoscopy and esophagastroduodenoscopy revealed no significant findings. Double-balloon enteroscopy of the small intestine revealed atrophic villi and mild erosions (Fig. 1). Histological examinations of the small intestine showed marked proliferation of histiocytes without infiltration of inflammatory cells, and Ziel-Nielsen staining detected numerous acid-fast bacilli in the histiocytes (Fig. 2a, b). Acid-fast bacilli found in the stool were negative for a PCR assay specific for *Mycobacterium tuberculosis*. Based on these findings, a diagnosis of intestinal NTM infection was made, and the combination therapy of clarithromycin (800 mg/day), ethambutol (1,000 mg/day), rifampicin (450 mg/day), and gatifloxacin (400 mg/day) was initiated on day 279 post-transplant. All of the symptoms were completely relieved within 14 days of initiating the therapy. After the 30-day treatment, the therapy was discontinued because of severe toxicoderma, which was treated with high-dose prednisolone (2 mg/kg). Although the patient was asymptomatic, the culture of the stool continued to grow NTM, and clarithromycin and ethambutol were re-started day 327. The patient died of central line-associated septicemia due to methicillin-resistant *Staphylococcus aureus* on day 355, and the autopsy showed intestinal NTM infection completely localized in the jejunum.

**Discussion**

Although NTM infection after allogeneic HSCT is considered rare, the incidence seems relatively higher than that in the general population (3). An increased incidence of NTM infection has been reported among allogeneic HSCT recipients in recent years, ranging from 0.4% to 9.7% of cases (3-7). However, intestinal NTM infection is quite rare, and there has been only one other reported case after allogeneic HSCT (5). In the present case, NTM was completely localized in the small intestine, which made it difficult to make a diagnosis of intestinal NTM. Although double-balloon enteroscopy led to the diagnosis in our case, the culture for acid-fast bacilli was thoroughly positive. Thus, the culture for acid-fast bacilli of the stool could be a useful, non-invasive method to diagnose intestinal NTM infection.

Impairment of cellular immunity is one of the remarkable immune dysfunctions after allogeneic HSCT. Delayed immune reconstitution could be caused by the administration of systemic glucocorticoid, which is verified by the increased incidence of CMV infection in patients receiving glucocorticoid after allogeneic HSCT (8). Thus, long-term administration of systemic glucocorticoid, which was given for persistent GVHD, is considered to have played an important role in the susceptibility of our patient to NTM infection.

Regarding solid organ transplantation, several cases of intestinal NTM infection have been reported. An extensive review of the literature uncovered five cases of intestinal NTM infection after solid organ transplantation (heart 1, liver 1, and kidney 3) (9-13). The characteristics of these cases including the present case and one case after HSCT are described in Table 1. All 7 patients were adults, and in 4 of these, the affected site was the small intestine with or...
been longer than that in the two recipients of HSCT included in this study. The time from transplantation to onset in solid organ transplantation seems to have been generally effective, although there were variations in the drugs used. The time from transplantation to onset of intestinal NTM infection was 3 to 5 years after solid organ transplantation with one exceptional case (7 months). The time from transplantation to onset in these recipients of solid organ transplantation seems to have been longer than that in the two recipients of HSCT including our case (3 and 11 months).

We conclude that NTM infection should be recognized as one of the causes of intestinal infection after hematopoietic stem cell or solid organ transplantation, and a culture for acid-fast bacilli should promptly be performed if other causes have been excluded. An accumulation of such cases is required to further elucidate the clinical characteristics and prognosis of intestinal NTM infection.

Table 1. Reported Cases of Intestinal NTM Infection after Solid Organ or Hematopoietic Stem Cell Transplantation

<table>
<thead>
<tr>
<th>Reference (No.)</th>
<th>Age /Sex</th>
<th>Time from transplant to onset</th>
<th>Gastrointestinal symptoms</th>
<th>Involved sites</th>
<th>NTM species</th>
<th>Treatment</th>
<th>Response to treatment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>9 (Kidney)</td>
<td>20/Male</td>
<td>4 years</td>
<td>Diarrhea</td>
<td>Colon</td>
<td>Not specified</td>
<td>INH, EB, SM</td>
<td>ineffective</td>
<td>Died of NTM infection</td>
</tr>
<tr>
<td>10 (Kidney)</td>
<td>24/Male</td>
<td>5 years</td>
<td>Diarrhea</td>
<td>Colon</td>
<td>Not specified</td>
<td>INH, RFP EB</td>
<td>effective</td>
<td>Died of other cause</td>
</tr>
<tr>
<td>11 (Kidney)</td>
<td>35/Male</td>
<td>7 months</td>
<td>Abdominal pain</td>
<td>Ileum</td>
<td>M.gordonae</td>
<td>INH, RFP, EB</td>
<td>effective</td>
<td>Alive</td>
</tr>
<tr>
<td>12 (Liver)</td>
<td>66/Male</td>
<td>4 years</td>
<td>Asymptomatic</td>
<td>Jejunum, cecum</td>
<td>M.gordonae</td>
<td>CPFX, CAM</td>
<td>effective</td>
<td>Died of other cause</td>
</tr>
<tr>
<td>13 (Heart)</td>
<td>56/Male</td>
<td>3 years</td>
<td>Abdominal pain</td>
<td>Duodenum, jejunum</td>
<td>M.avium/intracellulare</td>
<td>CAM, CPFX, EB</td>
<td>effective</td>
<td>Alive</td>
</tr>
<tr>
<td>5 (BM)</td>
<td>32/Male</td>
<td>11 months</td>
<td>Diarrhea</td>
<td>Not specified</td>
<td>M.avium/intracellulare</td>
<td>CAM, EB, MFLX</td>
<td>effective</td>
<td>Died of other cause</td>
</tr>
<tr>
<td>Present case</td>
<td>32/Male</td>
<td>3 months</td>
<td>Diarrhea</td>
<td>Abdominal pain</td>
<td>Not specified</td>
<td>CAM, EB, RFP, GFLX</td>
<td>effective</td>
<td>Died of other cause</td>
</tr>
</tbody>
</table>

NTM, non-tuberculous mycobacteria; BM, bone marrow; M, Mycobacterium; INH, isoniazid; EB, ethambutol; SM, streptomycin; RFP, rifampicin; CPFX, ciprofloxacin; CAM, clarithromycin; MFLX, moxifloxacin; GFLX, gatifloxacin.

without the cecum. The response to combination chemotherapy seems to have been generally effective, although there were variations in the drugs used. The time from transplantation to the onset of intestinal NTM infection was 3 to 5 years after solid organ transplantation with one exceptional case (7 months). The time from transplantation to onset in these recipients of solid organ transplantation seems to have been longer than that in the two recipients of HSCT including our case (3 and 11 months).

We conclude that NTM infection should be recognized as one of the causes of intestinal infection after hematopoietic stem cell or solid organ transplantation, and a culture for acid-fast bacilli should promptly be performed if other causes have been excluded. An accumulation of such cases is required to further elucidate the clinical characteristics and prognosis of intestinal NTM infection.

References


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