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Case Report **Pathology**

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PLASMA CELL LEUKAEMIA

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ABSTRACT

Primary plasma cell leukemia (PCL) is a rare plasma cell disorder, and current knowledge regarding survival in this disease is limited to small series of patients. Although there has been significant improvement in the survival of patients with multiple myeloma (MM) over the past few decades, it is not known whether there has been a similar trend for PCL. The incidence of adverse prognostic factors is significantly higher in PCL versus MM. Although similar,PCL exhibits distinct clinical,immunophenotypic and cytogenetic features that distinguish it from MM.We report three cases of Plasma cell leukaemia of which one was a primary plasma cell leukaemia and the other two cases were secondary plasma cell leukaemias.

Key words:plasma cell leukaemia, multiple myeloma,immunophenotyping

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INTRODUCTION

Plasma cell leukemia (PCL) is a rare and aggressive variant of multiple myeloma with poor prognosis characterized by peripheral blood involvement. It is defined by the presence of circulating plasma cells exceeding 20% of peripheral blood leukocytes or 2 x 10^9/L .PCL is classified as either primary (60%) or secondary (40%). In primary PCL, a malignant plasma cell clone is thought to arise de novo and the peripheral blood proliferation is the presenting condition.Secondary PCL occurs through clonal evolution of an underlying multiple myeloma and is a terminal event. PCL occurs in 2 to 4 percent of myeloma cases and is seen more frequently in light-chain only, IgE, and IgD myeloma, and less frequently in IgG or IgA myeloma .Although similar, PCL exhibits distinct clinical, immunophenotypic, and cytogenetic features that distinguish it from multiple myeloma.[1]

CASE REPORTS

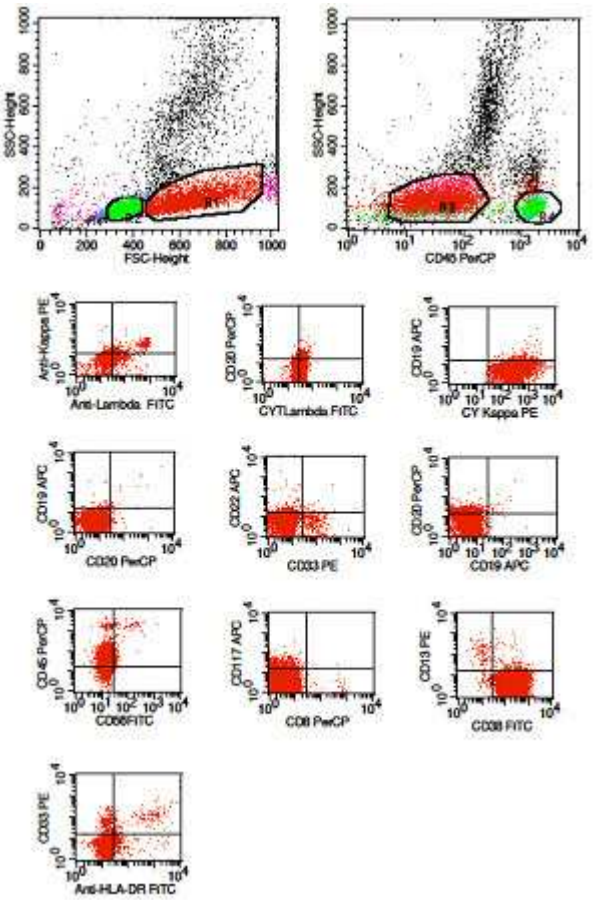
We report three cases of Plasma cell leukaemia of which one was a primary plasma cell leukaemia and the other two cases were secondary plasma cell leukaemias.

Case1:A 45 year old female presented with complaints of low back pain in January 2011 to our medical oncology OPD, following a fall about a year ago. On examination, her general condition was fair .There was pallor but no organomegaly. Her complete blood picture revealed Hb:7.3g/dl,WBC count of 49,500cells/c.mm,platelet:45,000/c.mm.Differential count showed 81% plasma cells and 6% plasmablasts..Serum creatinine was 0.7mg/dl,calcium 10.1mg/dl,uric acid 6.8mg/dl,serum β_2 microglobulin 16.18mg/dl.Serum protein electrophoresis showed total protein 5.9g/dl,albumin 3.03,$\alpha_1$globulin 0.37g/dl, $\alpha_2$globulin 1.16g/dl,β globulin 0.74g/dl,γ globulin 0.6g/dl.A/G ratio 1.05. Diagnosed to have increased $\alpha_2$globulin with no M band.

Imageology revealed multiple lytic lesions in the vault ,both clavicles and ribs, fractures in the pelvic bone ,left suprapubic ramus ,neck of femur and mild anterior wedging of D12 vertebral body.

Bone marrow aspiration and biopsy were performed from right posterior superior iliac crest.Bone marrow aspirate smears showed increased cellularity.Plasma cells and plasmablasts comprised 70% and 24% of the marrow nucleated cells respectively.Immunophenotyping was done on peripheral blood sample(Fig 1) .The gated population of neoplastic cells showed bright antigenic expression of CD38 and cytoplasmic kappa and dim expression of cytoplasmic lambda.The neoplastic cells were negative for expression of surface anti kappa,surface anti lambda,CD56,CD19,CD20,CD117,CD8,CD13 and CD33. Diagnosis rendered was Primary plasma cell leukaemia.

Figure 1
Immunophenotyping of peripheral blood sample showing antigenic expression of CD38 and loss of CD56.



Case 2:A 56 year old male patient presented with history of back pain to the medical oncology unit of our institute . MRI of the dorsal spine revealed a left paravertebral soft tissue mass involving D5-D7 which was suggestive of marrow infiltrative disease with a possibility of multiple myeloma. FNAC of the same was performed and a diagnosis of plasmacytoma was offered.His peripheral smear showed rouleaux formation and occasional nucleated RBC's.Total leucocyte count and platelet count were reduced.Differential count showed 40%plasma cells and 6%plasmablasts.(this sentence to be deleted)Serum β_2 microglobulin 6.34mg/dl.Serum protein electrophoresis showed albumin 18.3,$\alpha_1$globulin 10.3g/dl, $\alpha_2$globulin 42.8g/dl,β_1 globulin 16.9g/dl, β_2 globulin 5.4 .γ fraction was massively raised with a thick monoclonal band in the slow moving region along with a small but discrete oligoclonal spike in fast moving region. Total protein was 65.1mg/dl,IgG was 66.5 g/l.Bone marrow aspirate and biopsy were performed which confirmed the diagnosis of multiple myeloma.He was put on chemotherapy.In November 2011, he developed paraplegia for which he underwent vertebral decompression and sustained a fracture of left humerus for which he underwent fixation.He was diagnosed as a case of refractory myeloma.He was hospitalized in March 2012 with difficulty in breathing.On examination his accessory

muscles were active and his conjunctiva was muddy.He developed respiratory distress with bilateral pneumonia.His complete blood picture revealed a Hb of 8.4g%,WBC count of 45,700cells/cu.mm and platelets <10,000/cu.mm. Peripheral smear showed rouleaux formation with 78% circulating plasma cells.His biochemical parameters were as follows alkaline phosphates 127 U/l,serum creatinine 1.4mg/dl,total bilirubin0.9mg/dl,serum albumin 2.5.Bone marrow aspiration was performed from the left iliac crest.The aspirate was particulate with increased cellularity.The trilineage haemopoietic precursors were suppressed and replaced by atypical plasma cells and plasmablasts.Diagnosis of secondary plasma cell leukaemia was established..

Case 3: A 56 year old male diagnosed and treated elsewhere as light chain myeloma(kappa) in 2006 .In January 2009 he was diagnosed to have recurrence and was put on 6 cycles of Melphalan.In May 2010 on follow up there was persistence of disease and he was put on third line chemotherapy.Subsequent visit in August 2010 showed increased M band and later he was put on fourth line chemotherapy. In March 2012 he was admitted with pancytopenia ,his Hb was 9.2g/dl, peripheral smear was normocytic normochromic to microcytic with occasional nucleated RBC's,mild rouleaux formation seen.Total leucocyte count was moderately reduced with 34% circulating plasmablasts bearing prominent nucleoli,reticular chromatin and high nuclear-cytoplasmic ratio.Platelet count was reduced.

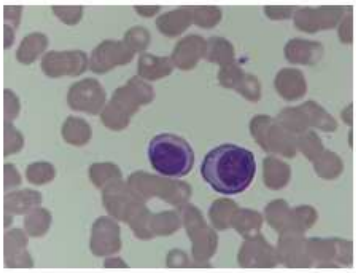


Figure 2
Peripheral blood film showing rouleaux formation and circulating plasma cells

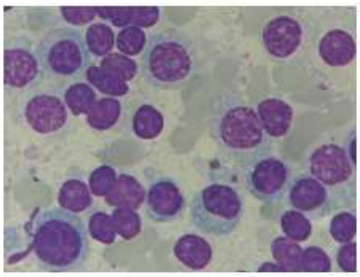


Figure 3
Bone marrow aspirate smear showing mature and immature plasma cells and plasmablasts

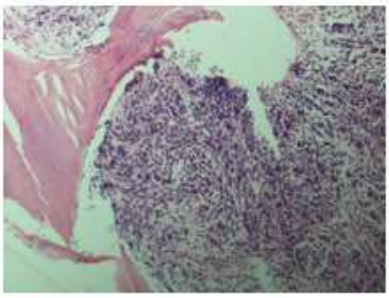


Figure 4
Bone marrow biopsy showing marrow

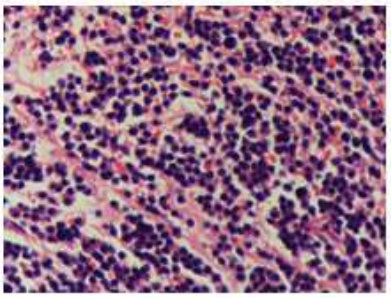


Figure 5
Biopsy showing sheets of replaced with neoplastic plasma cells plasma cells (40x)

DISCUSSION

Plasma cell leukaemia can be primary or secondary. The primary form occurs in individuals without preceeding multiple myeloma whereas the secondary form typically arises as a late manifestation in individuals with multiple myeloma. It develops in 1-2% of cases of multiple myeloma. The exact incidence of primary plasma cell leukaemia is unknown, but it is believed to be less than one case per million. Hepatosplenomegaly and lymphadenopathy are more common in primary than in secondary plasma cell leukaemia. The lytic bone lesions are more common in patients with secondary plasma cell leukaemia (100% versus 60%).[2]The median age of patients with PCL is 50-60 years with an approximately equal proportion of male and female patients.

In both its primary and secondary forms, PCL clinically resembles late-stage multiple myeloma. Patients may present with anemia, cytopenias, recurrent bacterial infections, or renal insufficiency.All our cases had anaemia and thrombocytopenia.. Rouleaux formation is usually evident on the peripheral blood smear; which was seen in our cases. Leucocytosis ranges from 20 to more than 100 X 10^9/L with 20% to 100% of plasma cells.In one of our secondary PCL case, there was moderate leucopenia however the differential count showed 34% plasmablasts.[2]

Pathologic diagnosis of PCL is based on histologic, immunophenotypic, and cytogenetic findings in addition to circulating plasma cell count. Bone marrow biopsy typically reveals aggregates or sheets of neoplastic plasma cells that displace normal marrow elements. Peripheral blood plasma cells range from mature forms with characteristic "clock-face" chromatin and perinuclear hof, to immature blastic forms with loose reticular chromatin, high nuclear/cytoplasmic ratio, and prominent nucleoli. Immature neoplastic cells may be indistinguishable from myeloblasts. In some instances, plasma cells display lymphoid morphology. PCL displays multiple adverse prognostic indicators at presentation such as elevated lactate dehydrogenase, elevated beta2-microglobulin, hypercalcemia, high percentage of Bence-Jones proteinemia, and extramedullary involvement.

Plasma cells in PCL frequently display a more immature phenotype. Expression of pan-B cell antigen CD20 has been shown in 50% of PCL cases compared to 17% of multiple myeloma cases .In addition, neoplastic cells in marrow and peripheral blood in both primary and secondary PCL typically do not express CD56, which is considered to have an important role in anchoring plasma cells to bone marrow stroma. Immunophenotypic differences could be relevant in explaining survival differences between the two entities. Expression of CD56 in a minority of PCL cases has been associated with a favorable prognosis, while CD20 expression has been associated with shorter survival .

An increased incidence of cytogenetic abnormalities has been reported in PCL compared to multiple myeloma. Conventional cytogenetic studies have shown abnormal karyotypes in 30 to 40% of myeloma cases compared to 68% of PCL cases .Complex karyotypes with multiple chromosomal gains and losses are the most frequent changes. Specific numeric chromosomal abnormalities described in PCL include monosomy 13, gains or losses in chromosome 1, trisomy 18, and monosomy X in women .Monosomy 13 may be present in up to 85% of PCL cases and, in multiple myeloma, has been associated with short post-treatment survival .The most common structural abnormality involves the immunoglobulin heavy chain (IgH) locus at 14q32, which is usually part of a translocation. Translocation t(11;14)(q13;q32) in particular has been associated with adverse outcome in patients with PCL .[3,4]

Patients with primary PCL may initially respond better to chemotherapy including single agent drugs commonly used in multiple myeloma.

However, resistant disease is expected and a median survival of less than six months for both types of PCL has been observed. Infection and haemorrhage contribute significantly to morbidity and mortality.

CONCLUSION

In summary, PCL is an aggressive and rare variant of multiple myeloma with poor outcome. No large trials are available on treatment of this disease but bone marrow/stem cell transplant has shown some long term survivals in individual cases.[5]

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