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Original Research Article

Morphological Patterns and Clinical Correlates in Multiple Myeloma: A Retrospective Analysis of 28 Cases

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Abstract

Background: Multiple myeloma (MM) is a malignant plasma cell neoplasm characterized by the clonal proliferation of plasma cells in the bone marrow, accounting for approximately 10% of hematologic malignancies. It predominantly affects older adults, with a median age of diagnosis around 70 years. Patients typically present with fatigue, bone pain, anemia, renal impairment, or hypercalcemia, collectively defined by the CRAB criteria. Despite advances in diagnostic modalities, bone marrow examination remains the cornerstone for establishing the diagnosis and evaluating disease morphology. Morphological variations of plasma cells provide prognostic information, with mature forms associated with favorable outcomes and plasmablastic variants linked to aggressive disease.

Methods: A retrospective observational study was conducted at the Department of Pathology, KIMS& RF, Amalapuram, including 28 cases of MM diagnosed over a 5-year period. Demographic details, clinical presentation, hematological and biochemical profiles, radiological findings, and bone marrow aspirates were reviewed. Morphological subtypes of plasma cells were categorized into mature, immature, plasmablastic, and pleomorphic types, with additional evaluation of multinucleation and cytoplasmic inclusions such as Russell bodies and Mott cells.

Results: The mean age of presentation was 57 years (range: 37–75), with a male-to-female ratio of 1.3:1. The most frequent presenting symptoms included bone pain (71.4%) and generalized weakness (46.4%). Anemia was present in 92.8% of patients, with hemoglobin values as low as 2.8 g/dL. ESR was universally elevated, and M-band positivity was detected in the majority. Radiological lytic lesions were observed in 57%. Bone marrow plasmacytosis ranged between 20–70%. Morphological distribution revealed mature plasma cells in 61%, plasmablastic in 10%, pleomorphic in 11%, and mixed mature/immature in 18%. Multinucleation was present in 46.4% of cases, while Mott cells and Russell bodies were rarely encountered.

Conclusion: Bone marrow morphology continues to be central to the diagnosis and prognostication of MM. The predominance of mature plasma cell morphology suggests a relatively favorable pattern, whereas plasmablastic morphology was rare but clinically significant due to its poor prognosis. Morphological assessment of plasma cells, integrated with clinical, biochemical, and radiological findings, remains indispensable in the comprehensive evaluation of MM patients.

Keywords: Multiple myeloma, Plasma cell morphology, Bone marrow aspiration, Plasmablastic myeloma, Prognosis, Hematological malignancy.

Introduction

Multiple myeloma (MM) is a malignant hematological disorder characterized by the uncontrolled proliferation of a single clone of plasma cells in the bone marrow. It represents the second most common hematologic malignancy in adults, following non-Hodgkin's lymphoma, and accounts for nearly 10% of all blood cancers worldwide [1]. The disease is primarily one of older adults, with the median age at diagnosis approximating 70 years, although younger cases are not uncommon [2]. The pathogenesis involves clonal expansion of B-cell–derived plasma cells, accompanied by production of abnormal monoclonal immunoglobulin (M-protein), which

can be detected in the serum or urine [3]. Clinically, MM presents with a constellation of symptoms summarized by the CRAB criteria: Calcium elevation (hypercalcemia), renal dysfunction, Anemia, and Bone lesions [4]. Bone pain, pathological fractures, recurrent infections, and generalized fatigue are common manifestations, leading to significant morbidity. The diagnostic framework for MM has evolved to incorporate advanced imaging and laboratory techniques, including serum protein electrophoresis, immunofixation, and free light chain assays, yet bone marrow examination remains the cornerstone for diagnosis [5].

Bone marrow aspirates in MM reveal varying proportions and morphologies of plasma cells. The percentage of plasma cell infiltration correlates with disease burden, while morphological subtyping provides insights into prognosis [6]. Mature plasma cells are typically associated with better outcomes, whereas plasmablastic and pleomorphic morphologies correlate with more aggressive disease and reduced survival [7]. Additional morphological features, such as multinucleation, Russell bodies, and Mott cells, though less common, contribute to the understanding of disease biology [8].

The study of MM morphology remains clinically relevant despite advances in molecular and cytogenetic characterization. Recent research emphasizes the integration of morphological assessment with cytogenetics and molecular markers to refine prognostic models [9]. However, in resource-limited settings, morphological examination of bone marrow continues to provide invaluable diagnostic and prognostic guidance at low cost.

In India, where access to advanced molecular techniques may be inconsistent, morphological analysis assumes even greater importance.

Regional variations in presentation, age of onset, and subtype distribution further highlight the need for population-specific data [10].

The present study was undertaken to analyze the clinical presentation and bone marrow morphology of MM cases diagnosed over a 5-year period at a tertiary care hospital. By correlating plasma cell morphology with clinical and laboratory findings, this study aimed to reinforce the diagnostic value of morphological assessment and contribute to the growing body of literature on MM in the Indian context.

Methodology

Study Design and Setting: This was a retrospective observational study conducted in the Department of Pathology, KIMS& RF, Amalapuram, and Andhra Pradesh, India. The study included cases diagnosed as multiple myeloma (MM) over a five-year period between January 2016 and December 2020. All cases were retrieved from departmental records, and relevant clinical and laboratory information was extracted for analysis.

Participants: A total of 28 patients diagnosed with MM during the study period were included. Diagnosis was established based on a combination of bone marrow examination, clinical features, radiological imaging, and laboratory parameters, in accordance with the World Health Organization (WHO) diagnostic criteria for multiple myeloma.

Inclusion Criteria

- Patients diagnosed with MM based on WHO diagnostic criteria.
- Availability of complete records, including bone marrow aspirates, peripheral smears, and supporting laboratory and radiological data.
- Age ≥18 years.

Exclusion Criteria

- Patients with incomplete records or unavailable bone marrow aspirates.
- Cases of plasma cell leukemia or solitary plasmacytoma without systemic features.
- Patients with other concurrent hematological malignancies.

Data Collection

Clinical and demographic information was collected from patient case files, including:

- Age and sex
- Presenting complaints (bone pain, backache, fatigue, fever, weight loss, pathological fractures)
- CRAB criteria (hypercalcemia, renal impairment, anemia, bone lesions)
- Relevant medical history
- Laboratory investigations recorded were:
- Complete blood counts (CBC) with hemoglobin, total leukocyte count, platelet count, and erythrocyte sedimentation rate (ESR)
- Peripheral blood smear (PBS) examination for rouleaux formation and other changes
- Biochemical parameters including serum calcium, renal function tests, and serum protein levels
- Serum protein electrophoresis for detection of M-protein (M-band)
- Radiological investigations such as skeletal surveys to detect lytic bone lesions and pathological fractures

Bone Marrow Examination: Bone marrow aspiration was the primary diagnostic tool. The

smears were stained with Leishman's stain and Giemsa stain, and examined under light microscopy. The following parameters were evaluated:

- Percentage of plasma cells in the bone marrow.
- Morphological classification of plasma cells into four subtypes:
    1. Mature
    2. Immature
    3. Plasmablastic
    4. Pleomorphic
- Cytoplasmic inclusions such as Russell bodies, Mott cells, Dutcher bodies, and flame cells.
- Nuclear characteristics, including multinucleation, binucleation, and Quadri nucleation.
- Presence of abnormal forms, such as giant plasma cells or pleomorphic cells.

Outcome Measures

The primary outcomes assessed were:

- Distribution of morphological subtypes of plasma cells in the study population.
- Frequency of morphological variations, including multinucleated plasma cells and cytoplasmic inclusions.
- Correlation of morphology with clinical features, hematological findings, and radiological evidence.

Statistical Analysis: Data were compiled in Microsoft Excel and analyzed using SPSS version 25.0. Descriptive statistics were used to summarize baseline characteristics. Continuous variables, such as age and hemoglobin, were expressed as mean ± standard deviation, while categorical variables were expressed as frequencies and percentages.

The correlation between plasma cell morphology and clinical/laboratory features was analyzed using chi-square test or Fisher's exact test, where applicable. A p-value <0.05 was considered statistically significant.

Ethical Considerations: This was a retrospective study using previously collected patient data. Patient confidentiality was maintained by anonymizing records before analysis.

Institutional ethical clearance was obtained from the Institutional Ethics Committee of KIMS& RF, Amalapuram prior to commencement of the study.

Results

Demographic Characteristics: A total of 28 patients diagnosed with multiple myeloma were included in this study. The age range was 37–75 years, with a mean age of 57 years. The male-to-female ratio was 1.3:1, with 16 males (57%) and 12 females (43%).

Table 1: Age and Sex Distribution of Patients

Parameter	Findings
Age range	37 – 75 years
Mean age	57 years
Males	16 (57%)
Females	12 (43%)

Clinical Presentation: The most common presenting complaint was bone pain (71.4%), followed by loss of weight and appetite (57.1%) and generalized weakness (46.4%). Other manifestations included fever (32%) and pathological fractures (7.1%). Lytic lesions on radiographs were observed in 57% of cases.

Table 2: Clinical Features of Patients with Multiple Myeloma

Clinical Feature	No. of Cases (%)
Bone pain / low backache	20 (71.4%)
Generalized weakness	13 (46.4%)
Weight loss / anorexia	16 (57.1%)
Fever	9 (32.0%)
Lytic bone lesions	16 (57.0%)
Pathological fractures	2 (7.1%)

Laboratory Findings: Anemia was present in 92.8% of cases, with hemoglobin as low as 2.8 g/dL. Based on severity, mild anemia was seen in 39.2% (11 cases), moderate anemia in 28.5% (8 cases), and severe anemia in 25% (7 cases). The erythrocyte sedimentation rate (ESR) was elevated in all patients, with a maximum recorded value of 140 mm/hr in the first hour. Serum electrophoresis demonstrated M-band positivity in the majority of patients. Peripheral smear examination showed rouleaux formation in 35.5% of cases.

Table 3: Hematological and Biochemical Findings

Parameter	Findings
Anemia	26 cases (92.8%)
– Mild (Hb 10–11.9 g/dL)	11 cases (39.2%)
– Moderate (Hb 7–9.9 g/dL)	8 cases (28.5%)
– Severe (Hb <7 g/dL)	7 cases (25.0%)
ESR	Elevated in 28 cases (100%)
Rouleaux formation (PBS)	10 cases (35.5%)
Serum M-band (electrophoresis)	Positive in majority of patients
Hypercalcemia (>11 mg/dL)	2 cases (7.1%)

Bone Marrow Morphology: Bone marrow aspirates revealed a plasma cell burden between 20%–70% across the cases. The predominant morphological subtype was mature plasma cell myeloma (61%), followed by mixed mature/immature (18%), pleomorphic (11%), and plasmablastic (10%) types. Morphological variations included binucleated and multinucleated plasma cells in 46.4% of cases, binucleation alone in 10%, and rare Quadri nucleated forms (3.5%). Mott cells were identified in 2 cases and Russell bodies in 1 case. Notably, Dutcher bodies and flame cells were absent in this cohort.

Table 4: Morphological Variants of Plasma Cells

Morphological Pattern	Cases (%)
Mature plasma cells	17 (61%)
Mixed mature + immature	5 (18%)
Pleomorphic plasma cells	3 (11%)
Plasmablastic plasma cells	3 (10%)
Multinucleated plasma cells	13 (46.4%)
Binucleated plasma cells	3 (10%)
Quadrinucleated plasma cells	1 (3.5%)
Mott cells	2 (7.1%)
Russell bodies	1 (3.5%)
Dutcher bodies / Flame cells	None observed

Summary of Key Findings

- Median age: 57 years, male predominance (1.3:1).
- Most common symptoms: bone pain (71.4%), weakness (46.4%), and weight loss (57.1%).
- Anemia (92.8%) and raised ESR (100%) were almost universal findings.
- Radiological lytic lesions (57%) were frequently detected.
- Bone marrow morphology was dominated by mature plasma cells (61%), with plasmablastic and pleomorphic types less common.
- Multinucleation was a common feature, whereas Dutcher and flame cells were absent.

Discussion

The present study analyzed 28 cases of multiple myeloma (MM) diagnosed over a five-year period, with emphasis on demographic patterns, clinical presentation, hematological findings, and morphological characteristics of plasma cells in the bone marrow. Our results reaffirm the centrality of bone marrow morphology in both diagnosis and prognostication of MM while also providing insights into the variability of clinical and morphological profiles within the Indian population.

Demographic Characteristics: The mean age of patients in our cohort was 57 years, with a range of 37–75 years. This is slightly younger than the mean age of 65–70 years reported in Western populations [11,12].

A modest male predominance (male-to-female ratio 1.3:1) was observed, consistent with findings from Robert et al. and Zervas et al., who reported similar ratios [13,14]. Regional variability may partly explain the relatively younger onset observed in our study, as previous Indian studies have also reported median ages between 55 and 60 years [15].

Clinical Presentation: Bone pain was the most frequent symptom (71.4%), followed by generalized weakness (46.4%) and weight loss with anorexia (57.1%). These findings align with Shaheen et al. and Kyle et al., who reported bone pain as the dominant presenting complaint in more than two-thirds of their patients [16,17]. The presence of lytic lesions in 57% of our cohort is comparable to the 60–75% frequency reported by Kaur et al. and other Western series [18]. Pathological fractures, though uncommon in our study (7.1%), represent a recognized complication of skeletal involvement in advanced disease.

Generalized weakness and constitutional symptoms, including weight loss and anorexia, reflect the systemic burden of the disease and correlate with anemia and hypermetabolic activity of plasma cells. Fever was present in 32% of patients, which, though nonspecific, may be attributed to recurrent infections secondary to immunoparesis.

Hematological and Biochemical Findings: Anemia was nearly universal (92.8%) in our study population. This figure is higher than the 68% reported by Bartl et al. and the 30% observed in the series by Singhal et al. [19,20]. The disparity may stem from differences in inclusion criteria, nutritional status, or stage of disease at presentation. Anemia in MM is typically multifactorial, resulting from bone marrow infiltration, renal dysfunction, and cytokine-mediated suppression of erythropoiesis.

ESR was elevated in all patients, consistent with the role of increased immunoglobulin production and altered plasma viscosity. Serum electrophoresis revealed M-band positivity in the majority of cases, reaffirming the utility of electrophoresis as a first-line laboratory diagnostic test.

Interestingly, hypercalcemia was detected in only 7.1% of our patients, which is lower than the 23–51% reported in studies by Mansoor et al. and Shaheen et al. [21,16]. The relatively low incidence of hypercalcemia in our series may reflect earlier diagnosis or differences in tumor biology.

Bone Marrow Morphology: Bone marrow aspirates showed a plasma cell burden ranging between 20–70%. The morphological distribution was dominated by mature plasma cells (61%), followed by mixed mature/immature forms (18%), pleomorphic (11%), and plasmablastic types (10%). This predominance of mature morphology parallels observations by Carter et al. and Subhramanian et al. [22,23]. In contrast, Kuriakose et al. reported a much higher proportion of immature and plasmablastic variants, highlighting inter-study variability [24].

The plasmablastic variant is of particular clinical importance due to its association with aggressive disease, high proliferative index, and poorer prognosis. Although present in only 10% of our patients, recognition of this subtype is essential for early identification of high-risk cases. Similarly, pleomorphic morphology, seen in 11% of our patients, has been linked to advanced disease and poor survival.

Multinucleation was a prominent finding in nearly half of our cases (46.4%). Binucleation and quadrinucleation represent cytological abnormalities reflecting dysregulated mitosis and genomic instability, features often associated with disease progression. Cytoplasmic inclusions such as Mott cells and Russell bodies, though rare in our series, underscore the diversity of morphological manifestations of plasma cell neoplasms. The absence of Dutcher bodies and flame cells may be incidental, given their relatively low frequency in most reported series.

Comparison with Literature: The overall spectrum of plasma cell morphology in our study demonstrates concordance with several previously published cohorts, but with important differences. Griepp et al. reported 28% mature, 19% immature, and 15% plasmablastic cases in their study of 100 patients [25], contrasting with the higher frequency of mature plasma cells in our population. This difference may be attributable to genetic, environmental, or diagnostic variations. Similarly, while Carter et al. observed pleomorphic variants in 11.5% of cases, our findings of 11% suggest comparable trends.

The presence of Mott cells and Russell bodies in a subset of our patients emphasizes the need to carefully evaluate cytoplasmic features, as these may occasionally lead to diagnostic confusion with reactive plasmacytosis. However, the high plasma cell burden and associated clinical features in our patients supported the diagnosis of MM.

Clinical Implications: The morphological assessment of bone marrow aspirates remains a low-cost, highly informative diagnostic modality, especially in resource-limited settings where advanced cytogenetic and molecular testing may not be readily available. The predominance of mature morphology in our study suggests a relatively favorable prognostic trend. Conversely, plasmablastic and pleomorphic morphologies, although less frequent, highlight the heterogeneity of MM and the need for stratified therapeutic approaches. Moreover, the high prevalence of anemia and skeletal lesions underscores the importance of early diagnosis and supportive care in improving quality of life. Clinicians should remain vigilant for subtle morphological cues that may indicate aggressive disease, as these can guide treatment decisions and follow-up strategies.

Strengths of the Study: A notable strength of this study is the detailed morphological characterization of plasma cells across multiple subtypes, supported by correlation with clinical and laboratory parameters. The inclusion of consecutive cases over a defined period minimizes selection bias and provides a realistic snapshot of MM presentation in our setting.

Limitations: The primary limitation lies in the retrospective design and the relatively small sample size of 28 cases, which restricts the generalizability of our findings. Lack of cytogenetic and molecular

data also limits the ability to integrate morphological observations with underlying genomic alterations.

Future Directions: Future research should aim to correlate plasma cell morphology with cytogenetic markers such as del (17p), t(4;14), and gain(1q21), which have well-established prognostic implications. Prospective, multicenter studies with larger sample sizes will help validate the prognostic significance of morphological variants.

Additionally, the incorporation of digital pathology and image analysis may allow for more objective classification of plasma cell morphology and identification of subtle morphological features that are often overlooked during manual evaluation.

Conclusion

In summary, our findings reinforce the diagnostic and prognostic relevance of bone marrow morphology in MM. While the majority of patients in our cohort exhibited mature plasma cell morphology, the presence of plasmablastic and pleomorphic variants in a subset underscores the heterogeneity of the disease and its prognostic implications.

Careful morphological evaluation, integrated with clinical, biochemical, and radiological findings, remains indispensable in the comprehensive management of MM, particularly in regions where advanced diagnostics may not be widely accessible.

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