CASE REPORT

# REACTIVE PLASMACYTOSIS: A DIAGNOSTIC CONUNDRUM IN ACUTE MYELOID LEUKAEMIA

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Bone-marrow being a home to various kinds of normal hematopoietic cells, sometime becomes overcrowded by abnormal cell population in malignancies like in acute myeloid leukaemia. One such dilemma in diagnosis betides when two abnormal cell populations in bone-marrow occur at the same time. A prime example is when reactive plasmacytosis in bone-marrow eventuate in relation with acute myeloid leukaemia (AML). Due to scarce amount of such cases reported, it is imperative to understand the difference between reactive plasmacytosis which arises after induction of chemotherapy and the one which is diagnosed along with AML, during initial diagnosis due to other causes, like infections and IL-6 production by the leukemic blast population. To substantiate these erstwhile arguments, the brief case history of a 45 years old female patient diagnosed with acute myeloid leukaemia with coincident reactive plasmacytosis having no previous history of chemotherapy is presented along with review of past published literature.

**Keywords:** Acute myeloid leukaemia; Polyclonal; Reactive Plasmacytosis; Monoclonal; Plasma cell myeloma

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## INTRODUCTION

The contemporaneous presence of acute myeloid leukaemia and plasmacytosis in the same patient is a well-known fact but a rare phenomenon. Various underlying pathological mechanisms associated with this condition have been reported in previous studies. The flowchart in figure-1 illustrated various underlying pathological mechanisms causing bone marrow plasmacytosis in patients with acute myeloid leukemia.[1] These causes should be clearly identified because of different therapeutic approaches linked with these conditions. In our case report of acute myeloid leukaemia (AML-M2) with reactive bone marrow plasmacytosis presumably due to infection, with no previous history of induction chemotherapy in 45 years old female patient is presented.

## CASE REPORT

A female patient of 45 years of age having two months history of low-grade episodic fever, gradually progressive weakness, fatigue, anorexia, dry cough and dyspnoea. She was neither diabetic nor hypertensive. On examination, patient appeared acutely ill. She was pale, lethargic, and unable to walk due to weakness and her temperature was 100 $^{o}$F. No organomegaly or lymphadenopathy was detected. She had a history of antibiotic therapy for acute pharyngitis diagnosed by a general practitioner two weeks earlier; but her condition deteriorated and her complaints aggravated despite antibiotic therapy. After re-evaluation, she was referred to our setting by her physician. Routine blood tests were performed. Her hemogram revealed pancytopenia with total leukocyte count of 2.43×10^9/L, haemoglobin concentration of 6.5 g/dl, haematocrit of 19.3% and platelet count of 45×10^9/L. Rouleaux formation was noticed on peripheral film. ESR of the patient was 90mm Hg/1$^{st}$ hour and renal profile was normal. Bone marrow aspiration for cytomorphological assessment along with trephine biopsy for histomorphological evaluation were advised and performed. Cytological evaluation of marrow aspiration revealed 75% blasts and plasmacytosis with plasma cells accounting for 18% of non-erythroid cells as illustrated in figure-2 (A,B). Blasts were myeloperoxidase positive (Figure-2 C). Bone marrow trephine biopsy showed hyper cellularity with extensive marrow replacement by myeloblasts along with increased plasma cells scattered interstitially and in small clusters (Figure-3 A,B). The provisional diagnosis of acute myeloid leukaemia (AML-M2: FAB classification) with plasmacytosis was made. Further investigations were performed to investigate the cause of plasmacytosis (reactive /plasma cell myeloma). Serum calcium level was 9.5mg/dl. Urinalysis for Bence Jones proteinuria was negative and there was no lytic lesion on skeletal survey.

No Para protein band was noticed on serum protein electrophoresis. The immunohistochemical analysis of biopsy specimen revealed malignant blast population showing strong, uniform expression of CD45, MPO, CD117, and CD33 with variable expression of CD34. There was negative expression of CD64 and Tdt in this blast population. CD138 positivity with polyclonal expression of κ and ʎ was noticed in abnormal bone marrow plasma cells as displayed in figure-3 (C-F). Due to lack of facility, serum free light chain assay and cytogenetic analysis were not performed. Based on these findings the patient was diagnosed with "acute myeloid leukaemia (AML-M2) with polyclonal reactive bone marrow plasmacytosis" and referred to the oncologist for further management.

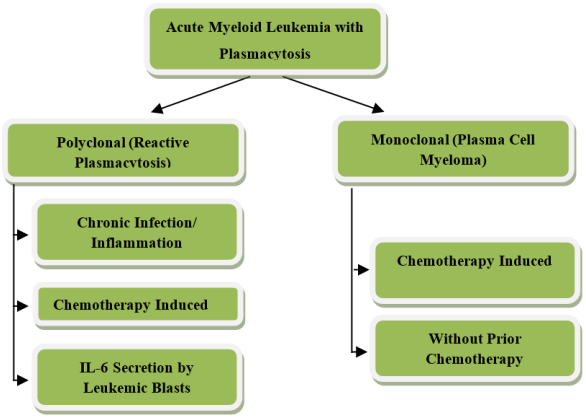


**Figure-1: Flowchart showing causes of acute myeloid leukaemia with plasmacytosis**

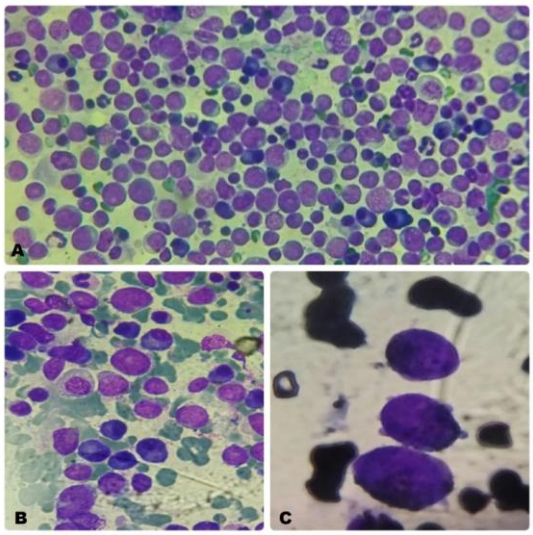


**Figure-2: AML with bone marrow plasmacytosis. A, B: Wright-Giemsa-stained bone marrow aspirate images (Magnification: 40x & 100x under oil immersion). C: Myeloperoxidase stain positivity in blasts.**

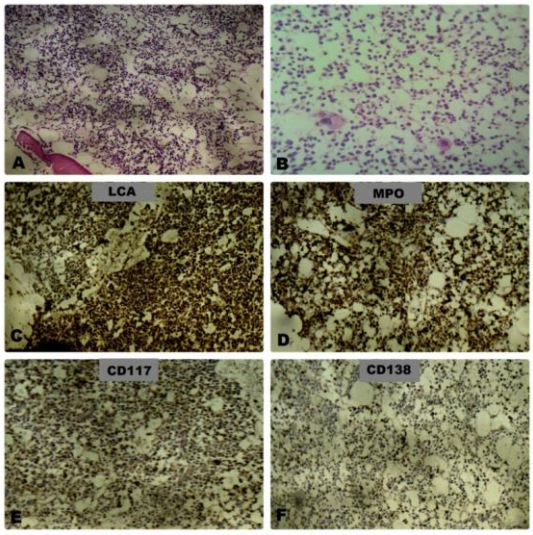


**Figure-3: AML with bone marrow plasmacytosis. A,B: Hematoxylin-Eosin stained images of bone marrow trephine biopsy (Magnification: 10x & 40x ).C-F: Immunohistochemical positive stains**

## DISCUSSION

The coincidental association of plasmacytosis with acute myeloid leukaemia is an established phenomenon. Various pathological mechanisms have been proposed in the past published literature in the context of acute myeloid leukaemia's association with plasmacytosis, whether polyclonal /reactive or monoclonal as a second malignancy in the form of plasma cell myeloma (Figure-1). Reactive bone marrow plasmacytosis in a patient of acute myeloid leukaemia can be due to infections, autoimmune disorders, hypersensitivity states, diabetes mellitus or post-chemotherapy.[1,2] Role of increasingly released cytokine IL-6 by the leukemic blast cells have also been postulated as underlying cause.[3,4] It is also thought as a physiological immunologic response or hypersensitivity reaction to a poorly defined or unknown antigenic stimulus.[2,5]

Previously acute leukaemia was also considered to be the part of natural course of plasma cell myeloma. In 1974, fifty-seven cases of plasma cell myeloma and concurrent acute leukaemia has been reported. Most of these were presented with multiple myeloma terminating into chemotherapy induced acute myeloblastic or acute myelomonocytic leukaemia. Melphalan therapy alone or along with other cytotoxic drugs/irradiation was considered to be the main culprit.[6] Although the association of chemotherapy induced acute myeloid leukaemia with plasma cell myeloma is identified in clinical settings, yet the combination of these two malignant disorders without prior chemotherapy is unusual finding.[7] Until 2003, only 9 patients had been reported suffering from acute myeloid leukaemia and plasma cell myeloma with no prior history of chemotherapy exposure.[6] Moreover the aetiology of this class still remains unclear.[8,9]

There are different concepts about the definition of reactive plasmacytosis and application of morphological criteria in differentiation of polyclonal/reactive or monoclonal plasmacytosis. Few previous reports discourage the use of morphological criteria because of their findings of very high plasma cell count (up to fifty percent), binucleated or immature forms with cytoplasmic inclusions and prominent nucleoli in cases of reactive plasmacytosis.[10] While others mentioned not more than 20% increase in marrow plasma cells with infiltration of more mature forms and plasmacytic satellitosis as characteristics of reactive plasmacytosis.[1,4,11] In our case, 18% plasma cells of non-erythroid series with variation in size and maturation stages were observed, having the cytological features of low N:C ratio, abundant cytoplasm, eccentric nuclei with coarse chromatin and only rare nucleoli; few showing loose chromatin and prominent nucleoli. Occasional binucleated forms were also noticed. Therefore, no clearly defined cut off percentage of bone marrow plasma cells and morphological criteria has been documented.

Detailed history, thorough clinical examination and more specific investigations like serum protein electrophoresis for the assessment of monoclonal band, serum free light chain analysis and whole-body skeletal survey for lytic lesions must be made for the differentiation of reactive plasmacytosis and other plasma cell neoplasms in acute myeloid leukaemia. Although, due to lack of specific clinical, morphological, cytogenetic and molecular findings acute myeloid leukaemia with reactive plasmacytosis is still not included as a separate entity in the classification of acute myeloid leukaemia, yet it will need an international registry because of its rare occurrence.

## CONCLUSION

Identification of underlying mechanism of plasmacytosis whether reactive or monoclonal as dual malignancy is requisite in cases of acute myeloid leukaemia. An errant procedure must be followed to curb such dire situations for the better guidance regarding therapeutic management and prognostic factors related to these conditions.

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