

CASE REPORT

PLASMA CELL LEUKAEMIA: A RARE YET AGGRESSIVE PLASMA CELL DYSCRASIA WITH A VERY POOR RESPONSE TO CONVENTIONAL THERAPY

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Plasma cell leukaemia (PCL) is a very rare plasma cell dyscrasia with a significant number of monoclonal plasma cells in the peripheral blood. It is diagnosed by the presence of $\geq 2 \times 10^9$ /L plasma cells in the blood or by plasma cells making up $\geq 20\%$ of the leukocyte count. It can arise from a leukemic transformation of multiple myeloma, or more commonly it can be primary. Regardless of its origin, it carries a very dire prognosis. It responds very poorly to the traditional chemotherapy regimens used for multiple myeloma. We present the case of a 50 years old female who presented to our hospital with a complicated UTI and severe generalized body aches. She was diagnosed as a case of plasma cell leukaemia and was treated with cyclophosphamide and dexamethasone, however she failed to go into remission. Her condition deteriorated and she ultimately passed away 1.5 months after diagnosis. The recommended treatment for PCL is aggressive combination chemotherapy followed by stem cell transplantation. However, there is no consensus regarding the treatment of plasma cell leukaemia, and treatment should be individualized based on the patient profile. Once diagnosed, the prognosis is poor.

Keywords: Plasma Cell Leukaemia; Multiple Myeloma; Plasma Cell Dyscrasia; Bortezomib

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INTRODUCTION

Plasma cell leukaemia is a very rare lymphoproliferative disorder that represents only a small proportion of the plasma cell dyscrasia. It was initially described by Gluzinski and Reichenstein in 1906.¹ PCL is a rare type of plasma cell dyscrasia. It is characterized by a large number of plasma cells in varying stages of maturation in the peripheral blood. It can be diagnosed if the plasma cells exceed 2×10^9 cells/L in the blood or if the plasma cells make up more than 20% of the TLC.² It can either be primary PCL which arises de novo or it can be secondary PCL which arises secondary to multiple myeloma. It is estimated that approximately 1–4% cases of multiple myeloma progress to PCL. Primary PCL is more common (60–70%) occurs at a younger age (55 years vs 66 years) and has a more aggressive presentation.^{3,4}

It is thought to account for 2–4% of the plasma cell dyscrasia. Its estimated incidence in Europe is 4 cases per 10,000,000 population.⁵ Its worldwide incidence is not known because of a paucity of cases and a very short post diagnosis survival. The mean survival varies from 2–11 months without and 12–18 months with combination chemotherapy. PCL like other plasma cell dyscrasia occurs mostly in the elderly population, though

primary PCL has a relatively younger onset. PCL has been described in all races and geographic locations. Multiple genetic aberrations have been described with PCL, but none of them is specific for PCL. These include deletion of chromosome 13, t(4;14), t(14;16) and del 17q13 with abnormalities of chromosome 13 the most common defect. PCL presents similarly to multiple myeloma and other leukaemia, though the frequency of specific signs and symptoms vary.⁶ The most common clinical features are reported to be anaemia, thrombocytopenia, raised WBC count, lytic lesions, hepatosplenomegaly and extramedullary plasmacytoma.^{7,8}

CASE REPORT

A 50 years old female presented to the out-patient department with a 2-week history of high-grade fever that was of acute onset, continuous with no rigors and chills. It was relieved temporarily by medications. The fever was associated with dysuria and frequency. The patient also had severe body aches that were insidious in onset over the last 2 months, and were more pronounced in the lower back and lower limbs.

Patient had no past medical history of any known illness. No previous hospital admissions. No known family history of any illness. Patient had no known allergies and was not on any regular medications. She completed a course antibiotic for UTI

two weeks before admission with minimal improvement. Patient is non-smoker and was postmenopausal. Up until this illness, she was independent and self-caring and currently has reduced appetite and sleep.

On general physical examination, patient appears pale, emaciated and dehydrated. Her BP was 110/70 mm Hg, Pulse was 78 bpm, temperature is 100 F and respiratory rate was 16 per minute. There was no lymphadenopathy or jaundice. Abdominal examination revealed splenomegaly of 3 cm below the left costal margin with abdomen soft and nontender. Musculoskeletal exam showed a moderately tender lower lumbar spine. Cardiovascular, respiratory and neurological examinations were unremarkable.

Her full blood count showed haemoglobin of 7.3 gm/dl, white cell count of 96,000/ccm with 68% lymphocytes & a platelet count of 52,000/ccm. The ESR was 90 mm/1st hour. The urinalysis showed 10–15 WBCs, 10–12 RBCs, 1+ albumin but no casts. The serum urea was 97 mg/dl and creatinine was 4.37 mg/dl. Serum calcium was 14.3 mg/dl. A gamma globulin Spike was seen on serum electrophoresis. The LFTs and Serum electrolytes were normal. Abdominal ultrasound showed an enlarged spleen measuring 13.5 cm along with bilaterally increased echogenicity (grade II) of the renal pyramids. Her urine culture and sensitivity showed a growth of *E. coli* sensitive to a wide range of antibiotics. A pelvic and lumbar spine x-ray showed no apparent abnormality. A skull x-ray showed no lytic lesions.

A peripheral smear showed 60% plasma cells with RBCs in a rouleaux formation. Bone marrow biopsy showed suppressed erythropoiesis, myelopoiesis, and megakaryopoiesis with diffuse infiltrates of sheets of plasma cells. (Figure-1 & 2). Hyperplastic with almost 80% cells of the marrow plasma cells with cytological atypia on bone marrow aspirate.

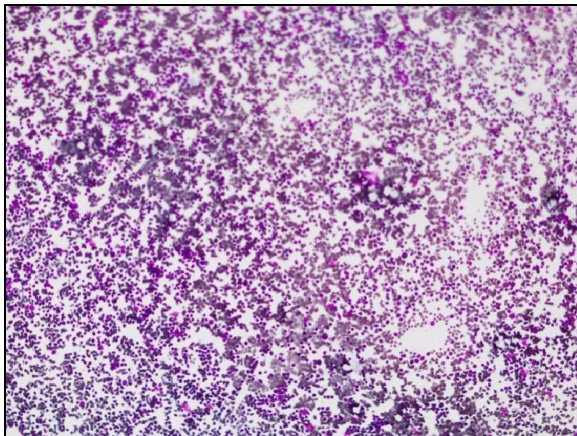


Figure-1: Sheet of plasma cells on bone marrow biopsy (4X Magnification)

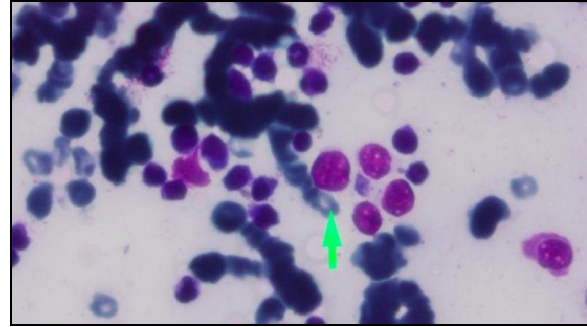


Figure-2: Increased plasma cells with cytologic atypia on bone marrow aspirate (100X Magnification)

The patient was initially treated for her infection and hypercalcemia. She was started on intravenous cefoperazone + sulbactam, and normal saline. She was given tramadol for pain relief. Her fever and dysuria improved, however she still complained of generalized body aches. She was then referred to an associated oncology unit where she was started on cyclophosphamide, dexamethasone and rasburicase as bortezomib was not available. The patient was not fit for bone marrow transplantation. The patient continued taking cyclophosphamide on an outpatient basis. The patient was initially suspected to be a case of multiple myeloma. After her initial full blood count showed a TLC of 92000/ccm with mostly lymphocytes, she was suspected to be suffering from chronic lymphocytic leukaemia or other lymphoproliferative disorder like hairy cell leukaemia. However, a peripheral smear and bone marrow biopsy confirmed the diagnosis.

The patient was followed up after one month but there was no significant subjective or objective improvement in her condition. Her CBC and renal function tests showed no significant improvement. Within two months of her initial diagnosis the patient again presented with high grade fever, respiratory distress and impaired consciousness. On examination, she was severely pale, with a fever of 102° F, a pulse of 112 bpm and BP of 90/70 mmHg. Her GCS was 5/15. She had bilateral coarse crepitation throughout her lung fields with decreased air entry and dullness on percussion in her lower lung fields. She still had a prominent splenomegaly. Her labs showed an Hb of 4.8gm/dl, TLC of 190,000/ccm with >90% lymphocytes (plasma cells), and platelets were 15,000/ccm. Her creatinine was 10.86 mg/dl; urea was 251 mg/dl. Her serum electrolytes were Na 140.4 mmol/L, K was 5.42 mmol/L and Cl was 106.3 mmol/L. Her prothrombin time was deranged by 6 seconds however her APTT was normal. The patient was treated as a case sepsis, with associated acute kidney injury. The patient was transfused 4 pints of 450 ml of packed cells and 4 pints of platelets in

addition to treatment for sepsis, likely source chest infection, with intravenous cefepime and dopamine support. She also underwent haemodialysis twice. However, on the 3rd day of her readmission, patient deteriorated quickly and started spiking fever again and GCS dropped to 3/15. Patient did not improve with treatment and died on this admission.

DISCUSSION

The diagnosis of PCL can be made on a peripheral smear. It will show an increased number of plasma cells with their morphologic features depending on the level of maturity. Immature cells are very similar to myeloblasts, while mature cells have abundant basophilic cytoplasm, an eccentrically placed nucleus with clock-face chromatin and a perinuclear clearing. Bone marrow aspiration will show an increased number of plasma cells (more than 20% is diagnostic). Serum protein electrophoresis will show a gamma spike and immunofixation will reveal the type of immunoglobulin secreted. A small number of cases can be non-secretors. Urine protein electrophoresis can be used to confirm the diagnosis. Immunohistochemistry usually shows elevated levels of CD138 and CD38, and low levels of CD19, CD20 and CD56. CD56 levels are especially useful in differentiating it from multiple myeloma in ambiguous cases as CD56 levels are elevated in Multiple Myeloma.^{9,10}

Plasma cell leukaemia responds very poorly to the conventional therapies used for multiple myeloma. The response rates for chemotherapy involving alkylating agents and/or vincristine, doxorubicin and carmustine range from 23–67%, however the median survival is still less than 1 year.⁸ There have been no clinical trials and treatment recommendations are based on retrospective studies of responses of individual cases and case series. Aggressive combination therapy is known to increase survival.

Younger and healthier patients are treated with aggressive induction therapy with combination chemotherapy including newer agents like bortezomib and lenalidomide. This is followed by autologous stem cell transplantation in eligible patients. The proteasome inhibitor bortezomib is associated with greater response rates and bortezomib based induction regimens are now recommended. Bortezomib based therapy was associated with a median survival period of 13 months vs a survival of only 2 months¹¹, with response rates of up to 92%¹². Lenalidomide can then be used for maintenance therapy. Our patient was given cyclophosphamide as the newer agents were not available and could not be arranged on a short notice. Our patient failed to go into remission.

Induction therapy is followed by hematopoietic cell transplantation (HCT) if there are no contraindications. Old age (age >70), end organ damage (conjugated bilirubin >2.0 mg/dl, serum creatinine >2.5 mg/dl, NYHA class III or IV failure) or severe bone pains are all contraindications for HCT in multiple myeloma and PCL. Induction therapy followed by HCT has a much better survival of 38 months vs 11 months for chemotherapy alone, however only younger and fitter patients are chosen for HCT. Similar results were reported by many other case series.^{7,8} Autologous HCT has a better outcome than allogeneic HCT with improved progression free survival and improved overall survival.¹³ Lenalidomide can then be used in all patients for maintenance therapy until disease progression or till the patient becomes intolerant to it.⁸ PCL carries a very poor prognosis with a mean survival ranging from 2–11 months without treatment, 12–18 months with aggressive chemotherapy and up to 38 months with HCT following aggressive chemotherapy.⁷ A case reported in Pakistan was treated on a regimen of treatment for hypercalcaemia with Melphalan/Prednisolone regime along with supportive care.¹⁴

Plasma cell dyscrasia can present with recurrent infections even though bone pain, anaemia or renal insufficiency are more classically associated with it. Any old patient with unprovoked severe bone pain must be investigated thoroughly for any underlying primary malignancy or metastasis. Plasma cell leukaemia has a very poor response to the traditional chemotherapy that is used for multiple myeloma, however newer agents including bortezomib and lenalidomide have proven to be more effective. Combination chemotherapy followed by autologous stem cell transplantation has been shown to improve survival significantly. There is no consensus regarding the treatment of plasma cell leukaemia, and treatment should be individualized based on the patient profile.

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