

Diagnostic and Prognostic Challenges in Cytology for Multiple Myeloma: A Case Series in a Resource-limited Setting

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Abstract

Background: Multiple myeloma (MM) is a malignancy of plasma cells characterized by clonal proliferation in the bone marrow and associated organ damage. In resource-limited settings, advanced diagnostic tools are often inaccessible, making conventional cytology a critical first-line diagnostic approach.

Objectives: To assess the advantages and limitations of using bone marrow cytology as the primary diagnostic method for MM in a resource-constrained environment.

Methods: A retrospective case series of four patients with suspected MM was conducted at a regional hospital in Senegal. Diagnosis was based exclusively on bone marrow cytologic evaluation using standard staining techniques. Demographic data, cytologic findings, and available clinical information were analyzed in comparison to established diagnostic criteria.

Results: Case 1 had 15% plasma cells but no clear CRAB features, suggesting smoldering MM. Case 2 exhibited 35% plasma cell infiltration, but staging was not possible due to the absence of biochemical and immunophenotypic data. Case 3 demonstrated significant plasmacytosis with pancytopenia, raising concerns about aggressive disease versus metastatic marrow involvement. Case 4 presented with systemic symptoms indicative of plasma cell leukemia, but cytologic evaluation alone was insufficient for definitive classification.

Conclusions: Although bone marrow cytology is a rapid and accessible diagnostic tool in low-resource settings, it is inadequate for risk stratification and precise subclassification of MM. Additional diagnostic techniques—such as basic immunophenotyping and serum studies—are necessary to optimize patient management and inform healthcare policy improvements.

Keywords: Multiple myeloma, Cytology, Plasma cell neoplasm, Resource-limited setting, Risk stratification, Case series, Hematology

Introduction

Multiple myeloma (MM) is a clonal disorder of plasma cells characterized by monoclonal immunoglobulin production and subsequent organ damage [1]. Accounting for approximately 1% of all cancers and 10% of hematologic malignancies

worldwide [2], MM is increasingly prevalent, particularly in low- and middle-income countries where diagnostic resources remain scarce [3]. The disease is driven by genetic mutations that promote plasma cell survival and proliferation, resulting in bone marrow infiltration, immunosuppression, and osteolytic lesions [4].

Clinically, MM is diagnosed using the CRAB criteria (hypercalcemia, renal failure, anemia, and bone lesions), with precursor conditions such as monoclonal gammopathy of undetermined significance (MGUS) and smoldering myeloma often preceding the overt disease [5]. The standard diagnostic approach includes bone marrow biopsy with immunophenotyping, serum protein electrophoresis, and imaging studies [6]. However, in many resource-constrained regions, cytologic evaluation is the only available diagnostic tool.

This study presents a case series highlighting both the potential benefits and limitations of using cytology for MM diagnosis in a low-resource setting.

Materials and Methods

This retrospective case series was conducted at Ziguinchor Hospital in Senegal. Four patients with suspected multiple myeloma (MM) were assessed using bone marrow aspirates and cytological smears stained with May-Grünwald-Giemsa. Due to financial constraints, ancillary tests such as immunophenotyping, serum protein electrophoresis,

and cytogenetic analysis were not performed. Patient data—including age, clinical presentation, and plasma cell percentage from cytology—were extracted from medical records and evaluated against the International Myeloma Working Group's diagnostic criteria [7].

Results

Case 1

A patient presented with mild anemia. Bone marrow cytology revealed 15% plasma cells with characteristic features such as eccentric nuclei and prominent nucleoli (**Figure 1**). The findings were consistent with early or smoldering MM, but the absence of biochemical and cytogenetic data prevented complete risk stratification [7].

Case 2

This patient exhibited high plasma cell infiltration (35%) (**Figure 2**). Despite strong morphological evidence for MM, staging could not be performed due to the unavailability of immunophenotyping and serum analysis, which are required for the Revised International Staging System (R-ISS) [8].

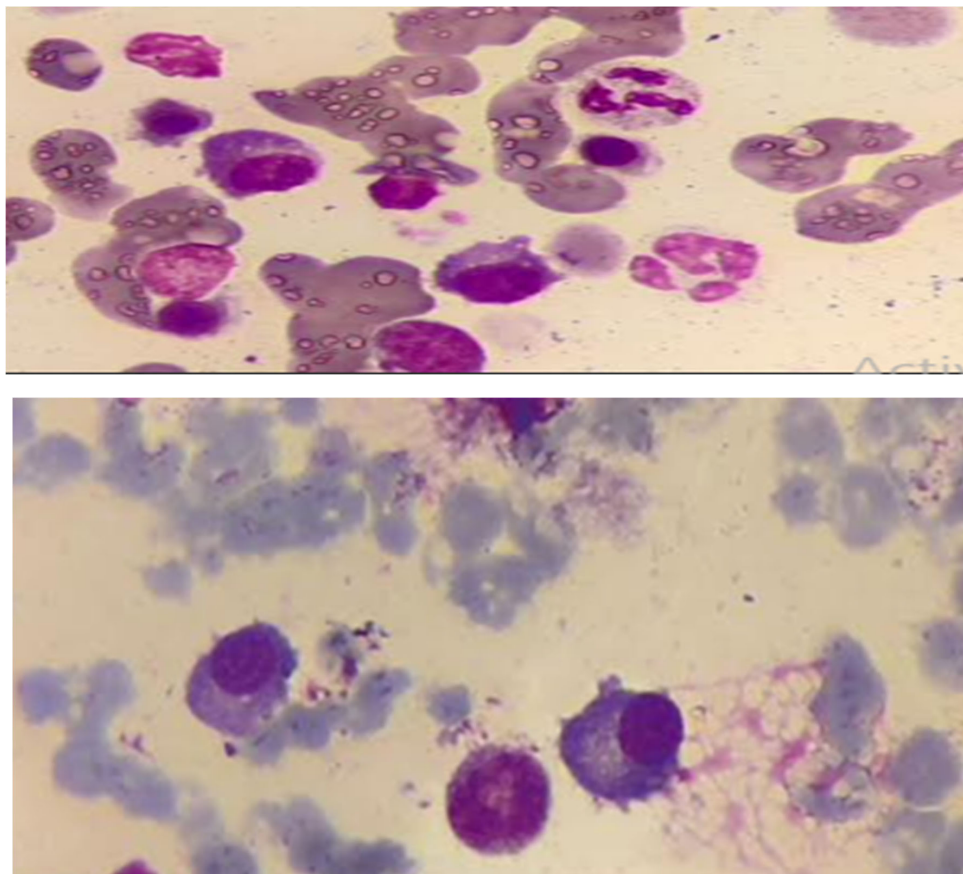


Figure 1. Dystrophic plasmocytosis in the bone marrow at a rate of 15% with anemia and absence of other MM positive diagnosis signs according to the WGMM.

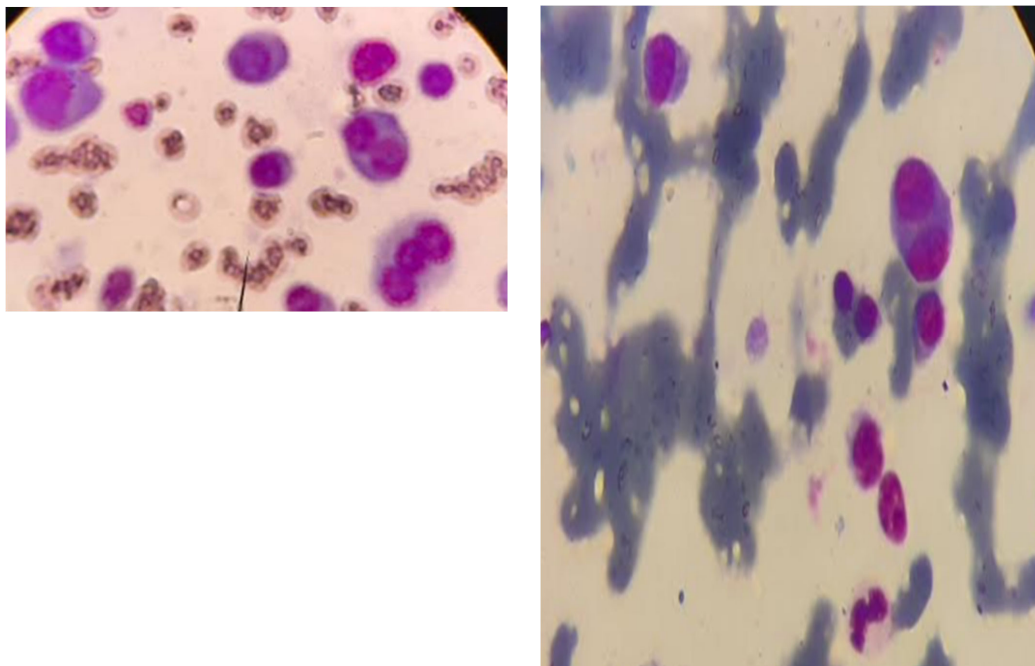


Figure 2. Bone marrow cytology shows bi or multinucleated plasmacytosis.

Case 3

The patient had pancytopenia and significant plasmacytosis. The cytological findings raised differential diagnostic concerns between aggressive MM and bone marrow metastases (**Figure 3**). However, cytology alone was insufficient to differentiate between these conditions [9].

Case 4

A patient with systemic symptoms, fever, and lymphadenopathy showed cytological features suggestive of plasma cell dyscrasia (**Figure 4**). Plasma cell leukemia was suspected, but confirmation required peripheral blood immunophenotyping [10].

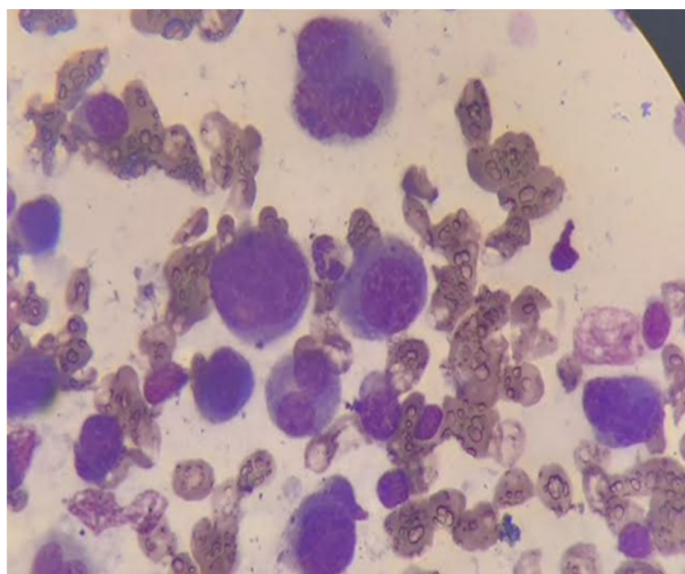


Figure 3. Bone marrow cytology in Case 3: Solid tumor cell infiltration from thyroid cancer or plasmacytosis in the context of positive CRAB criteria?

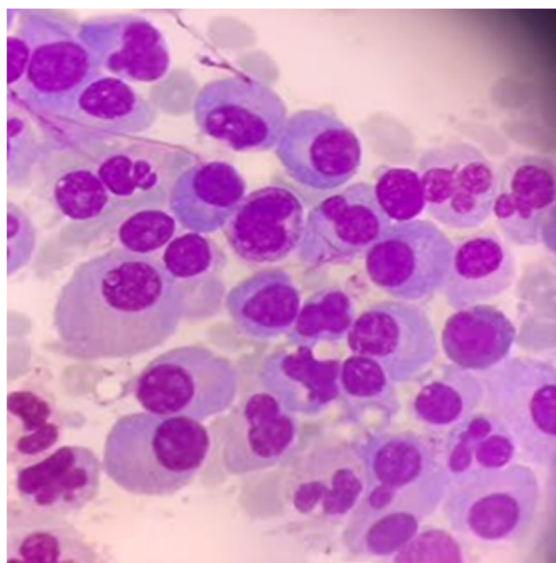


Figure 4. Bone marrow cytology in Case 4 showing features suggestive of a monoclonal gammopathy—type to be determined.

Discussion

Strengths of cytology

Bone marrow cytology with routine staining is a rapid, cost-effective method for assessing marrow cellularity and identifying abnormal plasma cell morphology [6]. Features such as increased plasma cell counts, binucleation, eccentric nuclei, and prominent nucleoli allow for a preliminary diagnosis of MM [6]. In low-resource settings, cytology serves as a crucial first-line screening tool, prompting further investigation when additional diagnostic resources become available [11].

Limitations in risk stratification and disease classification

Proper MM management relies on risk stratification using clinical, biochemical, and cytogenetic markers [7]. The R-ISS staging system incorporates serum β_2 -microglobulin, albumin, lactate dehydrogenase, and cytogenetic abnormalities (e.g., del(17p), t(4;14)) to classify patients [8]. In Cases 2 and 3, although cytology revealed high plasma cell infiltration, the absence of these complementary markers made accurate staging impossible, potentially leading to suboptimal treatment choices [8].

Challenges in differential diagnosis

Cytology alone is often inadequate to distinguish MM from reactive plasmacytosis or plasma cell leukemia [5]. Immunophenotypic analysis using markers such as CD38, CD138, CD56, and CD45 improves diagnostic accuracy by confirming clonality and malignant transformation [12]. Minimal flow cytometry panels feasible in low-resource settings can enhance diagnostic confidence [13].

Strategies for improving diagnosis

Several cost-effective approaches can help bridge the diagnostic gap in resource-limited settings:

- Basic Immunophenotyping: Implementing simple flow cytometry panels (e.g., CD38, CD138, CD45) can confirm plasma cell malignancy and assist in risk stratification [12-14].
- Regional Referral Networks: Collaborations with central laboratories enable referral of samples for essential tests, such as serum protein electrophoresis and cytogenetic analysis, improving diagnostic accuracy [11,14].
- Targeted Training: Enhanced training programs for cytologists improve recognition of subtle morphological changes in plasma cell dyscrasias, leading to earlier diagnosis [13].
- Utilization of Low-Cost Biomarkers: Affordable point-of-care tests may supplement cytological evaluation with additional data for risk stratification [11].
- Emerging Prognostic Biomarkers: Raghunathachar *et al.* recently reviewed diagnostic and prognostic biomarkers in MM, highlighting emerging plasmatic markers (sFLC, soluble BCMA, microRNAs) and low-cost molecular assays suitable for regional centers to improve risk stratification and guide therapy [15].
- Telemedicine Integration: Telecytology adoption allows remote experts to assist local clinicians in interpreting complex cases, reducing diagnostic delays [16].

Broader implications and policy recommendations

The limitations observed in this case series reflect broader healthcare disparities in low-income regions. Expanding access to basic diagnostic tools is essential for improving MM management [17]. Policy initiatives should subsidize essential diagnostic technologies and establish regional centers of excellence to facilitate early detection and risk-adapted therapy [17,18]. Additionally, integrating telemedicine and affordable biomarker testing could provide sustainable solutions to address diagnostic limitations [19,20].

Conclusion

Key findings

This case series highlights the importance of bone marrow cytology as an accessible diagnostic tool for MM in resource-limited settings. However, cytology alone is insufficient for comprehensive risk stratification and precise disease classification.

Clinical and research implications

The inability to perform additional tests, such as immunophenotyping and serum studies, limits accurate staging and individualized treatment plans. The adoption of cost-effective diagnostic improvements is essential for optimizing patient outcomes.

Policy recommendations

Investment in affordable diagnostic technologies, the establishment of regional referral networks, and the integration of telemedicine are critical steps toward improving MM care. These measures will enhance diagnostic capabilities, ensure better disease management, and help reduce healthcare disparities in low-income settings.

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Authors' Contributions

Mame Ngone Coly conceptualized the study and prepared the manuscript. All authors contributed to data analysis and critical manuscript revisions. All authors reviewed and approved the final manuscript.

Ethical Approval and Consent

Informed consent was obtained from all patients included in the study. The research was conducted in accordance with the ethical guidelines of the Institutional Review Board of the Hospital of Peace.

Competing Interests

The authors declare no conflicts of interest.

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