Concurrent Hepatic Tuberculosis and Hepatic Graft-versus-host Disease in an Allogeneic Hematopoietic Stem Cell Transplant Recipient: A Case Report

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ABSTRACT

Background. Infection and graft-versus-host disease (GVHD) are among the most common complications after hematopoietic stem cell transplantation (HSCT). With well-known risk factors including allogeneic HSCT and GVHD, tuberculosis (TB) has a higher incidence and shorter survival rate in HSCT recipients than in the general population.

Case Report. A 55-year-old Indonesian female with a history of latent TB was found to have acute myeloid leukemia 3 months after allogeneic HSCT. She presented with fever, abdominal pain, and predominant cholestatic-type liver function tests derangement. Computed tomography scans showed a relatively unremarkable liver. Liver biopsy specimens revealed multiple necrotizing granulomas with numerous acid-fast bacilli shown using Ziehl-Neelsen histochemical stain. No fungal organisms are detected by Grocott's methenamine silver and periodic acid–Schiff stains. There was also mild portal hepatitis with prominent bile duct injury and scattered apoptotic bodies, compatible with GVHD. In addition, the patient was also discovered to have cutaneous and intestinal TB as well as cutaneous and colonic GVHD during investigation. She was started on anti-TB treatment and adjusted immunosuppression scheme accordingly. Unfortunately, our patient died of spontaneous intracranial haemorrhage approximately 2 months after the diagnosis of post-transplantation TB and GVHD.

Conclusion. We report a case of concurrent hepatic TB and GVHD in an allogeneic HSCT recipient. Recognition of the dual pathology in the biopsy results aids proper treatment.

INFECTION and graft-versus-host disease (GVHD) are among the most common complications after hematopoietic stem cell transplantation (HSCT) [1]. Patients receiving allogeneic HSCT are highly susceptible to infections because of immunodeficiency [2]. Tuberculosis (TB), however, is an uncommon post-transplantation complication, with an overall incidence of 0.4% [3]. On the other hand, up to 80% of patients suffered from GVHD after HSCT [1]. Here we report a case of concurrent hepatic TB and hepatic GVHD in an allogeneic HSCT recipient.

CASE REPORT

A 55-year-old Indonesian female with a history of latent TB, Sjogren's syndrome, and bipolar disorder, was found to have acute myeloid leukemia 3 months after allogeneic HSCT. She presented with fever, abdominal pain, and predominant cholestatic-type liver function tests derangement. Computed tomography scans showed two indeterminate sub-centimeter nodules in the upper lobes of both lungs (enlarged and necrotic mesenteric lymph nodes) and mild splenomegaly with segmental splenic infarction. The liver was relatively unremarkable. The overall radiologic findings suggested an infective/inflammatory etiology. Blood procalcitonin and C-reactive protein levels were elevated. Meanwhile, bone marrow aspirate did not show any evidence of leukemic relapse. No bacteria or acid-fast bacilli (AFB) were found on the repeated blood, urine, and stool

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cultures. Her blood TB quantiferon test (QuantiFERON-TB, Qiagen, USA) was positive, which however would not help differentiate active from latent TB. Polymerase chain reaction tests for cytomegalovirus and Epstein–Barr virus were negative, despite persistent cytomegalovirus antigenemia. While under investigation, the patient was started with empiric antibiotics and antifungal agents, and added anti-TB medicine afterwards because of persistent fever.

Liver biopsy was performed for deteriorating liver function. Two cores of liver tissue with approximately eight portal tracts showed multiple necrotizing granulomas composed of aggregates of epithelioid histiocytes rimming areas of necrosis, located not only within the portal tracts but also throughout the hepatic lobule (Fig 1A). Numerous AFB were demonstrated within the granulomas with Ziehl-Neelsen (ZN) histochemical stain (Fig 1B). No fungal organisms were observed with Grocott's methenamine silver and periodic acid–Schiff stains. Although only few portal tracts were visualized, most of them showed a sparse mixed inflammatory infiltrate composed of lymphocytes, histiocytes, plasma cells, and neutrophils (Fig 2A). Eosinophils were not readily observed. The bile ducts also showed features of injury, with attenuated small profiles coupled with reactive nuclear atypia. Furthermore, few scattered eosinophilic apoptotic bodies were discerned (Fig 2B). Patchy mild areas of intracanalicular cholestasis were noted. There was no periportal inflammation. Few foci of lobular inflammation were present (3 foci on a 10× objective). There was no significant steatosis. Features of mild portal hepatitis with prominent bile duct injury and scattered apoptotic bodies were compatible with GVHD. Connective tissue stains showed portal-only fibrosis. There was grade 1 hemosiderosis with Perls' Prussian Blue histochemical stain. Diagnosis of concurrent hepatic TB and GVHD was made on the liver biopsy.

During investigation, the patient was clinically suspicious for intestinal TB due to several enlarged and necrotic mesenteric lymph nodes shown on the computed tomographic scan. The patient also had a papule over her left thigh, skin biopsy of which revealed a dermal necrotic focus containing nuclear debris and AFB (Fig 1C and 1D). Immunohistochemical stains, including myeloperoxidase, CD34, CD117, and MIB1, suggested no obvious features of a leukemic infiltrate. Approximately 2 weeks later, cutaneous and colonic GVHD was discovered through further biopsies as well. Skin biopsy from the right thigh showed interface and spongiotic dermatitis, which is consistent with grade 2 GVHD. The epidermis showed basal vacuolation with mild spongiosis and a few scattered apoptotic keratinocytes (Fig 2C). Colonic biopsy, performed due to diarrhea, showed features of mild GVHD. There were small numbers of basal apoptotic cells in several crypts associated with focal crypt distortion (Fig 2D).

DISCUSSION

In this case, our patient presented with post-HSCT fever and was administered broad spectrum anti-infective agents empirically, despite initial negative microbiologic findings.

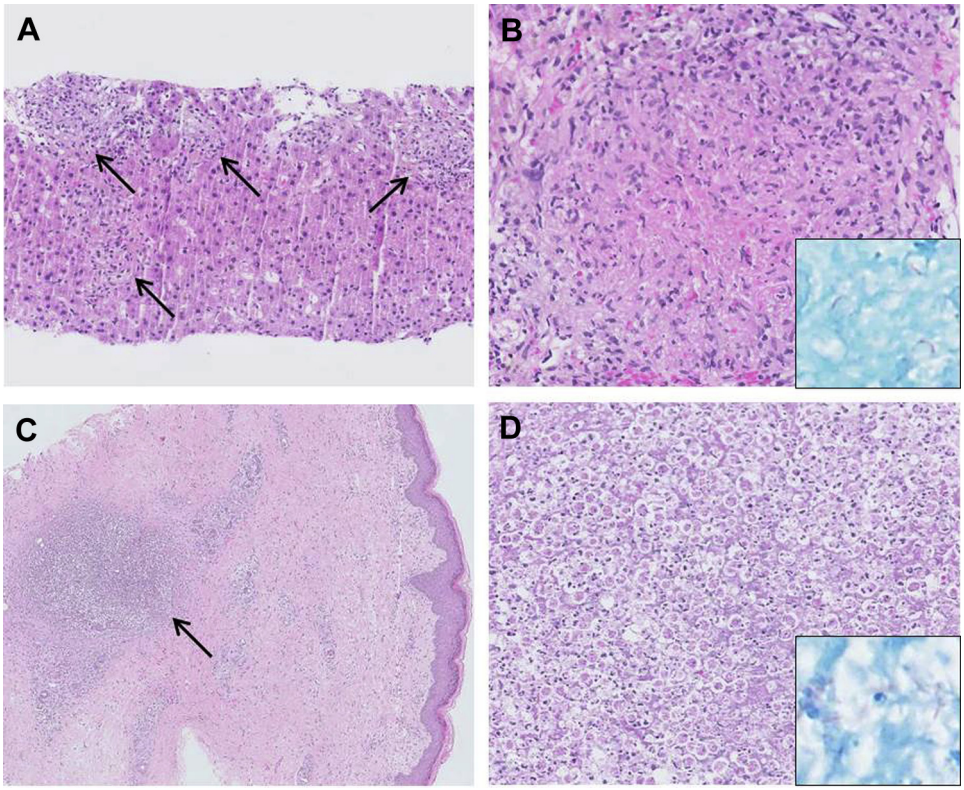

Fig 1. Disseminated tuberculosis. Liver biopsy showed multiple granulomas in portal tracts and throughout the hepatic lobules (**A**, original magnification ×100). The granulomas are of necrotizing type (**B**, original magnification ×400), with numerous acid fast bacilli (AFB) detected by Ziehl-Neelsen (ZN) histochemical stain (*inset*, original magnification ×1000). Skin biopsy specimen of a papule from left thigh showed a dermal necrotic focus (**C**, original magnification ×20); with the presence of AFB highlighted by ZN stain (**D**, original magnification ×100 and *inset*, original magnification ×1000).