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Case Report OMICS International

Primary Plasma Cell Leukemia Presenting as Heart Failure: A Case Report

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Abstract

Plasma cell leukemia (PCL) is an uncommon and aggressive plasma cell dyscrasia characterized by malignant plasma cells in bone marrow and peripheral blood. The prognosis of PCL patients treated with conventional chemotherapy remains poor. The clinical presentation of PCL features extensive abnormal plasma cells in the peripheral blood and a higher prevalence of organomegaly, with involvement of multiple tissues and organs, the symptoms usually include anemia, bleeding, infection, bone pain, and renal failure. However, PCL presenting as heart failure is very rare. We herein report a case of 45-year-old man primary PCL in which the patient presented atypically as heart failure.

Keywords: Plasma cell leukemia; Heart failure; Megakaryocyte

Introduction

Plasma cell leukemia (PCL) is a rare cancer involving plasma cells. It has an aggressive presentation that progresses rapidly, leading to a poor prognosis and short survival [1,2]. PCL has a slightly low incidence of bone lesions. Its clinical presentation is more like that of acute leukemia; the symptoms usually include anemia, bleeding, infection, bone pain, and renal failure [3,4]. PCL presenting as heart failure is very rare. To better understand PCL, we report a case that presented atypically as heart failure; we discuss our diagnostic approach as well as the clinical outcome of this case.

Case report

A 45-year-old man was admitted to our hospital for fatigue and shortness of breath. Over a period of 2 months his symptoms had become worse, leading to bloating for the last 2 weeks. The patient had previously had hepatitis (cured); the family history was unknown. Results of the physical examination were as follows: temperature, 36.5°C; respiration, 20 breaths per minute; pulse, 83 beats per minute; blood pressure, 113/55 mm Hg (1 mm Hg=0.133 kPa). The patient was conscious and experiencing orthopnea. There was no jaundice and no red spots were found on the skin; no enlargement of the superficial lymph nodes was palpable. Jugular venous distention was present, as were symptoms of hepatojugular reflux. The intercostal spaces of the right thoracic cage were enlarged, and the left thoracic cage had a pectus carinatum deformity. Dilated veins were observed on the upper chest. There were diminished lung sounds at the bases and no pulmonary rales. The location of the point of maximal impulse extended laterally and downward. The heart rate was 83 beats per minute with normal rhythms. Grade 3/6 systolic murmurs were heard over the mitral valve and pulmonary artery valves. The abdomen was soft, with pain/tenderness in the right upper quadrant; Blumberg's sign was negative. The upper border of the liver was located at the fourth intercostal space in the midclavicular line; the lower border was at 5 cm below the costal margin in the medial collateral ligaments and one finger above the navel at the xiphoid cross. The liver was firm and its edge felt sharp and rough. Percussion of the kidneys elicited no pain or tenderness. Edema was seen in the lower extremities and lumbosacral area.

Other examinations

ECG: normal sinus rhythm, T-wave changes (low I, avL, and V4-V6 T-wave).

Echocardiography: 2-dimensional echocardiography showed an enlarged heart (on anteroposterior view, left atrium diameter 56 mm; left ventricle diastolic diameter 60 mm; right atrium diameter 70 mm and right ventricle diameter 55 mm). Mild tricuspid valve regurgitation, mitral valve regurgitation and aortic valve regurgitation was observed. Elevated pulmonary artery pressure (51-56 mm Hg) and a moderate pericardial effusion were detected. Left ventricular ejection fraction (LVEF, M-type) and left ventricular fractional shortening (LVFS) were 60% and 30%, respectively. Left ventricular diastolic dysfunction had an E/A ratio greater than 1.

An abdominal ultrasound examination showed hepatomegaly with increased liver echogenicity, possibly suggesting hepatic congestion; also noted were a dilated hepatic vein and inferior vena cava, thickened gallbladder wall with coarse echo texture, slightly dilated intrahepatic bile ducts, splenomegaly, hypoechogenic nodules at the splenic hilum (possibly lymph nodes), and a small perihepatic effusion.

A hemogram revealed a white blood cell count of 7.71 × 109 cells/L, with 67.2% neutrophils, 13.4% lymphocytes, and 18.9% monocytes. Platelet counts were 30 × 109 per liter, red blood cells were 3.56 × 1012 per liter, and hemoglobin was 114 g/L.

Liver function tests showed the following: albumin-42.7 g/L; globulins-15.2 g/L; albumin-to-globulin (A/G) ratio- 2.81; proalbumin-162.0 mg/L; aspartate aminotransferase-30.0 U/L; alanine aminotransferase-15.0 U/L; γ-glutamyl endopeptidase-70.0 U/L; total

bilirubin-17.2 μmol/L; direct bilirubin-10.9 μmol/L; and indirect bilirubin-6.3 μmol/L.

Kidney function tests showed the following: blood urea nitrogen (BUN)-10.37 mmol/L; serum creatinine-120.6 μmol/L; and uric acid-627.2 μmol/L.

A lipid blood test showed the following: total cholesterol-1.55 mmol/L; high-density lipoprotein cholesterol (HDL-C)-0.60 mmol/L; low-density lipoprotein cholesterol (LDL-C)-0.58 mmol/L; and triglycerides-0.83 mmol/L.

Other laboratory tests included thyroid function tests, brain natriuretic peptide (BNP), high-sensitivity C-reactive protein (hs-CRP), erythrocyte sedimentation rate (ESR), alpha-fetoprotein (AFP), and carcinoembryonic antigen (CEA). The results of all were within normal limits.

Quantitative immunoglobulin analysis showed IgM at 0.15 g/L, IgA at 0.50 g/L, IgG at 3.0 g/L, and ferritin at 554.9 ng/mL.

Tests for hepatitis B surface antibody and hepatitis B virus core antibody were positive; those for hepatitis C virus antibody and hepatitis A virus antibody were negative.

Syphilis testing proved negative for *Treponema pallidum*-specific antibodies; the toluidine red unheated serum test was also negative. Tests for HIV antibodies and antinuclear antibody (ANA) were both negative, as was the test for antineutrophil cytoplasmic antibodies (ANCA), which showed negative results for both cANCA and pANCA. Complement 3 and complement 4 were both negative.

An antimyocardial antibody (AMA) test showed negative results for anti-ATP/ADP carrier antibody, anti-β1 receptor antibody, anti-M2-cholinergic receptor antibodies, and MHC anti-myosin heavy chain antibody. In addition, IgM antibodies against Coxsackie virus types B3 and B5, antibodies against enterovirus, as well as IgM antibodies against cytomegalovirus were all negative. The serum free κ-light chain level was less than 3.30 mg/L, while the serum free λ-light chain level was greater than 3900 mg/L.

Pulmonary vascular measurements using contrast-enhanced CT showed normal pulmonary arteries, bilateral pleural effusions with bibasilar atelectasis, and an enlarged cardiac shadow.

Examination of the liver, gallbladder, and spleen using contrast-enhanced CT showed a low-density lesion on right lobe of the liver (a 2.8-cm oval lesion, which was not clearly visualized during the arterial and delayed phases), hepatomegaly, splenomegaly, ascites, and tortuous dilated splenic veins.

Bone marrow biopsy examination revealed hypercellular marrow with good cellular trails and no fat cells (Figure 1). The proliferation was active, with G=21%, E=4%, and G/E=4.75/1. The percentages of granulocyte series and granulocytic precursors were decreased, while the percentage of segmented granulocytes was increased. The morphology of granulocytes at different maturational stages was normal. Erythroid series were rare; the size and morphology of mature RBCs were slightly heterogeneous. The percentage and morphology of lymphocytes were normal. The percentage of monocyte series was decreased but cell morphology was normal. Three granular megakaryocytes were detected, while platelets were rare. The percentage of plasma cells was increased with the presence of flame cells, Mott cells, and cells with cleaved nuclei. Iron staining showed extracellular iron; the intracellular iron was not determined because of a low erythrocytes count. PAS staining was negative for nucleated erythrocytes and megakaryocytes.

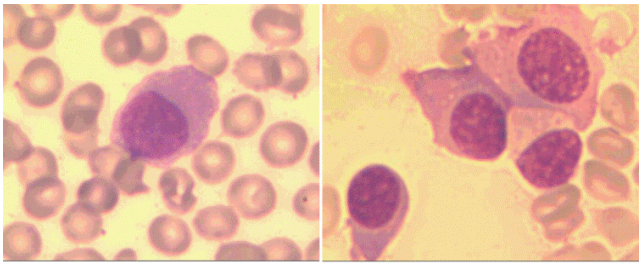

Figure 1: Bone marrow biopsy examination revealed hypercellular marrow with good cellular trails and no fat cells.

A peripheral blood smear showed increased white blood cells with a normal percentage of neutrophils and thrombocytopenia. Immature granulocytes were detected. The size of mature erythrocytes was slightly heterogeneous. No nucleated erythrocyte was found within the 100 white blood cells counted. The percentage of lymphocytes increased with 22% abnormal lymphocytes, most of which were plasma cell-like lymphocytes. The percentage and morphology of monocytes were normal. Conclusion: there were 57% plasma cells in the biopsy area, among which 40% were abnormal.

Peripheral blood was sent for immunophenotyping by flow cytometric analysis (Figure 2). Some 10,000 cells were counted in CD45/side scatter (SSC) gating. The percentages of lymphocytes, blast cells, abnormal cells, myeloid cells, and nucleated red blood cells, and the total nucleated cell population were 13%, 0.5%, 48%, 36.5%, and 2% respectively.

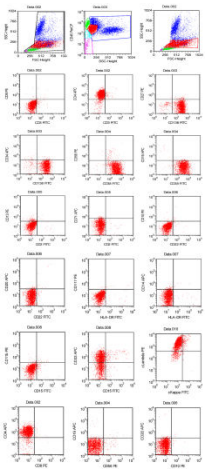

Figure 2: Peripheral blood was sent for immunophenotyping by flow cytometric analysis.

On the CD45/SSC histogram, an abnormal cell population with lower CD45 expression and larger size than that of the lymphocytes was observed. The percentage of this abnormal cell population within the total number of nucleated cells was 48%; the abnormal cells expressed CD4, CD33, C38, CD138, and cLambda, suggesting that these cells were abnormally proliferating plasma cells. Suggestions:

abnormal proliferative plasma cell disorders. The clinical presentation and other laboratory investigations to be considered for diagnosis include antigens examined: HLA-DR, CD2, CD3, CD4, CD8, CD10, CD11b, CD13, CD14, CD15, CD19, CD20, CD22, CD27, CD33, CD34, CD38, CD56, CD71, CD117, CD138, cKappa, cLambda, and CD45.

Protein electrophoresis and immunofixation testing of a serum sample revealed the presence of a monoclonal protein in the M protein peak, which formed specific immunoprecipitation with antibody against lambda light chains (L) but not with those against IgD or IgE (Figure 3A). Protein electrophoresis of a urine sample revealed an M protein peak, which formed specific immunoprecipitation with antibody against L and Lf (Figure 3B). Bence-Jones protein (BJP) analysis was positive, kappa light chain (KAP) was at 0.03 g/L and lambda light chain (LAM) at 0.65 g/L. The result pointed to M-type hypergammaglobulinemia.

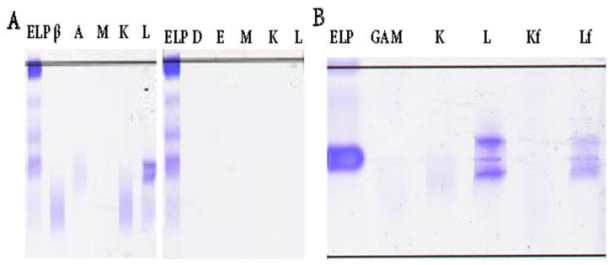

Figure 3: Protein electrophoresis and immunofixation testing of a serum (A) and urine sample (B).

The diagnosis of coronary heart disease with class IV heart failure was initially considered when the patient was admitted. After he was treated with diuretics, medications to improve cardiac output, and coronary artery dilators, the symptoms persisted. Comprehensive laboratory tests-including bone marrow biopsy, whole blood flow cytometry analysis, protein electrophoresis and immunofixation testing of serum samples-were conducted. Based on the test results and the fact that the patient had no previous multiple myeloma, proliferative plasma cells disorders, or other lymphoproliferative disorders, the diagnosis of primary PCL was made. The patient was then treated with bortezomib, but the treatment response was poor. What a pity, in this case report, the patient's symptoms deteriorated rapidly and proceeded to multi-organ failure. The patients and his family declined to further treatment. There had been only 80 days between the onset of the disease and the patient's death.

Discussion

PCL is a rare lymphoproliferative disorder involving plasma cells. It is highly aggressive associated with a poor prognosis (some patients have died within a month after diagnosis) and refractory to chemotherapy. The incidence of PCL ranges between 1.3% and 3.4% in patients with plasma cell neoplasms and 2% and 4% in patients with multiple myeloma (MM) [5]. New cases reported each year range from 0.5 to 1.5 per 100,000 [6]. The median age of onset ranges from 50 and 60 years. No significant gender difference is observed for PCL. The original diagnostic criteria of PCL were established by Kyle et al., requiring an absolute plasma cell count greater than 2 × 109/L or peripheral blood containing more than 20% plasma cells [7]. The presentation of PCL is primary and does not evolve from an existing case of MM as part of the terminal phase of the disease.

The clinical presentation of PCL features extensive abnormal plasma cells in the peripheral blood and a higher prevalence of organomegaly, with involvement of multiple tissues and organs. The significant and continuous increase of plasma cell count in peripheral blood is one of the most critical diagnosis criteria for PCL; it is also a main laboratory feature that differentiates PCL from MM. The presentation of PCL may be primary or secondary. Secondary PCL (SPCL) most often evolves from an existing case of MM as part of the terminal phase of the disease, but it may also evolve from macroglobulinemia, lymphoma, or chronic lymphocytic leukemia. SPCL is more common in clinical practice than primary PCL (PPCL). The age at which patients are diagnosed with PCL ranges from 45 to 48 years; that is, they are younger than the age observed in the general MM, and about 20% to 35% patients with PCL are under age 40. The clinical presentations of PCL include weight loss, fatigue, bleeding, bone pain, lower back pain, and so on. The involvement of extramedullary organs-such as liver, spleen, and lymph nodes-is more common in patients with primary PCL than that in those with SPCL and MM; however, the incidence of lytic bone lesions is slightly lower than that usually observed in SPCL and MM [8]. In this case report, the patient was 45 years old; he first presented with heart failure and no complaints of bone pain. The age of patient, his clinical presentation, and his laboratory investigations all supported the diagnosis of primary PCL.

Because of the relatively low incidence of primary PCL, the current clinical management of PPCL is unsatisfactory. Challenges include issues of the proper chemotherapy regimen, selection of the appropriate chemotherapeutic agents, optimal timing for bone marrow transplantation, whether or not to use bortezomib to stabilize disease after transplantation, as well as the treatment and prevention of remission. These issues need to be addressed through multicenter and multiaspects collaboration.

Disclosures

The authors have no conflicts of interest to disclose.

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