

## Case Report

### PLASMA CELL LEUKEMIA (PCL), A RARE AND AGGRESSIVE VARIANT OF MULTIPLE MYELOMA (MM)

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#### Abstract

Plasma cells can rarely be seen in the peripheral blood of the patients previously diagnosed with multiple myeloma or more often observed at the time of diagnosis of Multiple Myeloma. When the number of these circulating cells is more than 2000/uL or more than 20% of circulating Leukocytes, the term of Plasma Cell Leukemia (PCL) is used. To the best of our knowledge, we are reporting the second ever case of plasma cell leukemia from Pakistan in the light of review of the literature.

**Key words: Plasma cell leukemia, multiple myeloma, leukocytes**

#### Introduction

Plasma cell leukemia (PCL) is a rare but aggressive form of lymphoproliferative disorder which is distinguished from multiple myeloma (MM) by the presence of more than  $2 \times 10^9/L$  plasma cells in the peripheral blood, constituting at least 20% of the leukocytes<sup>1, 2</sup>. The incidence of PCL ranges between 2-4% of all myelomas<sup>3, 4</sup>. This rare variant of multiple myeloma (MM) is called Primary when it presents *de novo* in patients with no preceding MM or secondary in patients with established MM after leukemic transformation<sup>5</sup>. Although PCL and MM are closely related disease entities, the prognosis of PCL patients treated with standard chemotherapy has consistently

been shown to be inferior to that of MM patients<sup>6</sup>. The response to therapy in primary PCL is in the range of 37% to 47% in reported series with a median survival of 7-12 months while patients with secondary PCL are usually refractory to chemotherapy and have a median survival of less than 2 months<sup>7</sup>. Due to the rarity of PCL, there has been a paucity of studies evaluating optimal treatment strategies.

#### Case Report

A 55 years old previously well farming man presented to the Medical OPD of Khyber Teaching Hospital Peshawar with two weeks history of high grade fever, irritability, weakness and weight loss. He had generalized body aches and pains and was

oliguric over the preceding four days. On physical examination he was grossly pale and acidotic with a conscious level of 13/15 on Glasgow Coma Scale (GCS). Systemic examination revealed hepatomegally and a full blood count showed Hb: 9.2 g/dL, WBC count  $10 \times 10^9/L$  including 25% plasma cells which showed plasmablastic features with prominent nucleoli and basophilic cytoplasm, and platelets of  $87 \times 10^9/L$ . Other abnormal laboratory studies were: Serum creatinine 4 mg/dL, serum calcium 12.5 mg/dL, LDH: 2470 IU/L, a high sedimentation rate of 120 mm/h. Skeletal survey showed two lytic lesions in the skull while bone marrow examination revealed MM with immature plasma cells of 40%. Coagulation parameters indicated a probable ongoing disseminated intravascular coagulation (DIC) with Prothrombin time (PT): 17 seconds, activated partial thromboplastin time (aPTT): 53 seconds and FDPs and D-Dimers were positive. Serum protein electrophoresis and immunofixation showed a monoclonal component of IgG type (IgG: 7170 mg/dl. Immunophenotyping of peripheral blood cells with flow-cytometer disclosed 80% CD38- and CD138- positive plasma cells and the cells were negative for CD45, CD19 and CD56. The patient was given supportive treatment in the first instance including I/V antibiotics, fluids, blood products and haemodialysis. The patient was counseled for the option of Autologous Stem Cell Transplantation (ASCT) but the patient refused due to affordability issues. The patient was thus treated as non-transplant candidate and was discharged on Melphalan and Prednisolone. The patient was reviewed in 4 weeks time and had subjective and objective evidence of partial improvement. On follow up his lab parameters were as follows; Hb 10.5gm/dl, TLC  $11000/mm^3$ , Platelets  $100,000/mm^3$ . He still had 22% of plasma cells in peripheral circulation and had IgG

hypergammaglobulinemia while his renal functions had reverted back to normal. The patient was asked for monthly follow-ups for the first six months but we unfortunately lost contact with him after his first follow up visit.

### Discussion

Although PCL is a rare entity representing only 0.3% of acute leukemia cases, it is an aggressive disease with a median overall survival of less than one year with conventional chemotherapy alone. From 1960 till 2008 only 90 seen at The Mayo Clinic patients fulfilled the criteria for plasma cell leukemia<sup>8</sup>. Several genomic aberrations and immunohistochemical markers including t(11;14), cyclin D1 and deletion of p17 have been identified as prognostic indicators for MM<sup>9</sup>. In a study of 11 plasma cell leukemia patients, all showed clonal chromosomal abnormalities<sup>10</sup>. We did not do cytogenetic analysis of our patient due to lack of the facility in our setup.

From our case report it can be noticed that our patient was suffering from a Primary PCL. Primary PCL has a more aggressive clinical course than MM, with a higher frequency of extramedullary involvement (liver, spleen, lymph nodes, extraosseous plasmacytomas), anemia, thrombocytopenia, hypercalcemia and renal insufficiency<sup>11</sup>. Our patient did have hepatomegally, hypercalcemia, anemia and acute renal failure.

Our patient had two lytic lesions in the skull though in primary PCL the presence of lytic bone lesions seems to be lower than those usually observed in MM. Our patient also had findings of DIC at their presentation and despite administration of chemotherapy and fresh frozen plasma, coagulation abnormalities did not improve. In MM prolongation of thrombin time has been reported to be due to antibodies to thrombin

and impaired fibrin polymerization by paraproteins<sup>12,13</sup>.

Our patient stained positive for both CD 38 and CD 138. The malignant cells in PCL express CD38 and CD138 however unlike malignant cells in MM, they usually do not express CD56 which is a very good differentiating point on immunohistochemistry<sup>14</sup>.

The patient's response to the therapy in PCL is extremely poor. There is no confusion in that combination of Alkylating agent like Melphalan and Prednisolone (MP) is not appropriate choice for PCL patients and novel agents needs to added to the regimen followed by autologous stem cell transplantation (ASCT) in eligible patient, we had to put our patient on MP regimen only as our patient was neither willing for

ASCT not could afford the costs of the novel agents. Intensive chemotherapy with Bortezomib-based combinations can treat not only MM but also PCL. Although the data are still limited, the use of bortezomib likely improves disease outcome and this drug will likely become the backbone in the treatment of PCL<sup>15</sup>.

#### **Conclusion**

PCL is an aggressive and extremely rare variant of multiple myeloma with dismal outcome. Large trials examining the efficacy of various therapeutics regimens are lacking but novel agents-based combination therapies( Bortezomib, lenalidomide, thalidomide) with ASCT in transplant eligible patients is the current treatment modality of choice.

Fig 01: The magnified microscopic view of the plasma cells in the peripheral blood of our patient (taken with permission of our patient).

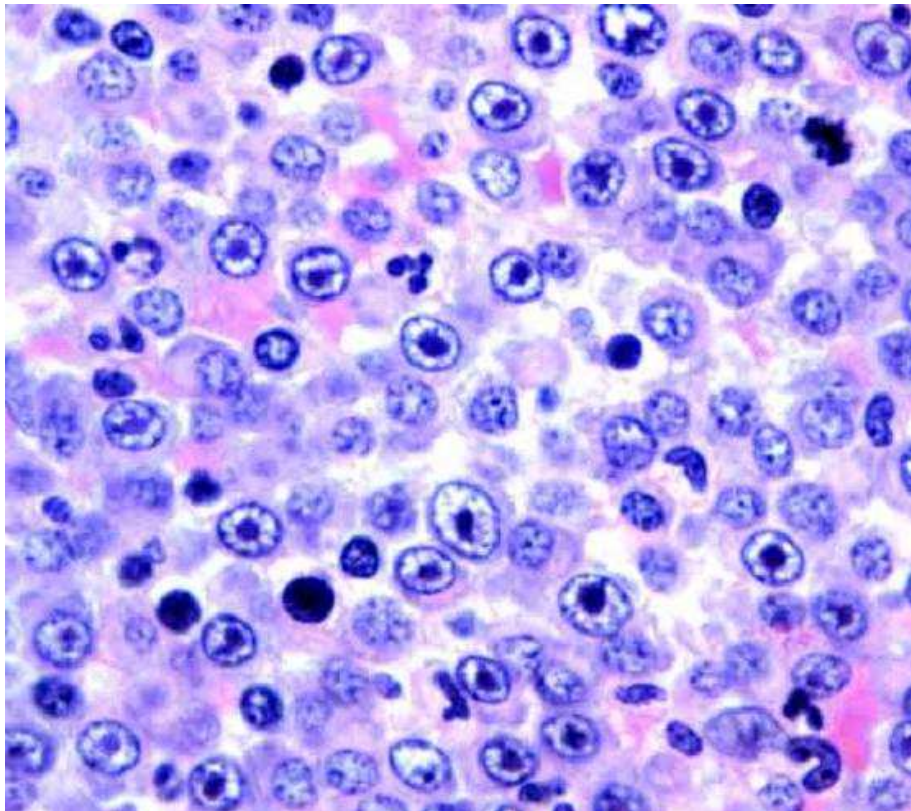
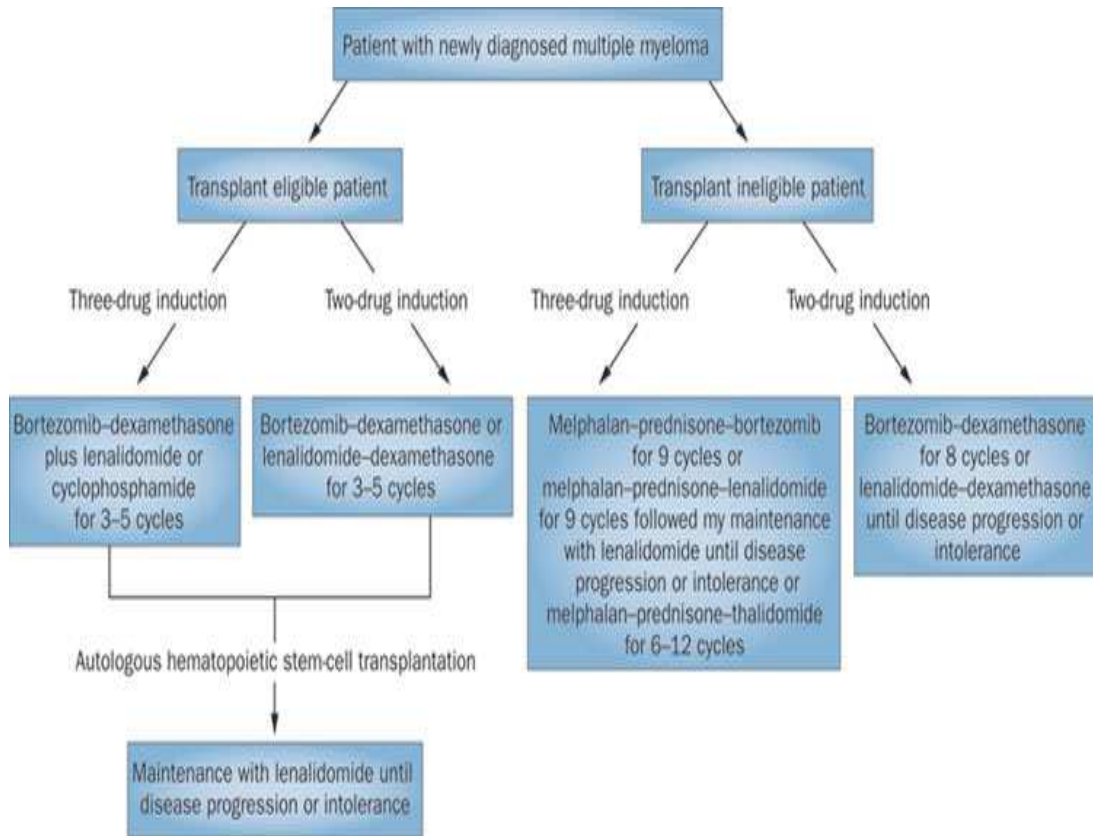


Fig 02: Treatment algorithm for PCL (taken with permission from International Myeloma Foundation and International Myeloma Working Group)



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