

Pancytopenia as Primary Presentation of Hodgkin's Lymphoma, a Unique Paradox: A Case Report

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ARTICLE INFO

Received:  August 19, 2021

Published:  September 01, 2021

Citation: Khalid Shahzad, Anum Ashfaq, Irshad Khan, Waqas Ahmad, Saif ul Haque, Usman Hameed Mian. Pancytopenia as Primary Presentation of Hodgkin's Lymphoma, a Unique Paradox: A Case Report. Biomed J Sci & Tech Res 38(3)-2021. BJSTR. MS.ID.006163.

Keywords: Pancytopenia; Reed-Sternberg cells; Hodgkin's lymphoma

ABSTRACT

Pancytopenia can be associated with wide variety of diseases of which some are life threatening. Hodgkin's lymphoma almost always initially presents with lymph node involvement. Pancytopenia without lymph node involvement as primary presentation of Hodgkin's lymphoma is extremely rare and only few cases have been reported in literature. This is a case of a 55-year-old male known asthmatic who presented with constitutional symptoms i.e. fever, generalized body weakness, lethargy and decrease appetite. On examination patient was anemic with hepatosplenomegaly but no lymph nodes. Labs showed Pancytopenia and raised C-reactive protein, raised LDH and ferritin. Liver function tests, Renal function tests, Serum electrolytes, Urine Routine examination were normal. Pan-cultures showed no growth. ECG, Echocardiography and chest x-ray were normal. Ultrasound abdomen showed Hepatosplenomegaly with no lymphadenopathy. PAN-CT only showed hepatosplenomegaly with no lymph node involvement. Bone marrow biopsy was done which showed Reed-Sternberg cells. Patient was diagnosed as a case of Hodgkin's Lymphoma with primary bone marrow involvement. High clinical suspicion is required for exact diagnosis of disease on lateral thinking.

Abbreviations: LDH: Lactate Dehydrogenase; CMV: Cytomegalovirus; TPHA: Treponema Pallidum Hemagglutination Assay; PBMHL: Primary Bone Marrow Hodgkin's Lymphoma; EBV: Epstein-Bar Virus; HIV: Human Immunodeficiency Virus; PET Scan: Positron Emission Tomography Scan; ABVD: Adriamycin Bleomycin Vinblastine Dacarbazine

Background

Hodgkin's lymphoma is a cancer of mature B-lymphocytes representing approximately 10% of all lymphomas diagnosed every year. About 90% of diagnosed cases of Hodgkin's lymphoma are Classical Hodgkin's lymphoma while remaining are Nodular lymphocyte predominant subtype. Reed Sternberg cells are diagnostic of Classic Hodgkin's Lymphoma which are usually PAX-5 (+ve) and also express CD15 and CD30. Hodgkin's lymphoma usually presents as lymphadenopathy most commonly in cervical,

axillary or mediastinal areas. About 25% of cases of Hodgkin's lymphoma present with B-symptoms like weight loss, night sweats and fever. Pruritis also occurs in 10-15%. Bone marrow infiltration usually occurs in advance stage and extensive disease in Hodgkin's lymphoma in which the patient usually presents with bone pain, symptomatic anemia or pancytopenia. Primary Bone marrow involvement in Hodgkin's lymphoma is extremely rare. Here is one such case of Hodgkin's lymphoma who presented with primary bone marrow involvement.

Case Report

A middle-aged male 51 years working as a ward attendant in a hospital, married belonging to the lower socioeconomic status, non-smoker admitted initially with fever, generalized body weakness and decreased appetite for 6 months. He had 3 such admissions in the past 1 year for same complaints. Detailed workup was done which was negative. Patient was discharged on symptomatic treatment. On this admission, fever was documented up to 102^oF, high grade, continuous and associated with rigors and chills. There was no history of weight loss, night sweats and any other systemic complaint. He had past history of bronchial asthma for which he took Foster Inhaler. On general physical examination, patient was well oriented in time, space and person. He had pallor with BP=120/78mmHg. Pulse was 83/minute, temperature of 102^oF, respiratory rate of 16/minute and saturation of 98% at room air. There were no palpable lymph nodes or edema or cachexia.

On Abdominal examination, the abdomen was soft, non-distended and non-tender. There was splenomegaly and palpable splenic notch. Bowel sounds were audible. Rest of systemic examination was unremarkable. Labs showed thrombocytopenia of 49000 and Hb of 11mg/dl on admission. This bicytopenia later progressed to pancytopenia with Hb of 6.6mg/dl, TLC count of 2730 and platelet count of 27000. ESR was 90. Peripheral film showed retics of 2.5%. LDH was 540 and Ferritin was 2000. Serum bilirubin was 0.3, ALT of 36 and ALP of 339. RFTs, Serum Electrolytes and Urine R/E were normal. PAN Cultures showed no growth. Hep B, C and HIV were negative. Brucella serology, Mantoux test and sputum for AFB were negative. USG Abdomen showed hepatosplenomegaly with no lymphadenopathy. Liver span was 18cm and splenic index was 80. ECG, Echocardiography and Chest X-ray were normal. CT Scan Chest, Abdomen and Pelvis showed only hepatosplenomegaly with no lymphadenopathy.

Our differentials were CMV, EBV, TB, Syphilis, HIV, Autoimmune disease and occult malignancy. Antibodies for CMV and EBV, ANA, Syphilis TPHA, HIV, Coomb's test, Tumormarkers were normal. Based on the diagnosis of PUO next step was bone marrow biopsy. Bone marrow showed Reed Sternberg Cells. On Immunohistochemistry, these were positive for PAX-5, CD30 and CD15 whereas negative for LCA. Background showed inflammatory infiltrates consisting of reactive lymphocyte plasma cell and eosinophils. CD3 and CD20 immunostaining were positive for scattered T and B lymphocytes respectively. Few megakaryocytes were identified. Granulopoiesis and erythropoiesis was suppressed. Patient was diagnosed as case of Hodgkin's lymphoma and referred to oncology department for treatment. He received ABVD protocol (6 cycles) and then declared as treated case.

Discussion

Hodgkin's lymphoma accounts for 30% of all lymphomas. It is a common lymphoproliferative disorder that primarily involve lymphoid tissues including lymphocytes, histiocytes and its precursors [1]. Hodgkin's lymphoma is mostly confined to lymph nodes entirely with only 2-16% of cases involving extranodal structures and almost always the initial presentation is progressive peripheral lymph node enlargement [2,3]. WHO classification of tumors of hematopoietic and lymphoid tissues divides Hodgkin's lymphoma into two main classes Classic Hodgkin's lymphoma and Nodular lymphocyte predominant Hodgkin's lymphoma [4]. In our case, patient initially presented just with thrombocytopenia which rapidly progressed to pancytopenia within no time and pan-CT scan did not showed any lymph nodes.

Extranodal lesions in Hodgkin's lymphoma mainly involve liver, spleen, lung, bone and bone marrow [1]. Staging of Hodgkin's lymphoma is done by location of lymph nodes whether present on one side of diaphragm or both, bulky disease or not, extranodal involvement or disseminated extranodal disease and presence of B-symptoms [3]. Although PET Scan/CT Scan is most important tool for staging of Hodgkin's lymphoma bone marrow biopsy from iliac crest is gold standard to confirm bone marrow infiltration which in turn guide treatment options and prognostic evaluation [3,5,6].

Bone marrow infiltration in Hodgkin's lymphoma is mostly associated with extensive lymphadenopathy and advanced stage disease and usually occur from disseminated disease arising somewhere else in the body [7,8]. The frequency of bone marrow involvement in Hodgkin's lymphoma ranges from 4-18% proven in various studies and once bone marrow is infiltrated it is considered as Stage IV disease [5]. The two subtypes with higher risk of bone marrow infiltration are Lymphocyte depleted and Mixed cellularity compared to other subtypes in one study [5]. New onset pancytopenia is a diagnostic dilemma and is caused by vast variety of conditions and is one of the most common indication for bone marrow biopsy [9].

Hodgkin's lymphoma involving primarily bone marrow without lymph node involvement is extremely rare with only few cases been reported in literature. It is extremely aggressive and rapidly progressing with very poor prognosis [10,11]. Primary bone marrow Hodgkin's lymphoma is mostly reported in HIV positive patients and rarely in HIV negative patients [7]. Usually HIV negative PBMHL occur in older patients aged more than 55 years compared to HIV positive PBMHL which has mostly been reported in young people [11]. PBMHL is relatively hard to diagnose due to either absence of typical Reed-Sternberg cells or difficult to detect the tumor cells due to focal pattern of bone marrow infiltration

or masking of cells by extensive fibrosis and florid inflammatory background [7,11,12].

In HIV associated PBMHL Epstein-Bar Virus is believed to play a pivotal role with 75-78% positivity for EBV in HIV associated PBMHL [2]. PBMHL is very easily associated with multiple complications with only few responding to conventional therapy especially those with HIV negative PBMHL respond very poorly to ABVD therapy [11]. Bone marrow infiltration is more common in patients who present with constitutional symptoms and decrease blood cell lineages compared to those in whom these are absent [5]. Patients presenting with leucopenia and thrombocytopenia are usually at higher risk [5]. Degree of cytopenias is an important prognostic factor in the severity of disease [10]. Some studies have showed that isolated thrombocytopenia is an important survival indicator in primary bone marrow lymphomas [10].

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ISSN: 2574-1241

DOI: 10.26717/BJSTR.2021.38.006163

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