*IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*
*e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 17, Issue 10 Ver. 1 (October. 2018), PP 30-33*
*www.iosrjournals.org*

# Incidental detection of Plasma cell leukemia, A case report

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***Abstract:*** *Plasma cell leukemia (PCL)is an uncommon, aggressive variant of lymphoproliferative disorder that may occur de novo (primary) or in association with multiple myeloma (secondary) . Primary PCL is a distinct clinicopathological entity with different cytogenetic abnormalities and molecular findings from multiple myeloma. Secondary PCL is seen in advanced myeloma. The diagnostic criteria are based on the percentage (>20%) and absolute number (2000/ml) of plasma cells in peripheral blood. Clinical course is aggressive with poor survival rate.We report a case of plasma cell leukemia detected incidentally when the patient was being evaluated for gastrointestinal symptoms. Peripheral blood showed >20 % plasma cells & absolute plasma cell count was much more than cut off limit of >2000/ml.Further bone marrow aspiration ,biopsy showed plasma cell precursors & sr electrophoresis showed M band , so diagnosis of secondary plasma cell leukemia was confirmed.PCL ,whether primary or secondry ,needs to be diagnosed early to initiate therapy immediately as it is known to have an aggressive clinical course & poor outcome .*

***KEY WORDS:*** *Plasma cell leukemia , secondary,primary*

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Date Of Submission: 20-09-2018 Date of acceptance: 08-10-2018

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## I. Introduction:

Plasma cell leukemia(PCL) is an aggressive & rare clonal plasma cell disorder characterized by malignant proliferation of plasma cells in bonemarrow and peripheral blood. It accounts for 1.3–3.4% of all plasma cell dyscrasias .[1]The first case of plasma cell leukemia was reported by Reichenstein Gluzinski almost a century ago. As per Kyle et al it is defined by the presence of absolute plasma cell count of $> 2 \times 10^9$/L or plasma cells comprising >20% of the total white cell count in the peripheral blood. It can be of two types, primary or secondary .Primary (pPCL) when it occurs de novo and secondary (sPCL) if it is associated with relapsing or refractory multiple myeloma .The primary type is more common,with incidence of 60-70% and rest 30- 40% is of secondary type.[2] Clinically it is characterized by non-specific symptoms and median age at presentation is usually more than 50 years. New therapeutic regimens have been introduced recently like bortezomib, immunomodulators and stem cell transplantation .[3]

## II. Case Report:

Case-1: A 59-year-old male with history of hypertension since 1 year, presented with loose stool with increased frequency since last 6 months & epistaxis . There was history of weight loss & fatigue. Physical examination was unremarkable except for mild splenomegaly. Due to persistent pain abdomen he was advised for upper GI endoscopy & routine haematological tests. Endoscopy showed focal gastric mucosal thickening ,so gastric biopsy was performed. Meanwhile laboratory investigations showed hemoglobin of 7.3 g/dl, TRBC 2.1x $10^6$µL, PCV 21.1 %,MCV 100.5 fl, MCH 32.4 pg/dl, MCHC 32.28 gm/dl, RDW 15.54,total white blood cell count of $24.3 \times 10^9$/L and a platelet count of $130 \times 10^9$/L. In peripheral blood smear excess rouleaux formation seen (fig-1). Differential count showed neutrophils were 24%, lymphocytes 02%,eosinophils 00%,monocytes 01% and predominant population of atypical cells were 73%.The atypical cells were large with high nuclear cytoplasmic ratio,many having bluish scanty to moderate amount of cytoplasm and nuclei with vesicular chromatin.Some cell were plasmacytoid with eccentrically placed round nuclei , perinuclear hof and coarse chromatin.(fig-2) Some cells had peripheral cytoplasmic reddish hue like flame cells.Based on the percentage of plasma cells(i.e.>20%) and absolute number(absolute count: $17.7 \times 10^9$/L) in peripheral smear, diagnosis of plasma cell leukemia was given. Further biochemical tests showed sr calcium of 11.9 mg/dL ,sr creatinine of 1.8mg/dl, sr urea 38 mg/dl,sr uric acid 8 mg/dl, sr phosphorus 6.8 mg/dl, PT 13.7 second and INR 1.27 ,SGOT 50 µ/L, SGPT 50µ/L,GGT 71µ/L, sr Alkaline phosphatase 65µ/L,sr lactate dehydrogenase (LDH) 373 U/L, Sr β2 microglobulin 1.9 mg/dl and Urine immunofixation electrophoresis showed kappa chains .The bone marrow

aspiration revealed hypercellularity with markedly decreased erythroid, myeloid and megakaryocytic cell lines. It showed numerous circulating atypical plasma cells and plasmablasts (> 90%) (Fig-3).Touch imprint smears of bone marrow biopsy showed similar features( fig-4). Bone marrow biopsy revealed hypercellularity with monotonous population of cells, many of which plasmacytoid .(fig-5) Immunohistochemical study with CD38 & CD138 was positive.(fig-6,7)Serum protein electrophoresis showed a gamma M-spike of 62 %. Total serum protein was 8.5 g/dL ,albumin was 3.5 g/dL & sr globulin 5 gm/dl. Serum protein electrophoresis showed M spike of 0.1 g/dL. Gastric biopsy histopathology report was mild chronic nonspecific gastritis. The patient received 16 cycles of Lenalidomide (25 mg × HS for 21 days), Bortezumib (2 mg × I/V weekly) and dexamethasone (8 mg × TDS for 4 days every week). (Figure 1).

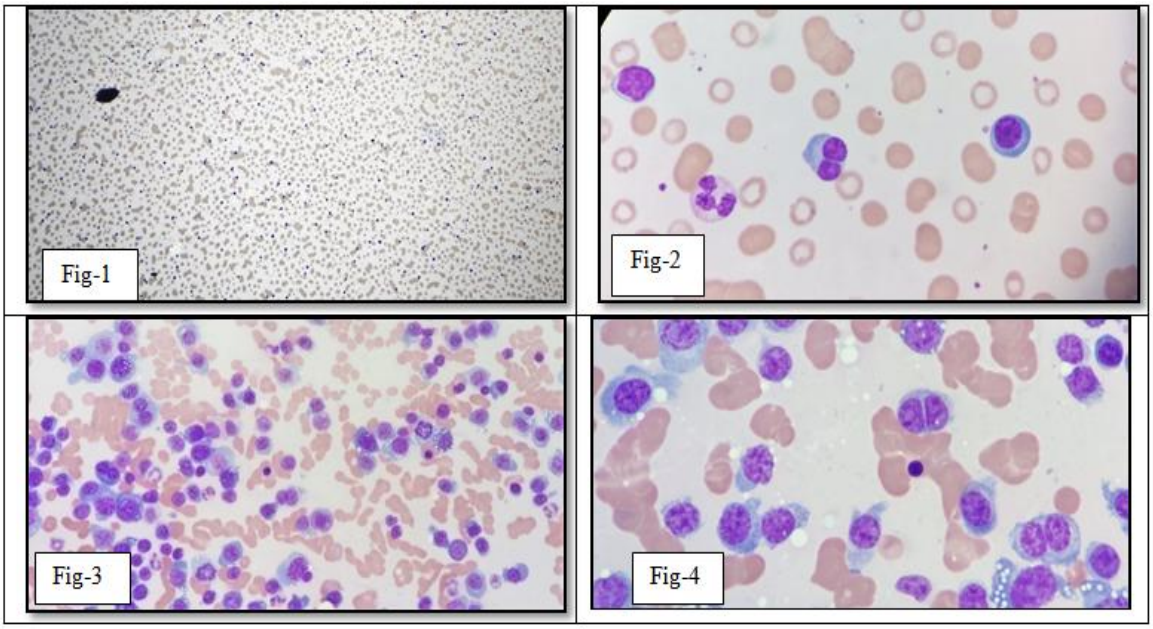


Fig-1: Rouleauex in peripheral smear, 40x

Fig-2: Plasma cells in peripheral smear, 400x

Fig-3: Mature & immature plasma cells in bone marrow aspiration smear, 100x

Fig-4: Immature plasma cells in bone marrow biopsy touch imprint smear, 400x

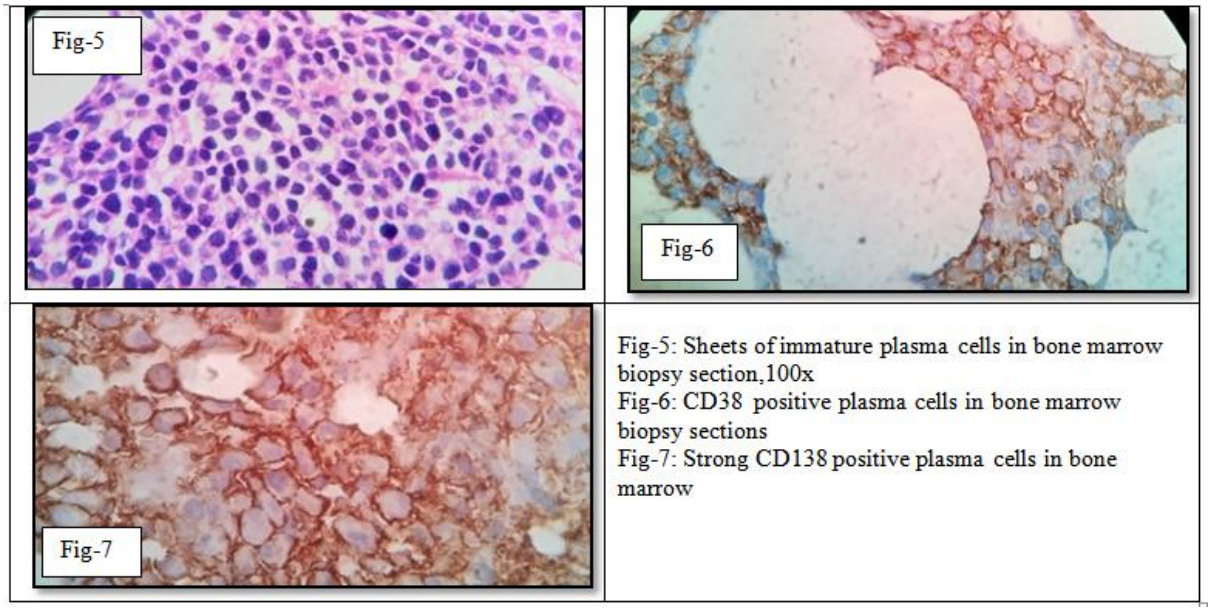


Fig-5: Sheets of immature plasma cells in bone marrow biopsy section,100x
Fig-6: CD38 positive plasma cells in bone marrow biopsy sections
Fig-7: Strong CD138 positive plasma cells in bone marrow

## III. Discussion:

Plasma cell leukemia accounts for 0.3% of acute leukemia cases and up to 4% are associated with multiple myeloma (MM) .[3] Characteristic features of PCL are extramedullary involvement, ability to circulate in blood, and expansion of plasma cells independent of the supportive bone marrow (BM) microenvironment. The biology of tumor cells dissemination is not only related to changes in expression of host of adhesion molecules and chemokine receptors like CD56, VLA-4,CD 54, HLA-1, CD40,neuronal cell adhesion molecule, CCR1, CCR2, CXCR4 and leukocyte function-associated antigen 1 but also due to the presence of other molecular aberrations,like presence of p53 deletion, hypodiploidy, 13q deletions and 1q gains .Consequently BM microenvironment-independent tumor growth, inhibition of apoptosis, poor prognosis and resistance to therapy occurs.[2,4,5] In pPCL, the genetic abnormalities like hyperdiploidy and primary IgH translocations are present at the time of disease inception itself , whereas during the progression of disease upto MM, and sPCL stage, there is a gradual accumulation of genetic abnormalities leading to the acquisition of more aggressive phenotype of malignant plasma cells.[5] Both pPCL and sPCL share similar biological and clinical courses cinically resembling advanced stage of multiple myeloma presenting with anemia, cytopenias, recurrent bacterial infections or renal insufficiency. PPCL usually presents a decade earlier and show a higher prevalence of hepatosplenomegaly, pleural effusion, lymphadenopathy, neurological deficits, anemia , thrombocytopenia, significant leukocytosis, hypercalcemia, elevated lactate dehydrogenase levels, high beta-2-microglobulin levels ,extra medullary plasmacytomas and higher incidence of tumor lysis syndrome , with higher lambda light chain restriction than kappa while osteolytic lesions are relatively few , pPCL (35%-67%) versus sPCL or MM (79%-81% ). As sPCL is a leukemic transformation of MM, no major differences in the clinical presentations between MM and sPCL is noted . Secondary PCL occurs only in 1-2% of advanced and refractory MM patients & has a median survival of a few months (1.3 months for sPCL versus 11.1 months for pPCL) [3, 6]

Non-neoplastic conditions causing severe transient peripheral blood plasmacytosis are sepsis (eg staphylococcal), pertusis, rubella ,dengue fever, infectious mononucleosis and parvovirus B19 infection which should be ruled out as differentials. Diagnosis of PCL requires a proper history & physical examination followed by laboratory and radiological investigations.[7] Although MM and PCL have an similar cell of origin , primary PCL has different clinical presentation, response to therapy and prognosis.Therefore early recognition of the characteristic bloodsmear can be key to diagnosis and initiating appropriate therapy.Greater awareness regarding markers of adverse prognosis(hypoalbuminemia, elevated β2-microglobulin, renal insufficiency , Bence-Jones proteinuria , hypercalcemia & extramedullary involvement), helps in early identification of aggressive nature of the disease.[2,4] Pathologic diagnosis of PCL is based upon histologic(bone marrow biopsy), immunohistocemical, and cytogenetic findings with circulating plasma cell count in peripheral blood. [8 ,9]

Management of PCL includes chemo therapy & immunomodulatory agents for rapid disease control and to minimize the risk of early death. Intensive chemotherapy regimens and bortezomib-based regimens, followed by autologous stem cell transplantation, are recommended. Allogeneic transplantation can be useful in younger patients.[10,11,12]

## IV. Conclusion:

PCL is an aggressive and uncommon variant of multiple myeloma with poor prognosis. Bone marrow/ stem cell transplant has shown promising long term survival in some cases. Peripheral blood smear examination is one of the vital steps in arriving at a diagnosis along with bone marrow examination, immunohistochemical study , immunophenotyping and serum protein electrophoresis for prompt initiation of therapy & favourable outcome .

**CONFLICT OF INTEREST:** None.

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Sarojini Raman. " "Incidental detection of Plasma cell leukemia, A case report. " IOSR Journal of Dental and Medical Sciences (IOSR-JDMS), vol. 17, no. 10, 2018, pp 30-33.