CASE REPORT

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Primary Bone Marrow Hodgkin's Lymphoma Presenting with Pancytopenia

Gavisiddappa, Nagaraja Kamath*, Vinay N *, Aravind GN***

Abstract

Pancytopenia can be sired by a myriad of diseases. Hodgkin's lymphoma (HL) usually presents with lymphadenopathy. Nevertheless, few patients can present with atypical symptomatology of HL which usually poses a clinical and diagnostic challenge. Very few cases of HL with first presentation as pancytopenia without lymph node involvement are described in the literature. Here we report a case of a young adult who presented with a history of fever, malaise and weight loss for one year. He had no lymphadenopathy on physical examination. Laboratory investigations showed pancytopenia with elevated LDH. Imaging confirmed no lymphadenopathy. Bone marrow biopsy was done which showed features of HL. FDG PET-CT scan done at the time of presentation after bone marrow biopsy showed hypermetabolic skeletal involvement. Patient was started on chemotherapy and responded well to the treatment. FDG PET-CT done after 6 cycles of chemotherapy revealed complete response to therapy. Atypical forms like primary bone marrow HL present with constitutional symptoms and have a protracted clinical course. Precise and prompt recognition of Primary HL is required for successful management of this rare entity.

Key words: Hodgkin's lymphoma, pancytopenia, Reed-Sternberg cells, primary bone marrow Hodgkin's lymphoma.

Introduction

Pancytopenia is a clinico-hematological entity which is characterised by reduction of all three cell lines. It can be a feature of a wide array of diseases, ranging from benign conditions to malignant neoplasms, either primary haematologic malignancies or non-haematologic metastatic malignancies. HL involves clonal proliferation of mature B lymphocytes. Around 90% of HL are classical, whereas the remaining 10% are lymphocyte predominant[1]. HL typically presents with lymphadenopathy, most commonly involving nodes of cervical, mediastinal or axillary region. In a few patients, B symptoms like fever, weight loss and night sweats can predominate. Bone marrow infiltration is usually known to occur in advanced stages of HL which can present with symptomatic anaemia, bony pain or pancytopenia[1,2]. Primary bone marrow involvement is uncommon and primarily reported in HIV-positive patients[3]. Here we describe a case of HL that primarily involved bone marrow and was successfully treated with conventional chemotherapy.

Case report

A thirty-five-year-old man, an event manager by occupation, reported with complaints of fever, malaise and weight loss for one year. Due to this, he had multiple admissions in the past year. Each time evaluation did not reveal anything significant. Patient was discharged with symptomatic treatment each time.

On general physical examination his vitals were stable and pallor was present. He was febrile with fever upto 101° F. There was no oedema or palpable lymph nodes. Abdominal examination showed mild splenomegaly. Rest of the clinical examination was unremarkable.

Initial laboratory tests showed pancytopenia with haemoglobin 5.7 g/dL, WBC 1,500 cells/mm^3, platelet count of 81,000 cells/mm^3. Liver function showed elevated total bilirubin 3.6 mg/dL, direct bilirubin 1.8 mg/dL, AST 35 U/L, ALT 49 U/L and ALP 180 U/L. Serum albumin was 3.2 g/dL. Renal function test, serum electrolytes (Sodium 142 mEq/L, Potassium 4.8 mEq/L) were normal. Fasting lipid profile showed triglycerides 120 mg/dL and LDL 102 mg/dL. Peripheral smear showed RBCs with normocytic normochromic anaemia with few tear drop cells and pencil shaped cells, WBCs and platelets were normal in morphology and distribution but reduced in number. Corrected reticulocyte count was 1.5%. ESR and LDH were elevated. Folic acid and Vitamin B12 levels were within limits. Serum ferritin was 2,000 ng/mL with elevated transferrin saturation. Hepatitis B, hepatitis C and HIV were negative. Antibodies for EBV and CMV were negative. Mantoux test, Weil Felix test and sputum CBNAAT were negative. Pan cultures did not yield anything significant. ANA profile was negative. Chest X-ray and 2D Echocardiogram were normal.

Junior Resident, **Professor and Unit Head, Department of General Medicine, Bangalore Medical College and Research Institute, Bengaluru - 560 002, Karnataka.

Corresponding Author: Dr Nagaraja Kamath, Junior Resident, Department of General Medicine, Bangalore Medical College and Research Institute, Fort, Krishna Rajendra Road, City Market, Bengaluru - 560 002, Karnataka. Tel: 8762957560, E-mail: Nagaraj.kamath1998@gmail.com

USG of the abdomen evinced mild splenomegaly and liver of normal size and shape. CT imaging of abdomen, chest and pelvis done revealed mild splenomegaly and no features of lymphadenopathy. Then the patient received two units of packed red blood cells.

Following this, a biopsy of the bone marrow was done. It showed Reed-Sternberg cells, epithelioid granulomas and a background composed of lymphocytes, eosinophils and histiocytes. Granulopoiesis and erythropoiesis were suppressed (Fig. 1) Immunohistochemistry for CD30 and PAX5, was positive (Fig. 2). They were negative for CD 15, CD 79a, CD 3, CD 45 and EMA. To evaluate the spread of disease throughout the whole body FDG PET CT was done which showed avid bony lesions noted in few vertebrae, bilateral scapulae, pelvic bones, bilateral femurs and humeri (Fig. 3). Liver appeared normal with no evidence of FDG avid lesion. Spleen appeared slightly enlarged in size with no evidence of FDG avid lesion. Hepatosplenic ratio was maintained. Based on the above features he was diagnosed to have Hodgkin's lymphoma. Medical oncologist consultation was sought and he was initiated on chemotherapy. He received ABVD protocol (6 cycles) as an out-patient with an excellent response. Serial monitoring done with PET CT showed interval resolution of hypermetabolic bone lesions. Following six cycles of chemotherapy, an FDG PET scan demonstrated a complete metabolic response, with no evidence of active trace uptake at any site (Fig. 4). Then he was declared as a treated case. He is currently on regular follow-up by clinical and laboratory examination every 3 months. During his most recent follow-up, conducted two years after his diagnosis, CBC showed haemoglobin 13.4 g/dL, WBC 5,990 cells/mm^3 and platelets 1.52 lakhs/mm^3.

Discussion

Hodgkin's lymphoma (HL) is typically limited to lymph nodes alone, with 2 - 16% of cases incriminating extranodal structures. Peripheral lymph node enlargement is almost always the initial presentation[1,2]. Liver, lungs, spleen, bone and bone marrow are the commonly involved extranodal sites. In HL, bone marrow involvement is uncommon between 4 - 18%, with average incidence around 10%[1]. If present, it is usually associated with extensive lymphadenopathy and advanced disease. It is reckoned a feature of generalised disease with primary arising somewhere else in the body. Bone marrow infiltration can be expected to occur more often in those who turn up with constitutional symptoms and cytopenias compared to those in whom these are absent. Typically, bone marrow involvement is designated as stage IV disease. This is because clinical stages I and II have a very meager percentage of patients with bone marrow involvement (<1%)[4,5].

HL primarily incorporating bone marrow without involvement of lymph nodes is an infrequent presentation with negligible number of reports in the literature. The reported cases are from HIV positive individuals, which is rapidly progressive. Reports from HIV negative individuals are uncommon. Amongst the cases described, patients with HIV negative Primary bone marrow Hodgkin's lymphoma (PBMHL) were more than 50 years old. Whereas HIV positive PBMHL were reported in younger patients[6]. PBMHL can pose a diagnostic difficulty as Reed-Sternberg cells may be absent in the bone marrow or tumour cells may be difficult to detect due to focal involvement of the marrow or tumour cells may be masked by expansive inflammatory cell infiltrates or fibrosis. PBMHL is usually known to be associated with a myriad of complications and poor response to conventional treatment. Mostly those with HIV negative PBMHL seldom improve with ABVD regimen[7]. Bone marrow aspiration has a limited role in prognosis of patients in early stages presenting with classical symptoms, but plays a role in patients presenting with elevated LDH, elevated ALP and cytopenias. Despite the fact that PET-CT scan plays an important role in staging HL, biopsy of bone marrow remains the gold standard test and thus helping in modulating

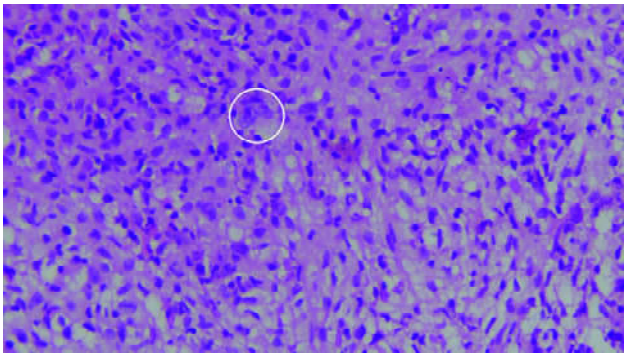

Fig. 1: *Bone marrow biopsy showing Reed-Sternberg cells (circled in white) and background composed of lymphocytes, eosinophils and histiocytes.*

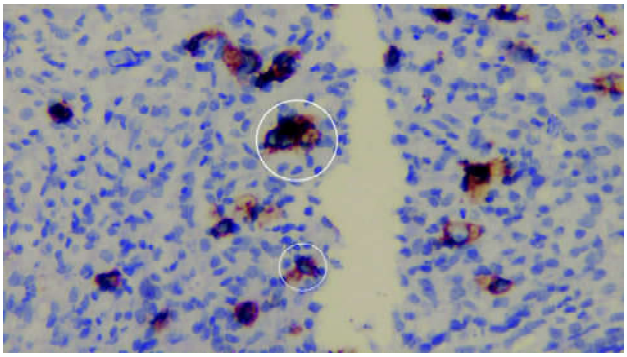

Fig. 2: *Immunohistochemistry of the bone marrow biopsy sample showing positive CD 30 staining.*

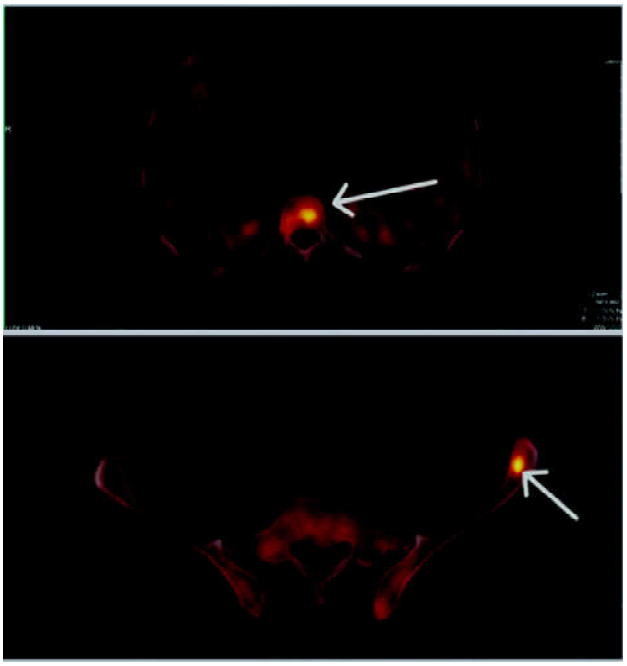

Fig. 3: *PET-CT images showing intense FDG uptake in the right ileum and thoracic vertebrae.*

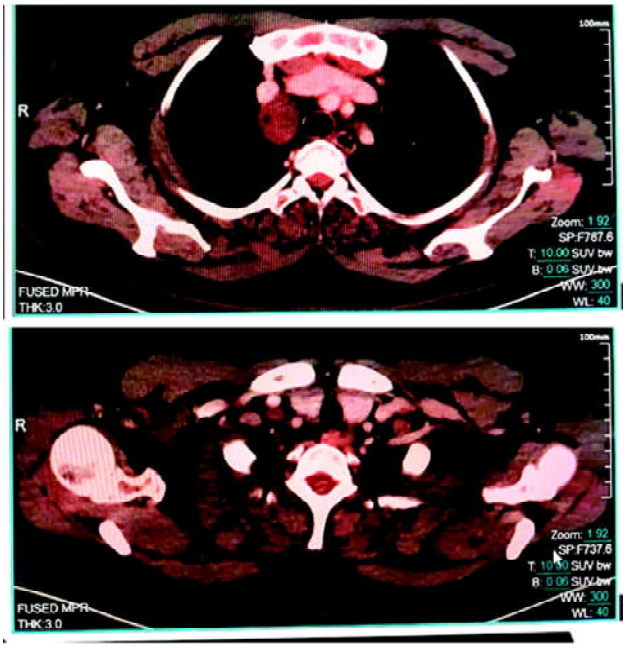

Fig. 4: *PET-CT images showing resolution of hypermetabolic bone lesions.*

treatment options and prognostic evaluation[8].

Conclusion

Primary bone marrow HL often exhibits B symptoms, cytopenias and a protracted clinical course. It poses a diagnostic dilemma and is often associated with delayed diagnosis and treatment. If a form of PBMHL is suspected, physicians should perform a bone marrow biopsy and consult a medical oncologist as soon as possible. Finally, typical Reed-Sternberg cells are not always observed in the pathological findings in patients with PBMHL. Immunophenotypic assessments should include examinations with a panel of antibodies, including HL and keep low threshold for ordering bone marrow examination in patients presenting with fever of unknown origin associated with pancytopenia.

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