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Isolated splenic mycobacterial disease: a cause of persistent fever in a hairy cell leukemia patient

Abstract

We describe a 69-year-old male patient who was referred for the investigation of long-lasting fever, anemia and neutropenia. Hairy cell leukemia was diagnosed and treated successfully. However, fever persisted despite thorough investigation and use of broad-spectrum antibiotics.

Four months after the initial diagnosis, the patient underwent explorative laparotomy and splenectomy. Spleen biopsy revealed multiple necrotizing mycobacterial granulomata while the patient's fever disappeared permanently. Isolated splenic mycobacterial disease is very rare. This case report emphasizes that investigation of chronic fever in hairy cell leukemia requires a high level of clinical suspicion.

Early diagnostic procedures for evidence of a typical mycobacterial infection should be considered. When everything else fails, surgery can be helpful in selected cases.

Keywords

Hairy cell leukemia, Mycobacteria, Infection, Spleen, Fever

Disciplines

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Isolated Splenic Mycobacterial Disease: A Cause of Persistent Fever in a Hairy Cell Leukemia Patient

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Key Words
Hairy cell leukemia · Mycobacteria · Infection · Spleen · Fever

Abstract
We describe a 69-year-old male patient who was referred for the investigation of long-lasting fever, anemia and neutropenia. Hairy cell leukemia was diagnosed and treated successfully. However, fever persisted despite thorough investigation and use of broad-spectrum antibiotics. Four months after the initial diagnosis, the patient underwent explorative laparotomy and splenectomy. Spleen biopsy revealed multiple necrotizing mycobacterial granulomata while the patient's fever disappeared permanently. Isolated splenic mycobacterial disease is very rare. This case report emphasizes that investigation of chronic fever in hairy cell leukemia requires a high level of clinical suspicion. Early diagnostic procedures for evidence of atypical mycobacterial infection should be considered. When everything else fails, surgery can be helpful in selected cases.

Introduction

Hairy cell leukemia (HCL) is an uncommon chronic lymphoproliferative disease in which malignant B-lymphocytes infiltrate bone marrow, spleen, liver and rarely lymph nodes. Although the survival of patients with HCL has been improved by the therapeutic introduction of interferon alpha and purine analogues, it is still worsened by

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complications such as severe infections [1–3]. We present a unique case of HCL associated with localized splenic mycobacterial infection, and review the available literature.

Case Report

In October 2008, a 69-year-old male patient was referred for the investigation of long-lasting fatigue, fever (up to 39°C), sweats and nausea. Full blood count showed: hemoglobin (Hb) level 10.9 g/dl, white cell count (WBC) 2.4×10^9/l, neutrophils (NEU) 1.12×10^9/l, monocytes 0.02×10^9/l and platelets (PLTs) 249×10^9/l. Blood film, bone marrow biopsy and immunophenotyping confirmed HCL. A computed tomography (CT) scan showed normal lung fields and a slightly enlarged spleen.

Initially, the patient was put on empirical piperacillin/tazobactam and amikacin which failed to control his fever. Cultures of blood, bone marrow, urine and induced sputum for common bacteria, acid-fast bacilli and *Pneumocystis* were negative. Serology for human immunodeficiency and hepatitis viruses was also negative. Quantitative real-time PCR failed to detect cytomegalovirus or Epstein-Barr virus transcripts in the blood. Transesophageal echocardiogram was normal. Consequently, the fever was considered to be a symptom of the underlying hematological disease and therapy was started. The patient had 4 weekly infusions of rituximab 375 mg/m^2 because he was neutropenic and then cladribine 0.1 mg/kg/day on continuous intravenous infusion for seven days.

Three months after admission the patient's full blood count returned to normal (WBC/NEU $8.6/7.5 \times 10^9$/l, Hb 13.6 g/dl, PLTs 166×10^9/l) and bone marrow immunophenotyping for minimal residual disease was negative (detection limit 0.1%). Nevertheless, fever and sweat persisted despite the successive administration of antibiotics such as quinolones, meropenem, linezolid, teicoplanin and liposomal amphotericin B. Empirical antimycobacterial therapy with isoniazid 600 mg/day, rifampicin 300 mg/day and ethambutol 1,500 mg/day proved also unsuccessful. A new CT scan of the chest and abdomen was performed and multiple low-density lesions on the spleen and liver were detected (**fig. 1**a). Fine-needle biopsy of the liver revealed chronic nonspecific granulomatous inflammation while hepatic tissue cultures were sterile. Subsequently, an atypical mycobacterial infection was suspected and the patient was put on clarithromycin 500 mg twice daily. This intervention led only to partial control of symptoms, with relapses of low-grade fever still present.

Four months after symptom onset, the patient underwent explorative laparotomy and splenectomy. The resected spleen had a weight of 600 g. On histological examination, splenic tissue was replaced by multiple necrotizing granulomata and Ziehl-Nielsen staining was positive for acid-fast bacilli (fig. 1b). However, cultures failed to grow mycobacteria. The patient's fever disappeared permanently 2 days post operation. Antimycobacterial therapy with isoniazid, rifampicin and ethambutol was given for 6 months. HCL remains in complete remission until now.

Discussion

HCL has shown a good long-term prognosis since the therapeutic introduction of purine analogs [2–7]. The predominant disease complication is infection, and early clinical studies have demonstrated a link between infection and poor survival [8, 9]. In patients with HCL, neutropenia and monocytopenia have been related to the occurrence of infection [8–10]. Additionally, in a recent study by Damaj et al., an absolute lymphocyte count $<1 \times 10^9$/l at diagnosis was found to be the sole independent factor associated with increased risk of severe infections [3]. The relationship between lymphopenia and the incidence of severe infection may be explained by the fact that nucleoside analogs aggravate preexisting lymphopenia and immunodeficiency [3].

Fever in HCL has been related to a wide range of infections. Half of those are caused by common microbes like *Pseudomonas aeruginosa, Staphylococcus aureus, Streptococcus*

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pneumoniae, and *Escherichia coli* [11]. In the remaining half, the causative agent can be an intracellular pathogen (*Listeria, Legionella, Coxiella, Mycobacterium tuberculosis*, atypical mycobacteria), a fungus *(Candida*, *Aspergillus*, *Cryptococcus*, *Rhizomucor*, *Sporothrix)*, a virus (hepatitis B, respiratory syncytial virus, cytomegalovirus, herpes, influenza), or a parasite like *Toxoplasma* or *Pneumocystis* [11]. Apart from infections, fever in HCL has been described in the context of vasculitis, such as polyarteritis nodosa and leukocytoclastic vasculitis [12]. In an early report by Bouza et al., 30% (6/20) of febrile patients with HCL were diagnosed with fever of unknown origin [8]. Half of these patients had well-documented infectious episodes later in their courses while no infection was found in the other half. Fever was controlled with steroids in 4/6 patients [3]. This could mean that fever in HCL is sometimes attributed to the disease itself. Initially, we believed that this was the case in our patient. This conclusion was not correct and the patient's outcome highlights the need of increased clinical suspicion when investigating fever in HCL.

The association between HCL and mycobacterial disease has been established [13]. To the best of our knowledge, a case of coexistent HCL and isolated splenic mycobacterial infection has never been reported in the literature. The vast majority of published reports describe disseminated mycobacterial disease, related to *Mycobacterium kansasii* infection, in patients with active HCL [13, 14]. Splenic granulomata due to mycobacteria are very rare, mostly diagnosed in immunocompomised hosts or as part of miliary tuberculosis [15]. This includes patients with HIV infection, organ transplantation, steroid therapy and chemotherapy [15]. Isolated hepatosplenic tuberculosis has been reported previously in the setting of acute lymphoblastic and acute myeloid leukemia [16, 17]. In both reports, the disease typically presented during the recovery phase of neutropenia post chemotherapy and was characterized by the absence of organomegaly, non-involvement of other sites, poor inflammatory response and a high bacillary load. It is worth noting that ultrasound or CT findings of such lesions, in a neutropenic individual, are not specific. Fungal hepatosplenic abscesss due to *Candida* species are included in the differential diagnosis, and they have been widely reported [17].

In conclusion, this case demonstrates that investigation of chronic fever in a patient with HCL requires a high level of clinical suspicion. Early diagnostic procedures for evidence of atypical mycobacterial infection should be considered. When everything else fails, surgery can be helpful in selected cases.

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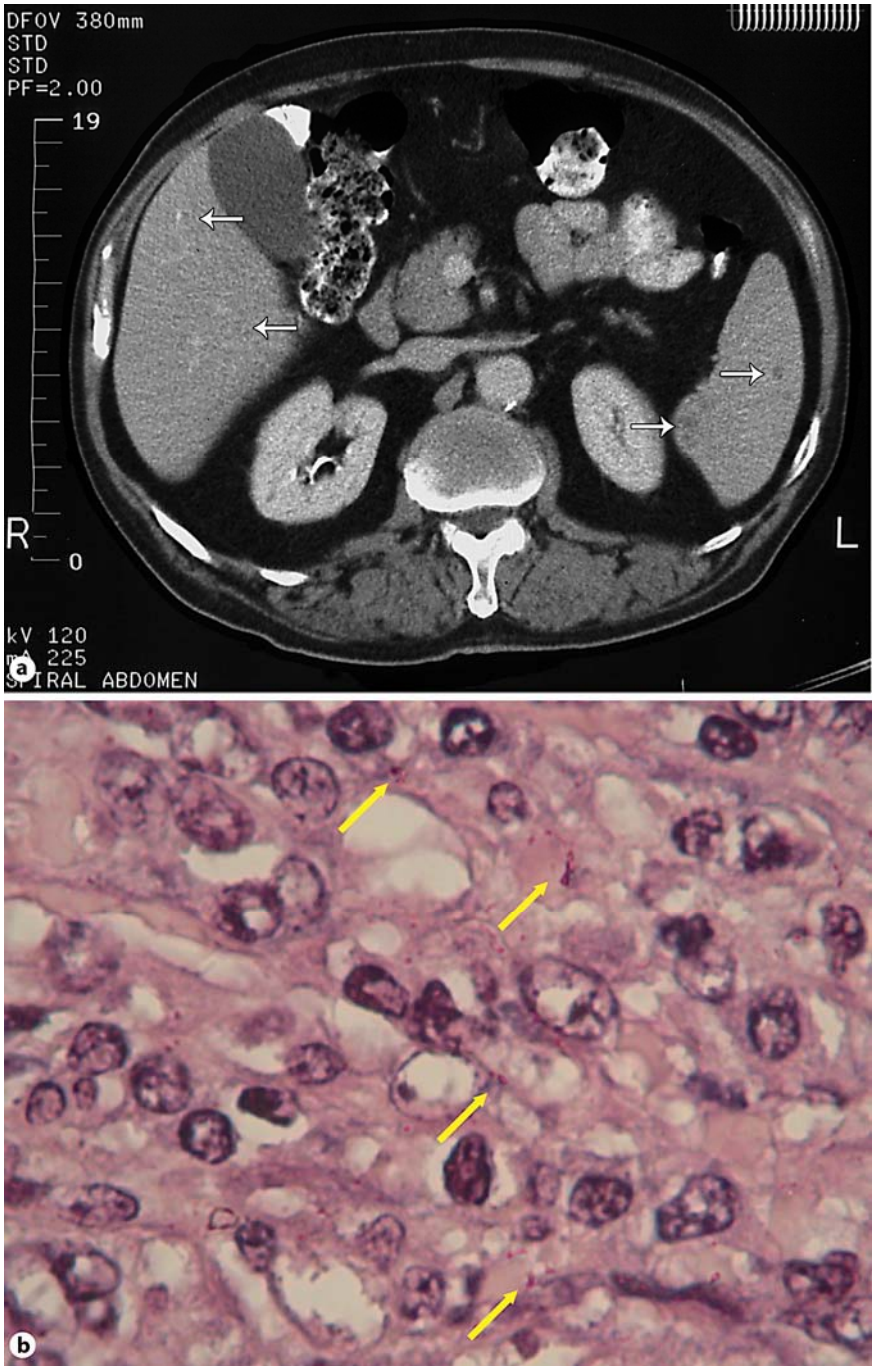

Fig. 1. **a** CT scan of the abdomen showing multiple low-density lesions on the spleen and liver. **b** Positive Ziehl-Nielsen staining for acid-fast bacilli on splenic tissue.

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References

1 Flinn IW, et al: Long-term follow-up of remission duration, mortality, and second malignancies in hairy cell leukemia patients treated with pentostatin. Blood 2000;96:2981–2986.

2 Goodman GR, Burian C, Koziol JA, Saven A: Extended follow-up of patients with hairy cell leukemia after treatment with cladribine. J Clin Oncol 2003;21:891–896.

3 Damaj G, et al: Risk factors for severe infection in patients with hairy cell leukemia: a long-term study of 73 patients. Eur J Haematol 2009;83:246–250.

4 Zinzani PL, et al: Long-term follow-up of front-line treatment of hairy cell leukemia with 2-chlorodeoxyadenosine. Haematologica 2004;89:309–313.

5 Else M, et al: Long remissions in hairy cell leukemia with purine analogs: a report of 219 patients with a median follow-up of 12.5 years. Cancer 2005;104:2442–2448.

6 Chadha P, et al: Treatment of hairy cell leukemia with 2-chlorodeoxyadenosine (2-CdA): long-term follow-up of the Northwestern University experience. Blood 2005;106:241–246.

7 Maloisel F, et al: Long-term outcome with pentostatin treatment in hairy cell leukemia patients. A French retrospective study of 238 patients. Leukemia 2003;17:45–51.

8 Bouza E, Burgaleta C, Golde DW: Infections in hairy-cell leukemia. Blood 1978;51:851–859.

9 Golomb HM, Hadad LJ: Infectious complications in 127 patients with hairy cell leukemia. Am J Hematol 1984;16:393–401.

10 Bourguin-Plonquet A, et al: Severe decrease in peripheral blood dendritic cells in hairy cell leukaemia. Br J Haematol 2002;116:595–597.

11 Kraut EH: Clinical manifestations and infectious complications of hairy-cell leukaemia. Best Pract Res Clin Haematol 2003;16:33–40.

12 Hasler P, Kistler H, Gerber H: Vasculitides in hairy cell leukemia. Semin Arthritis Rheum 1995;25:134–142.

13 Bennett C, Vardiman J, Golomb H: Disseminated atypical mycobacterial infection in patients with hairy cell leukemia. Am J Med 1986;80:891–896.

14 Thaker H, et al: Remember mycobacterial disease in hairy cell leukaemia (HCL). J Infect 2001;42:213–214.

15 Jain M, Singh S, Thomas S, Jain D: Acid-fast bacilli positive isolated tubercular splenic abscess in a HIV-negative patient. Indian J Pathol Microbiol 2008;51:74–75.

16 Chang MC, Lin SC, Jeng KS, Shih CC: Tuberculous splenic abscess in a patient with acute myeloblastic leukemia. Taiwan Yi Xue Hui Za Zhi 1985;84:1173–1179.

17 Chakrabarti S, Varma S, Kochhar R, Gupta S, Gupta SK, Rajwanshi A: Hepatosplenic tuberculosis: a cause of persistent fever during recovery from prolonged neutropenia. Int J Tuberc Lung Dis 1998;2:575–579.