Human Pathology (2010) 41, 1646–1649

Human PATHOLOGY

www.elsevier.com/locate/humpath

Case study

Disseminated *Mycobacterium genavense* infection in a healthy boy

Hiroaki Miyoshi MD[a,*], Gen Tamura MD, PhD[a], Toshihiko Satoh MD, PhD[b], Riko Homma MD[c], Eijiro Omoto MD, PhD[c], Noriyuki Nakano[d], Ryuichi Wada MD, PhD[d]

[a]*Department of Pathology and Laboratory Medicine, Yamagata Prefectural Central Hospital, Yamagata 990-2292, Japan*
[b]*Department of Surgery, Yamagata Prefectural Central Hospital, Yamagata 990-2292, Japan*
[c]*Department of Internal Medicine, Yamagata Prefectural Central Hospital, Yamagata 990-2292, Japan*
[d]*Department of Pathology and Molecular Medicine, Hirosaki University Graduate School of Medicine, Hirosaki 036-8562, Japan*

Received 3 January 2010; revised 1 February 2010; accepted 8 February 2010

Keywords:
Mycobacterium genavense;
Immunocompetent individuals;
Ileus

Summary *Mycobacterium genavense* (*M genavense*) has been recognized as a life-threatening pathogen in severely immunocompromised patients. To our knowledge, disseminated *M genavense* infection has never been described in immunocompetent individuals. Here, we report a case of disseminated *M genavense* infection in a healthy Japanese boy. A 15-year-old boy who had never been diagnosed with an immunodeficiency disorder was hospitalized because of ileus. Tumorous lesions were identified in the ileum, cecum, and ascending colon, resulting in stenosis of ileocecal valve. There was diffuse proliferation of histiocytes throughout the intestinal wall, along with lymphocytic infiltration. No nuclear or cellular atypia was present in these cells. Ziehl-Neelsen staining revealed numerous acid-fast bacteria in histiocytes. After surgery, systemic lymph node swelling was noticed by generalized examination, including the mesenteric and cervical lymph nodes. *M genavense* DNA was identified by direct sequencing of 16S ribosomal DNA that had been amplified by polymerase chain reaction.

1. Introduction

Mycobacterium genavense (*M genavense*) was identified as one of the nontuberculous mycobacteria in 1992 [1]. Since then, there have been many reports that have described *M genavense* as a life-threatening pathogen in severely immunocompromised patients with human immunodeficiency virus (HIV) infection [1-6]. Disseminated *M genavense* infection has also been described in HIV-negative patients, such as in those with chronic lymphocytic leukemia, patients undergoing immunosuppressive therapy, and heart transplant recipients [7-9]. By contrast, in immunocompetent patients, *M genavense* infection has only resulted in cervical lymphadenitis [10,11]. To our knowledge, disseminated *M genavense* infection has never been described in immunocompetent individuals. Here, we report a case of disseminated *M genavense* infection in a healthy Japanese boy.

2. Case report

A 15-year-old boy who had never been diagnosed with an immunodeficiency disorder was hospitalized at Yamagata Prefectural Central Hospital in October 2007 because of

* Corresponding author.
E-mail address: miyoshi_hiroaki@med.kurume-u.ac.jp (H. Miyoshi).

0046-8177/$ – see front matter © 2010 Elsevier Inc. All rights reserved.
doi:10.1016/j.humpath.2010.02.017

abdominal pain that had become progressively worse over several weeks before admission. On admission, abdominal distention was noticed; and abdominal computed tomography indicated thickening of the intestinal wall from the ileocecum to the ascending colon, along with dilation of the small intestine, and ascites. Hematologic and serologic examinations revealed no abnormalities except for elevated immunoglobulin E (547 IU/mL). Ileocecal resection with partial enterectomy was performed because of persistent ileus. Swollen mesenteric lymph nodes were resected during surgery. After the surgery, systemic lymph node swelling was noticed by general examination. One of the swollen cervical lymph nodes was also removed for histopathologic evaluation. Following the histopathologic diagnosis of nontuberculous mycobacterial infection, the patient's immune condition was investigated. The CD4+ and CD8+ lymphocyte counts were 298/μL and 631/μL, respectively. Serum complement value was 34.1 U/mL. The result of an intracutaneous tuberculin test was negative. The result of serologic screening for HIV, human T-cell leukemia virus type 1, cytomegalovirus, Epstein-Barr virus, and antinuclear antibody was negative. The patient did not have a familial history associated with immunodeficiency. He had kept many kinds of pet since infancy, including tropical fishes, dogs, rabbits, and turtles, and sometimes played in the river. After the patient was treated with clarithromycin, ethambutol, and rifampicin, his swollen lymph nodes gradually diminished in size.

3. Materials and methods

Surgically resected materials were fixed in formalin, embedded in paraffin, cut into 3-μm sections, and then stained with hematoxylin and eosin. The sections were also stained by the method of Ziehl-Neelsen. Immunohistochemical stains were performed on formalin-fixed, paraffin-embedded tissue sections using antibodies against CD68 (DAKO, Glostrup, Denmark) and S-100 (Nichirei Corp, Tokyo, Japan) and using the universal immunoenzyme polymer method (Histofine Simple Stain MAX-PO, Nichirei Corp).

DNA was isolated from paraffin sections of colon. As control, DNA extracted from paraffin sections of tuberculous lymphadenitis was used. Mycobacterial 16S ribosomal DNA (rDNA) was amplified by polymerase chain reaction. *M genavense*–specific sequence was amplified with primers MG22 and MG23 [12]. The polymerase chain reaction (PCR) products were all sequenced.

4. Results

Grossly, tumorous lesions were identified in the ileum, cecum, and ascending colon, resulting in stenosis of ileocecal valve (Fig. 1). Histologically, there was diffuse proliferation of histiocytes throughout the intestinal wall along with infiltration by lymphocytes (Fig. 2A). Proliferating histiocytes had abundant clear cytoplasm and small round nuclei (Fig. 2B). No nuclear or cellular atypia was present in histiocytes or lymphocytes (Fig. 2B). The histiocytes were positive for CD68 (Fig. 2C) and negative for S-100 protein by immunohistochemistry. Ziehl-Neelsen staining revealed numerous acid-fast bacteria in histiocytes (Fig. 2D). Similar findings were also observed in mesenteric and cervical lymph nodes, although fewer numbers of acid-fast bacteria were seen than in the intestinal lesions. Acid-fast bacteria could not be cultivated on conventional solid media. Mycobacterial 16S rDNA was amplified both in tuberculous lymphadenitis and the current case (Fig. 3A). With primers MG22 and MG23, PCR products were obtained only in the current case (Fig. 3A). The sequence of 16S rDNA hypervariable region in the current case was homologous with that of *M genavense* (X60070) (Fig. 3B). The sequence of the MG22-23 product was homologous with *M genavense* hypothetical 21-kd protein gene (AF025995).

5. Discussion

Since Böttger et al [1] identified *M genavense* as one of the nontuberculous mycobacteria in 1992, this pathogen has been described to cause disseminated infection in severely immunocompromised patients [1-9]. Infection with *M genavense* is reportedly responsible for more than 10% of disseminated nontuberculous mycobacterial infection in

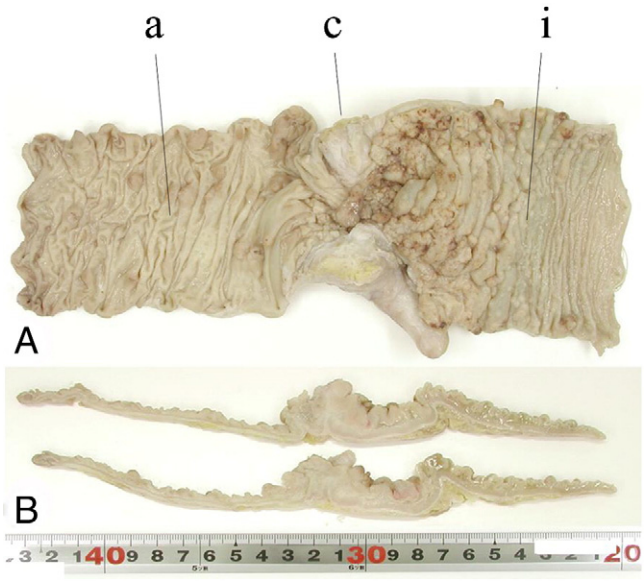

Fig. 1 Gross findings of resected ileocecum and ascending colon (A) and longitudinal cross sections (B). A number of tumorous lesions in varying sizes are present in ileum (i), cecum (c), and ascending colon (a), resulting in stenosis of ileocecal valve.