ORIGINAL RESEARCH PAPER
Volume - 10 | Issue - 09 | September - 2021 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

PLASMA CELL LEUKEMIA: A CASE REPORT FROM A TERTIARY CARE CENTRE OF NORTH EAST INDIA WITH REVIEW OF LITERATURE

Pathology

Jina Bhattacharyya Professor and Head of the Department of Haematology, Gauhati Medical College and Hospital, Guwahati, Assam, India.

Asreen Suhana* Post graduate trainee, Department of Pathology, Gauhati Medical College and Hospital, Guwahati, Assam, India. *Corresponding Author

ABSTRACT

Plasma Cell Leukemia is a rare and aggressive haematogical malignancy with poor prognosis when treated with conventional therapy for Multiple Myeloma. Here we report a case of PCL in a 45 years old male with no significant past history or comorbidities, presenting with fever, weakness, vomiting, passage of tarry black stools and loss of appetite for 2 months, who later developed difficulty in breathing and chest pain. Initial investigations revealed anemia, thrombocytopenia and leukocytosis with 68% plasma cells in the peripheral blood. After all the necessary investigations and no previous history in support of Multiple Myeloma, he was diagnosed as a case of Primary Secretory PCL. He has received one cycle of Bortezomib, Cyclophosphamide and Dexamethasone. He is clinically better with reduction in the total leucocyte count and is being planned for the next cycle of treatment. With the advent of newer and aggressive targeted therapies, the survival and prognosis of PCL will hopefully improve in the near future.

KEYWORDS

Plasma Cell Leukemia, plasmablast, Kyle criteria

INTRODUCTION

Plasma cell leukemia is rare and aggressive form of plasma cell dyscrasias with a median survival of maximum 12 months following diagnosis. Plasma cell leukemia is diagnosed based on Kyle's criteria of more than 20% circulating plasma cells or absolute count of plasma cells in peripheral blood more than $2x10^9/L$.[1,2] It represents mere 2-4% of plasma cell dyscrasias.[3] It is subdivided into primary PCL, arising de novo and secondary PCL, arising from known MM cases following relapse or in refractory cases.[4,5] Primary PCL accounts for 60-70% of the cases and presenting earlier(median age 52-65 years) than secondary PCL(median age 65-70 years).[6,7] Both the subtypes have poor prognosis, secondary PCL being worse than primary PCL.[6,7,8] The median survival ranges 6.8-12.6 months, which has increased following autologous stem cell transplant to more than three years.[2,9]

CASE REPORT

A 45 years old male presented with fever, vomiting, tarry black stools, loss of appetite, generalized weakness for 2 months. He went to the nearest health centre where his hemoglobin level was found to be low. He was transfused five units of blood and given symptomatic treatment, but his condition did not improve. He was then referred to a tertiary care centre in Guwahati. He was brought to Gauhati Medical College and Hospital, Guwahati. At presentation, pallor was present, blood pressure was 110/70 mm Hg, pulse rate was 92 beats per minute. On systemic examination, liver and spleen were palpable 2.5 cms below the costal margin, there was dullness on percussion and decreased breath sounds on both sides of his chest. Central nervous system and cardiovascular system were within normal limits. Following admission, he developed orthopnoea and chest pain.

A complete blood count revealed hemoglobin level of 5.6 gm/dl (severe anemia), total leucocyte count of 33,500(leukocytosis) and platelet count of 10,000(marked thrombocytopenia). Peripheral blood smear examination revealed leukocytosis with the presence of 68% plasma cells, predominantly normocytic normochromic RBCs and reduced number of platelets. (Figure 1,2) On biochemical assessment, serum creatinine was 3.13 mg/dl (↑), serum uric acid was 14.38 mg/dl (↑), serum calcium 9.7 mg/dl.

Serum protein electrophoresis revealed irregularities in beta-2 region. (Figure 3) Serum free light chain ratio(kappa/lambda) was 634.27(kappa ↑).

Immunophenotyping from peripheral blood revealed 79.7% CD45 negative population, positive for CD 38, CD 138 and negative for B and T markers confirming presence of plasma cells in the peripheral blood. Bone marrow aspiration revealed 90% of atypical mononuclear cells, morphologically suggestive of lymphoplasmacytoid cell. Bone marrow biopsy on morphology suggested bone marrow infiltration by low grade non-Hodgkin lymphoma. Immunohistochemistry done on bone marrow biopsy revealed tumor cells immunoreactive for CD 138(Figure 4) and CD 99, focal MUM1, negative for CD45, CD3,CD20, TDT, CK, Synaptophysin and INSM-1. Kappa/Lambda > 10:1(Kappa light chain restriction)(Figure 5).

Skeletal survey was normal.

Ultrasonography of abdomen revealed hepatomegaly(16.5cm) and splenomegaly(13.46 cm) with normal echotexture alongwith bilateral pleural effusion. HRCT thorax was done which revealed bilateral moderate to gross pleural effusion with underlying subsegmental collapse and consolidation.

Upper GI endoscopy revealed multiple erosions in body, fundus and antrum of stomach with a healed ulcer in the D1 region, that probably led to tarry black stools. Colonoscopy was normal.

A final diagnosis of Primary plasma cell leukemia was made. Treatment was started with bortezomib-based three drug induction regimen. The patient has clinically improved. His total count has come down to 8,000/uL, platelet count is 40,000/uL, hemoglobin level is 7.6gm/dl and there is reduction in the number of plasma cells in peripheral blood. He is now planned for the second cycle of treatment with addition of Cisplatin based regimen. He has three siblings and HLA has also been planned.

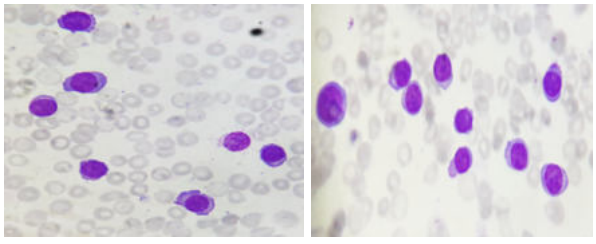

Figure 1: Plasma cells and occasional plasmablasts seen in the peripheral blood smear (40x objective)

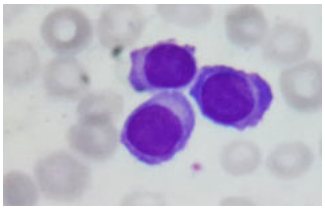

Figure 2: Circulating plasma cells showing perinuclear hof (100x objective)

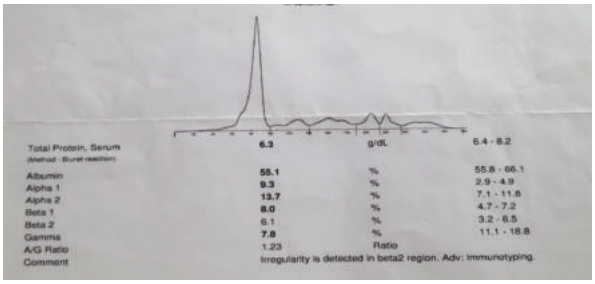

Figure 3: SPEP showing irregularities in beta-2 region

Figure 4: CD138 immunoreactivity on bone marrow biopsy

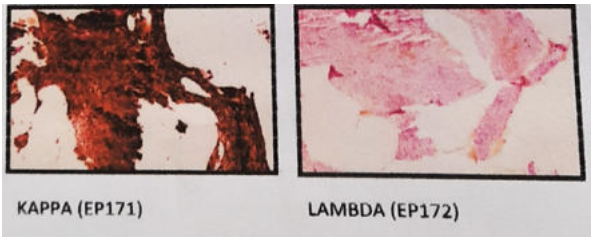

Figure 5: Kappa light chain restriction on IHC

DISCUSSION

As of now, both WHO and IMWG suggest the presence of any one of the two Kyle's criteria as sufficient for PCL diagnosis.[5,2] But this criteria does not take clonality of plasma cells into consideration[1], which at times, creates a problem in cases of reactive plasmacytosis like infectious mononucleosis, severe infections and serum sickness.[10,11] Also various studies are being done to find the prognostic threshold of circulating plasma cells. Granell et al. from their study in 2017 suggested 5% as cutoff for PCL diagnosis.[12] Another study using flow cytometry by Mayo Clinic in 2014 suggested that 0.26% plasma cells in circulation were related to reduced survival.[13]

Bone marrow microenvironment is very crucial for the survival and proliferation of myeloma cells.[14] In PCL, there is loss of CD56,a neuronal cell adhesion molecule that anchors myeloma cells to bone marrow stroma leading to their free peripheral circulation.[15] IL-6 also plays some role in myeloma cell proliferation and survival.[16]

Various genetic aberrations have been studied till date, hypodiploidy[17], IgH translocations in chromosome 14q32, MYC abnormalities, amplification of 1q21, Ras mutations[18],t(11;14) and Tp53 inactivation[6] are important and also help to differentiate PCL from MM .

Clinical presentation in PCL is earlier than in MM, with extensive infiltration of bone marrow and extramedullary sites, body cavities, CSF and less frequent lytic bone lesions and bone pain than MM.[5] Our patient is much younger, had involvement of bone marrow, liver, spleen and pleural cavity. The diagnosis of the patient was based on presentating complaints, examination, SPEP, original Kyle's criteria application on CBC and PBS examination aided by immunophenotyping, bone marrow aspiration, bone marrow biopsy including immunohistochemistry.

Treatment shows good response with proteasome inhibitor like bortezomib in both types of PCL.[19]In younger patients(<65 years) with good performance status, aggressive induction with VTD-PACE is advised.[20]Autologous stem cell transplant has shown that the patients go into complete remission and survival increases to 25.7 months (95% CI).[21] Bcl-2 inhibitor Venetoclax can be used in refractory cases with t(11;14).[22] Next generation Pis(carfilzomib, ixazomib), IMiDs (pomalidomide) and CD38 directed mAb(daratumab, isatuximab) have shown success in recent studies. Our patient is started on bortezomib based three drug induction regimen and he is clinically better.

Following treatment, International Myeloma Working Group suggested PCL remission based on (1) plasma cell count in peripheral blood (2) plasma cell count in the bone marrow (3) serum and urinary M-protein levels (4) assessment of extramedullary disease.[2]Complete remission is total absence of plasma cells from peripheral blood and relapse is the presence of >10% plasma cells in bone marrow.

CONCLUSION

Even though the first PCL case being reported in 1974, due to less number of reported cases, diagnosis, treatment and prognosis of PCL still remains a big challenge. Hopefully with more studies on the pathogenesis, prompt diagnosis and advent of newer modalities of treatment, the adverse outcome of PCL cases can be tackled well in the near future.

Conflicts of interest: None.

Financial support and sponsorship: Nil.

REFERENCES

1. Kyle RA, Maldonado JE, Bayrd ED. Plasma cell leukemia. Report on 17 cases. Arch Intern Med. 1974;133:813–818. [PubMed] [Google Scholar]
2. Fernández de Larrea C, Kyle RA, Durie BG, Ludwig H, Usmani S, Vesole DH, et al. Plasma cell leukemia: Consensus statement on diagnostic requirements, response criteria and treatment recommendations by the International Myeloma Working Group. Leukemia. 2013;27:780–91. doi: 10.1038/leu.2012.336. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
3. Dimopoulos MA, Palumbo A, Delasalle KB, Alexanian R. Primary plasma cell leukaemia. Br J Haematol. 1994;88:754–759. [PubMed] [Google Scholar]
4. Noel P, Kyle RA. Plasma cell leukemia: An evaluation of response to therapy. Am J Med. 1987;83:1062–8. doi: 10.1016/0002-9343(87)90942-9. [PubMed] [CrossRef] [Google Scholar]
5. Swerdlow SH, Campo E, Harris NL, Jaffe ES, Pileri SA, Stein H, et al., editors. WHO classification of tumours of haematopoietic and lymphoid tissues. 4th ed. [Accessed: Apr 2018]. From: http://publications.iarc.fr/Book-And-Report-Series/Who-Iarc-Classification-Of-Tumours/Who-Classification-Of-Tumours-Of-Haematopoietic-And-Lymphoid-Tissues-2017.
6. Tiedemann RE, Gonzalez-Paz N, Kyle RA, Santana-Davila R, Price-Troska T, Van Wier SA, et al. Genetic aberrations and survival in plasma cell leukemia. Leukemia. 2008;22:1044–52. doi: 10.1038/leu.2008.4. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
7. Bladé J, Kyle RA. Nonsecretory myeloma, immunoglobulin D myeloma, and plasma cell leukemia. Hematol Oncol Clin North Am. 1999;13:1259–72. doi: 10.1016/S0889-8588(05)70125-8. [PubMed] [CrossRef] [Google Scholar]
8. Katodritou E, Terpos E, Kelaidi C, Kotsopoulou M, Delimpasi S, Kyrtsonis MC, Symeonidis A, Giannakoulas N, Stefanoudaki A, Christoulas D, Chatziaggelidou C, Gastari V, Spyridis N, Verrou E, Konstantinidou P, Zervas K, Dimopoulos MA. Treatment with bortezomib-based regimens improves overall response and predicts for survival in patients with primary or secondary plasma cell leukemia: Analysis of the Greek myeloma study group. Am J Hematol. 2014 Feb;89(2):145-50. doi: 10.1002/ajh.23600. Epub 2013 Nov 21. PMID: 24123068.
9. Jelinek T, Kryukov F, Rihova L, Hajek R. Plasma cell leukemia: From biology to treatment. Eur J Haematol. 2015;95:16–26. doi: 10.1111/ejh.12533. [PubMed] [CrossRef] [Google Scholar]
10. Shtalrid M, Shvidel L, Vorst E. Polyclonal reactive peripheral blood plasmacytosis mimicking plasma cell leukemia in a patient with Staphylococcal sepsis. Leuk Lymphoma. 2003;44:379–80. doi: 10.1080/1042819021000029713. [PubMed] [CrossRef] [Google Scholar]
11. Touzeau C, Pellat-Deceunynck C, Gastinne T, Accard F, Jego G, Avet-Loiseau H, Robillard N, Harousseau JL, Bataille R, Moreau P. Reactive plasmacytoses can mimick plasma cell leukemia: therapeutical implications. Leuk Lymphoma. 2007 Jan;48(1):207-8. doi: 10.1080/10428190601016159. PMID: 17325872.
12. Granell M, Calvo X, Garcia-Guiñón A, et al. Prognostic impact of circulating plasma cells in patients with multiple myeloma: implications for plasma cell leukemia definition. Haematologica. 2017;102(6):1099-1104. [PMC free article] [PubMed] [Google Scholar]
13. Gonsalves WI, Rajkumar SV, Go RS, et al. Trends in survival of patients with primary plasma cell leukemia: a population-based analysis. Blood. 2014;124:907-912. [PMC free article] [PubMed] [Google Scholar]
14. Mitsiades CS, McMillin DW, Klippel S, Hideshima T, Chauhan D, Richardson PG, et al. The role of the bone marrow micro-environment in the pathophysiology of myeloma and its significance in the development of more effective therapies. Hematol Oncol Clin North Am. 2007;21:1007–34. doi: 10.1016/j.hoc.2007.08.007. [PubMed] [CrossRef] [Google Scholar]
15. Pellat-Deceunynck C, Barillé S, Jego G, Puthier D, Robillard N, Pineau D, et al. The absence of CD56 (NCAM) on malignant plasma cells is a hallmark of plasma cell leukemia and of a special subset of multiple myeloma. Leukemia. 1998;12:1977–82. [PubMed] [Google Scholar]
16. Zhang XG, Bataille R, Widjenes J, Klein B. Interleukin-6 dependence of advanced malignant plasma cell dyscrasias. Cancer. 1992;69:1373–6. doi: 10.1002/1097-0142(19920315)69:6<1373::AIDCNCR2820690612>3.0.CO;2-1. [PubMed] [CrossRef] [Google Scholar]
17. García-Sanz R, Orfão A, González M, Tabernero MD, Bladé J, Moro MJ, et al. Primary plasma cell leukemia: Clinical, immunophenotypic, DNA ploidy, and cytogenetic characteristics. Blood. 1999;93:1032–7. [PubMed] [Google Scholar]
18. Chiecchio L, Dagrada GP, Ibrahim AH, Dachs Cabanas E, Protheroe RK, Stockley DM, et al. Timing of acquisition of deletion 13 in plasma cell dyscrasias is dependent on genetic context. Haematologica. 2009;94:1708–13. doi: 10.3324/haematol.2009.011064. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
19. Esparís-Ogando A, Alegre A, Aguado B, Mateo G, Gutiérrez N, Bladé J, et al. Bortezomib is an efficient agent in plasma cell leukemias. Int J Cancer. 2005;114:665–7. doi: 10.1002/ijc.20793. [PubMed] [CrossRef] [Google Scholar]
20. Chauhan S, Jaisinghani P, Rathore J, Tariq H, Galan Y, Madhavan A, Rana H, Frenia D. Plasma cell leukemia. J Family Med Prim Care. 2018 Mar-Apr;7(2):461-465. doi: 10.4103/jfmpc.jfmpc_310_17. PMID: 30090796; PMCID: PMC6060942.

21. Drake MB, Iacobelli S, van Biezen A, Morris C, Apperley JF, Niederwieser D, Björkstrand B, Gahrton G; European Group for Blood and Marrow Transplantation and the European Leukemia Net. Primary plasma cell leukemia and autologous stem cell transplantation. Haematologica. 2010 May;95(5):804-9. doi: 10.3324/haematol.2009.013334. PMID: 20442444; PMCID: PMC2864387.
22. Gonsalves WI, Buadi FK, Kumar SK. Combination therapy incorporating Bcl□2 inhibition with Venetoclax for the treatment of refractory primary plasma cell leukemia with t (11;14). Eur J Haematol. 2018;100:215□217. [PubMed] [Google Scholar]