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Comparative Diagnostic Performance of Flow Cytometry, Aspiration, and Biopsy with Immunohistochemistry in Plasma Cell Neoplasms

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ABSTRACT

Background: Plasma cell neoplasms (PCNs) are a heterogeneous group of hematologic malignancies that require accurate and timely diagnosis for effective management. Despite the availability of multiple diagnostic tools, challenges remain due to clinical and morphological variability. This study aimed to compare the diagnostic performance of three key modalities, including flow cytometry (FCM), bone marrow aspiration (BMA), and bone marrow biopsy with immunohistochemistry (BMB+IHC) in patients with plasma cell neoplasms.

Materials and Methods: A cross-sectional study was conducted on 52 patients with confirmed PCNs. Diagnostic outcomes from FCM, BMA, and BMB+IHC were evaluated and compared. Sensitivity, specificity, predictive values, and inter-method agreement were calculated using SPSS version 27.

Results: BMB+IHC achieved the highest diagnostic yield (100%), followed by BMA (55.8%), while FCM demonstrated the lowest diagnostic rate (32.7%). Flow cytometry showed excellent specificity and a positive predictive value of 100%, but limited sensitivity (32.7–58.6%), resulting in a high rate of false negatives. BMA frequently underestimated plasma cell burden due to sampling variability and hemodilution. Collectively, integration of all three methods provided complementary diagnostic value, reducing the risk of misclassification.

Conclusion: Bone marrow biopsy with immunohistochemistry remains the gold standard for diagnosing PCNs. However, combining it with aspiration and flow cytometry offers a more comprehensive diagnostic framework, improving accuracy, minimizing false negatives, and supporting optimal patient management.

Keywords: Plasma cell neoplasms; Flow cytometry; Bone marrow aspiration; Immunohistochemistry; Diagnostic performance

INTRODUCTION

Plasma cell neoplasms (PCNs) comprise a spectrum of disorders characterized by clonal proliferation of plasma cells, ranging from solitary plasmacytoma to systemic multiple myeloma. These conditions account for a major category of hematologic malignancies and are associated with significant morbidity and mortality[1,2]. Accurate diagnosis of plasma cell myeloma is crucial because it determines treatment choices, prognosis, and overall patient

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management. Misdiagnosis can delay care and worsen outcomes. Updated consensus guidelines highlight the need for further enhance diagnostic accuracy and efficiency, strengthening clinical decision-making. Early diagnosis is especially important since symptoms are often nonspecific; delays can result in advanced disease, organ damage, and reduced survival. Approaches, including blood smear evaluation and detection of circulating plasma cells, allow earlier recognition. Importantly, circulating plasma cells at diagnosis correlate with prognosis and help identify aggressive variants, such as plasma cell neoplasms. Overall, integrating sensitive diagnostic strategies ensures timely treatment and better patient outcomes [3-8].

Accurate and early diagnosis of plasma cell neoplasia faces numerous challenges, largely due to the disease's heterogeneous clinical presentation and non-specific symptoms like bone pain, anemia, and renal impairment that can easily be mistaken for benign or chronic conditions. Many patients are initially seen by general practitioners who may lack awareness of the "red flags" for plasma cell malignancies, causing delays and frequent misdiagnosis. Additionally, plasma cell neoplasms exhibit diverse morphological and immunophenotypic profiles, sometimes mimicking other cancers or lacking classic markers such as CD138 or detectable serum monoclonal proteins, which complicates laboratory and imaging interpretation and may require sophisticated, but not always accessible, diagnostic technologies. System-related barriers—such as limited access to advanced tests, poor coordination among specialists, and delays in referral from primary care—further hinder prompt detection; overcoming these requires educational initiatives, implementation of rapid diagnostic algorithms, and broader integration of novel methods like AI-based decision support and genetic profiling [7, 8].

Currently, three modalities form the cornerstone of PCNs diagnosis: flow cytometry (FCM), bone marrow aspiration (BMA), and bone marrow biopsy with immunohistochemistry (BMB+IHC). FCM enables multiparametric immunophenotyping and sensitive detection of clonal populations, including minimal residual disease, but may underestimate plasma cell burden due to sample dilution or cell fragility. BMA allows rapid cytomorphologic evaluation but is limited by patchy infiltration and hemodilution. BMB+IHC, using markers such as CD138, remains the reference method for quantification and spatial assessment of plasma cell infiltration, although it is invasive and subject to sampling variability [9-12].

Taken together, these modalities underscore the necessity of a complementary diagnostic approach rather than reliance on a single technique. While flow cytometry offers unparalleled sensitivity for detecting clonal populations and minimal residual disease, bone marrow aspiration provides rapid cellular morphology, and biopsy with immunohistochemistry ensures reliable quantification and spatial resolution of plasma cell infiltration. Comparative evaluation of these methods not only clarifies their individual diagnostic performance but also highlights how their integration can overcome inherent limitations, reduce the risk of misdiagnosis, and ultimately improve clinical decision-making. In this context, systematically assessing their relative strengths and weaknesses is critical for establishing optimized diagnostic algorithms that support timely, accurate, and patient-centered management of plasma cell neoplasms.

Materials and Methods

Study Design, Population, and Sample Size

This descriptive–analytical cross-sectional study was conducted at the Cancer Institute of Imam Khomeini Hospital, Tehran, between 2021 and 2023 (1400–1402). The study population comprised patients with a confirmed diagnosis of plasma cell neoplasms, including multiple myeloma and related disorders, whose pathology records contained concurrent results from both bone marrow flow cytometry (FCM) and bone marrow biopsy with immunohistochemistry (BMB+IHC).

Eligibility criteria included patients with a definitive diagnosis confirmed by either FCM or IHC, availability of both FCM and IHC results in the electronic pathology system, and complete clinical and laboratory records. Patients were excluded if medical records were incomplete or if either FCM or IHC results were unavailable.

Based on an assumed correlation coefficient of 0.4 between FCM and IHC results, with a significance level of 0.05 and study power of 0.8, the minimum required sample size was calculated as 46 patients. To compensate for potential missing or incomplete data (approximately 10%), the final target sample size was set at 51 patients.

Data Collection

Following approval by the institutional ethics committee, data were extracted anonymously from patients' electronic pathology records. Bone marrow aspirates were analyzed using multiparameter flow cytometry panels including CD19, CD45, CD56, CD117, CD138, and light chains. Biopsy specimens were reviewed by hematopathologists for histomorphology and immunohistochemical staining with CD138, K, and λ to confirm plasma cell infiltration and clonality.

For each eligible patient, demographic and clinical variables (age, sex, erythrocyte sedimentation rate (ESR), presence of lytic bone lesions, anemia, elevated serum creatinine, hypercalcemia, and bone marrow cellularity) were extracted. Pathology-related variables included the percentage of plasma cells in bone marrow aspirate smears, plasma cell percentage in biopsy sections based on CD138 immunostaining, bone marrow infiltration patterns (diffuse, interstitial, focal aggregate, or multifocal), monoclonality (K or λ light chain restriction), proportion of atypical plasma cells in FCM, and aberrant expression of immunophenotypic markers (CD19, CD45, CD56, CD117, CD138).

Statistical Analysis

Data were analyzed using SPSS software version 27. Continuous variables were expressed as mean ± standard deviation (SD) and categorical variables as frequencies and percentages. Pearson's correlation coefficient (or Spearman's rank test when applicable) was used to assess associations between FCM and IHC results. Agreement between methods was evaluated, and a P-value < 0.05 was considered statistically significant.

RESULTS

Patient Characteristics

A total of 52 patients with plasma cell neoplasms were evaluated. The mean age was 60.6 ± 11 years (range: 36–86 years), with 63.5% males and 36.5% females. Bone lesions were present in 77.8% of evaluable cases, and the mean ESR was 80.2 mm/hr. Hematological analysis revealed a mean hemoglobin of 8.99 g/dL, mean serum creatinine of 1.96 mg/dL, and mean serum calcium of 9.65 mg/dL. Bone marrow aspiration (BMA) showed a wide plasma cell percentage (0–90%, mean 18.5%), while bone marrow biopsy (BMB) demonstrated a higher infiltration rate (10–100%, mean 50.1%). Bone marrow cellularity averaged 57.7%. The most frequent infiltration pattern was diffuse (28/52, 53.8%), followed by multifocal (14/52, 26.9%) and focal (5/52, 9.6%).CD138 immunohistochemistry demonstrated a mean positivity of 38.7%, and clonality assessment revealed kappa restriction in 36.6% and lambda restriction in 63.4% of evaluable cases (Table 1).

Table 1: Baseline clinical, laboratory, and bone marrow characteristics of patients with plasma cell neoplasms

Variable	N	Minimum	Maximum	Mean	Std. Deviation	Frequency / Percent
Age (years)	52	36.00	86.00	60.55	10.98	-
Gender (Male/Female)	52	-	-	-	-	Male: 63.5% | Female: 36.5%
ESR (mm/hr)	52	9	143	80.23	29.77	-
Bone Lesions (Yes/No)	45	-	-	-	-	Yes: 77.8% | No: 22.2%
Hemoglobin (g/dL)	52	5.5	15.7	8.99	2.10	-
Serum Creatinine (mg/dL)	52	0.5	7.3	1.96	1.75	-
Serum Calcium (mg/dL)	52	6.6	15.0	9.65	1.99	-
BMA Plasma Cell %	51	0	90	18.53	22.87	-
BMB Plasma Cell %	47	10	100	50.05	27.97	-
Bone Marrow Cellularity (%)	52	13	100	57.75	22.54	-
BM Pattern (Diffuse/Other)	52	-	-	-	-	Diffuse: 53.8% | Interstitial: 1.9% Focal: 9.6% | Multifocal: 26.9% Diffuse+Interstitial: 7.7%
CD138 IHC Positivity (%)	52	1.1	100.0	38.66	28.74	-
Monoclonality (Kappa/Lambda)	41	-	-	-	-	Kappa: 36.6% | Lambda: 63.4%
Flow Cytometry CD38+/CD138+ (%)	52	1.1	100	39.08	28.76	-
Flow Cytometry CD56 (%)	52	0.19	77.6	9.07	15.36	-
Flow Cytometry CD117 (%)	52	0.02	55.44	3.71	9.70	-
Flow Cytometry CD19-/CD138+/CD45- (%)	52	0	98	37.69	28.80	-
Flow Cytometry Myeloma Cells (%)	52	0	78.4	11.75	17.29	-

Flow Cytometry Findings

Flow cytometry identified clonal plasma cells with mean CD38+/CD138+ positivity of 39.1%. The aberrant phenotype CD19–/CD45– was observed in a mean of 37.7% of plasma cells, while CD56 (9.1%) and CD117 (3.7%) showed variable expression. The mean proportion of myeloma cells was 11.8% (range: 0–78.4%). Assessment of sample quality showed that 69.2% of preparations were good quality, while 23.1% were hemodilute and 7.7% hypocellular, indicating that although nearly one-third of samples were suboptimal, the majority provided reliable diagnostic material (Table 2).

Table 2: Flow cytometry sample quality in patients with plasma cell neoplasms

Category	Frequency	Percent	Valid Percent	Cumulative Percent
Good Quality	36	69.2	69.2	69.2
Hemodilute	12	23.1	23.1	92.3
Hypocellular	4	7.7	7.7	100.0
Total	52	100.0	100.0	100.0

Diagnostic Yield of Different Modalities

When comparing overall diagnostic performance, bone marrow biopsy combined with immunohistochemistry (BMB+IHC) achieved definitive diagnosis in 100% of cases (52/52), establishing it as the gold standard. In contrast, BMA was diagnostic in 55.8% (29/52), while flow cytometry yielded the lowest diagnostic capacity, with only 32.7% (17/52) being diagnostic (Table 3).

Table 3: Comparative diagnostic yield of flow cytometry, bone marrow aspiration, and bone marrow biopsy with immunohistochemistry in plasma cell neoplasms

Method	Diagnostic	Non-Diagnostic	Total	Diagnostic Percent	Non-Diagnostic Percent
Flow Cytometry	17	35	52	32.7	67.3
BMA	29	23	52	55.8	44.2
BMB + IHC	52	0	52	100.0	0.0

Comparative Diagnostic Performance of Flow Cytometry

Further analysis was performed to assess the relative diagnostic performance of flow cytometry against the two conventional methods. When compared with BMA, flow cytometry correctly identified 17 cases that were also diagnostic by aspiration (true positives), while 12 cases were missed despite being positive by BMA (false negatives). Twenty-three cases were negative in both methods (true negatives), and no false positives were observed. Based on these results, flow cytometry achieved a sensitivity of 58.6%, specificity of 100%, PPV of 100%, and NPV of 65.7%, with a moderate overall agreement (Kappa = 0.556, $p < 0.001$) (Table 4). When compared with BMB+IHC, flow cytometry demonstrated complete agreement for the 17 positive cases (PPV = 100%). However, 35 additional diagnostic cases were identified exclusively by BMB+IHC and missed by flow cytometry, resulting in a markedly lower sensitivity of 32.7%. These findings underscore that while flow cytometry provides excellent specificity and reliably confirms positive results, it substantially underestimates the true diagnostic burden when used alone, generating a considerable number of false negatives (Table 4).

Table 4: Diagnostic accuracy of flow cytometry relative to BMA and BMB with IHC

Comparison	Reference Method	Flow Cytometry Positive	Flow Cytometry Negative	Total	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Kappa (p-value)
Flow cytometry vs BMA	BMA Diagnostic	17 (TP)	12 (FN)	29	58.6	100	100	65.7	0.556 (<0.001)
	BMA non-diagnostic	0 (FP)	23 (TN)	23					
Flow cytometry vs BMB+IHC	BMB+IHC Diagnostic	17 (PPV = 100%)	35 (FN, Sensitivity = 32.7%)	52	32.7	100	100	–	–
	BMB+IHC Non-diagnostic	0	0	0					

BMA, bone marrow aspiration; BMB, bone marrow biopsy; IHC, immunohistochemistry; TP, true positive; FP, false positive; FN, false negative; TN, true negative; PPV, positive predictive value; NPV, negative predictive value

DISCUSSION

Plasma cell neoplasms, such as multiple myeloma (MM) and other terminally differentiated B-cell malignancies, are defined by the production of monoclonal immunoglobulins and typically evolve in a stepwise manner from a precursor condition known as monoclonal gammopathy of undetermined significance (MGUS), which represents a clonal proliferation of B or plasma cells. The diagnosis of these disorders relies on a combination of clinical findings, laboratory tests, and morphological evaluation [13]. Accurate and thorough diagnosis of plasma cell neoplasia is critically important because these disorders display wide morphological and immunophenotypic variability, often mimicking both hematopoietic and non-hematopoietic tumors, which can easily lead to diagnostic confusion and delayed treatment. Distinguishing plasma cell neoplasms from their mimics typically requires an integrated approach, employing morphologic analysis, immunohistochemistry, flow cytometry, and, when needed, molecular and cytogenetic studies to confirm clonality and exclude other malignancies. Ensuring diagnostic accuracy is crucial for selecting the proper therapy and implementing timely interventions, thereby improving patient outcomes and reducing the risk of complications arising from misdiagnosis or inappropriate management[14-16]. Here, we aimed to evaluate and compare the diagnostic performance of flow cytometry, bone marrow aspiration, and bone marrow biopsy with immunohistochemistry in patients with plasma cell neoplasms. The findings showed that although each method has its own value, bone marrow biopsy with immunohistochemistry provides the most reliable diagnostic accuracy, while flow cytometry and aspiration serve as important complementary tools. Overall, the study highlights that integrating morphological, immunophenotypic, and histological approaches enhances diagnostic precision and supports better clinical decision-making in plasma cell disorders.

Flow cytometry, bone marrow aspiration, and bone marrow biopsy with immunohistochemistry are considered among the main diagnostic tools in plasma cell neoplasms. Flow cytometry is a key diagnostic tool in plasma cell neoplasms, providing sensitive detection and quantification of normal and clonal plasma cells in bone marrow through multiparametric antigen analysis (e.g., CD38, CD138, CD45, CD56, CD19, CD27, CD81, and light chains). By distinguishing malignant from reactive plasma cells, it aids in differential diagnosis and excludes non-neoplastic conditions with greater sensitivity and specificity than standard histopathology. It is also indispensable for minimal residual disease (MRD) detection, with next-generation flow reaching sensitivities of 1 in 100,000–1,000,000 cells, now incorporated into treatment response criteria. Beyond diagnosis, it provides prognostic information on survival outcomes, helps predict progression in precursor states such as MGUS and smoldering myeloma, and supports therapeutic decision-making throughout disease monitoring[10,11,17-19]. Bone marrow aspiration (BMA) is a central diagnostic tool

in plasma cell neoplasms, enabling cytological evaluation and quantification of plasma cells, which is critical for distinguishing MGUS, smoldering multiple myeloma, and overt multiple myeloma. It provides essential diagnostic and prognostic information, with IMWG criteria requiring ≥10% clonal plasma cells or a biopsy-proven plasmacytoma plus myeloma-defining events. While BMA allows for morphology, flow cytometry, cytogenetics, and molecular analyses, its limitations include dilution with peripheral blood and patchy marrow involvement, which may underestimate plasma cell burden—reported in up to 30% of cases compared with biopsy or immunohistology. Despite these challenges, BMA remains indispensable for diagnosis, staging, treatment monitoring, and minimal residual disease assessment in plasma cell disorders[9,20-22]. Bone marrow biopsy (BMB) with immunohistochemistry (IHC) is essential for diagnosing and characterizing plasma cell neoplasms, as it enables evaluation of marrow architecture and detection of focal or patchy infiltrates often missed by aspiration. IHC improves diagnostic accuracy by identifying and quantifying plasma cells using markers like CD138, CD38, and light chains, while confirming clonality. This approach is particularly valuable in low-level or patchy disease, ambiguous morphology, or aspiration-limited samples, and also permits assessment of the marrow microenvironment, amyloid or pathological deposits, and distinction between reactive and neoplastic plasma cell proliferations. Together, BMB and IHC provide a comprehensive and reliable basis for diagnosis, classification, staging, and prognostication, guiding effective clinical management[9, 10, 23].

Flow cytometry, BMA, and bone marrow biopsy with immunohistochemistry (BMB+IHC) are complementary yet distinct diagnostic tools for plasma cell neoplasms (PCNs), each with unique strengths and limitations. Flow cytometry excels in rapidly identifying and quantifying circulating and marrow plasma cells, detecting minimal residual disease, and distinguishing neoplastic from normal plasma cells using multiparameter immunophenotyping; however, its accuracy depends on sample quality and may be affected by hemodilution or low tumor burden. BMA provides direct cytological assessment and plasma cell quantification, which is essential for initial diagnosis and classification, but may underestimate tumor load due to dilution or focal marrow involvement, thus missing PCNs cases with patchy or uneven infiltration. BMB combined with IHC enables detailed evaluation of marrow architecture, identifies focal infiltrates, and confirms clonality and plasma cell phenotype in situ, which is particularly valuable in ambiguous cases or when aspirate yields inconclusive results; nevertheless, it is invasive, more resource-intensive, and may suffer from sampling bias if disease distribution is uneven[9,17, 18, 21, 23].

In our cross-sectional of 52 patients, BMB+IHC demonstrated the highest diagnostic yield, achieving definitive diagnosis in 100% of cases, whereas BMA was diagnostic in 55.8% and non-diagnostic in 44.2%, and flow cytometry showed the lowest diagnostic capacity with 32.7% diagnostic and 67.3% non-diagnostic results. Comparative analysis showed that flow cytometry had excellent specificity and positive predictive value (PPV = 100%), but lower sensitivity when compared to both BMA (58.6%) and BMB+IHC (32.7%), resulting in a considerable number of false negatives.

Our findings are consistent with a growing body of literature emphasizing the strengths and limitations of each modality .Monteiro et al. compared BMB, BMA, BM IHC, and FCM in 67 patients with plasma cell disorders and found discrepancies in 55.2% of cases, with BMB consistently demonstrating higher plasma cell percentages than either BMA or FCM. Importantly, flow cytometry exhibited the lowest concordance with BMB (κ = 0.17), reflecting its tendency to underestimate infiltration, particularly in samples complicated by hemodilution or fibrosis. Their observations closely mirror our own, in which underestimation by FCM was common and contributed to a high false-negative rate[21].

Gjelberg et al. reached similar conclusions, showing that BMB consistently provided higher plasma cell percentages compared to aspirates or flow cytometry. They emphasized that discrepancies near diagnostic thresholds specifically 10% (distinguishing MGUS from SMM or MM) and 60% (diagnostic of

MM according to IMWG criteria) can lead to misclassification and inappropriate management. In our study, nearly half of the cases were underestimated by BMA, confirming that aspirates alone are insufficient for accurate quantification and classification[24].

Our findings also in line with Stifter et al. , demonstrate that bone marrow biopsy with immunohistochemistry (BMB+IHC) provides superior diagnostic sensitivity and more accurate plasma cell quantification compared to bone marrow aspiration and flow cytometry. This combined approach not only enhances diagnostic accuracy but also correlates with clinical staging and prognosis, supporting its role as the cornerstone in the evaluation of plasma cell neoplasms[25].

Flow cytometry and aspiration remain valuable complementary tools, particularly for MRD detection and rapid phenotypic assessment, but should not replace BMB+IHC as the primary diagnostic method. The role of sample quality in aspirate-based diagnostics has also been highlighted. A study investigating first-pull aspirates for FCM showed that early aspirates provided higher plasma cell yields and better diagnostic performance by minimizing peripheral blood contamination. Our findings, where approximately one-third of aspirates were hemodilute or hypocellular, echo this limitation and explain the lower diagnostic sensitivity of FCM (32.7%) observed in our cohort [26].

Further evidence comes from studies directly comparing IHC and FCM in large patient populations. Johnsen et al. and Paiva et al. showed systematic underestimation of plasma cell infiltration by FCM compared to morphology or biopsy. More recently, a large-scale series of 89 myeloma patients confirmed that plasma cell percentages were significantly higher by IHC (median 50%) than by FCM (median 6%), although the two modalities correlated positively ($R = 0.44$, $p < 0.001$)[20]. Importantly, IHC was superior in documenting light chain restriction (98% vs. 90%), while FCM excelled in identifying aberrant phenotypes such as CD19 loss and CD45 expression. These findings reinforce the complementary nature of both techniques: IHC as the most reliable method for quantification, and FCM as a valuable tool for clonality assessment, immunophenotypic characterization, and minimal residual disease monitoring [27, 28].

Earlier reports, including those by Rawstron et al., further demonstrated that BMB+IHC is particularly reliable in detecting clonal plasma cells in cases of patchy or low-level disease. Collectively, these studies highlight a consistent pattern across cohorts: BMB+IHC provides the most accurate baseline quantification, whereas FCM and BMA add complementary, but not interchangeable, diagnostic value [18].

Taken together, our results and those of prior studies support a consensus model in which BMB+IHC should be regarded as the gold standard for quantification and architectural assessment of plasma cell infiltration. BMA provides rapid cytomorphologic assessment and supports ancillary studies such as cytogenetics and molecular profiling, but is vulnerable to sampling variability and peripheral blood dilution. FCM, while prone to underestimation of plasma cell burden, offers unparalleled sensitivity for clonality assessment, detection of aberrant immunophenotypes, and longitudinal minimal residual disease monitoring.

The combined application of these modalities is not only complementary but also necessary. As recommended by the European Myeloma Network, an integrated diagnostic framework incorporating BMB+IHC for reliable quantification, BMA for cytology and ancillary testing, and standardized multiparametric FCM for clonality and MRD monitoring minimizes false negatives, reduces diagnostic uncertainty, and ensures more accurate risk stratification and disease classification [29].

Strengths and Limitation

This study's strengths include the direct comparison of three diagnostic modalities (flow cytometry, BMA, and BMB+IHC) within the same cross-sectional study, a sample of 52 cases, assessment of flow cytometry sample quality, and comprehensive statistical analysis of diagnostic performance. Limitations include its single-center design, relatively small sample size, potential sampling bias from focal marrow involvement, reliance on BMB+IHC as the gold standard without long-term clinical correlation, and the high dependence of flow cytometry on

specimen quality. In addition, only biopsy-confirmed plasma cell neoplasms were included, which may introduce selection bias and underestimate the role of flow cytometry in cases where biopsy is inconclusive. Overall, the findings highlight the superior sensitivity of BMB+IHC and the complementary role of BMA and flow cytometry, but larger multi-center studies with outcome-based validation are needed.

CONCLUSION

This study highlights the comparative diagnostic value of bone marrow biopsy with immunohistochemistry, bone marrow aspiration, and flow cytometry in plasma cell neoplasms. While BMB+IHC demonstrated superior sensitivity and established definitive diagnosis in all cases, both FCM and BMA provided important complementary information. Flow cytometry, despite its high specificity and prognostic utility, showed reduced sensitivity and was prone to false negatives, while bone marrow aspiration often underestimated disease burden due to patchy infiltration and hemodilution. Taken together, these findings confirm that an integrated approach, combining histopathology, morphology, and immunophenotyping, is essential for accurate diagnosis, timely treatment initiation, and improved patient outcomes in plasma cell disorders. Future multicenter studies with standardized protocols are warranted to further validate these observations.

Abbreviations

AI: Artificial Intelligence
BMA: Bone Marrow Aspiration
BMB: Bone Marrow Biopsy
BMB+IHC: Bone Marrow Biopsy with Immunohistochemistry
BM: Bone Marrow
CD: Cluster of Differentiation
ESR: Erythrocyte Sedimentation Rate
FN: False Negative
FP: False Positive
FCM: Flow Cytometry
IHC: Immunohistochemistry
IMWG: International Myeloma Working Group
MGUS: Monoclonal Gammopathy of Undetermined Significance
MM: Multiple Myeloma
MRD: Minimal Residual Disease
NPV: Negative Predictive Value
PCN: Plasma Cell Neoplasm
PPV: Positive Predictive Value
SD: Standard Deviation
SPSS: Statistical Package for the Social Sciences
TN: True Negative
TP: True Positive

CONFLICT OF INTEREST

The authors declare that they have no competing interests

Ethics approval and consent to participate

This study was approved by the Ethics Committee of Tehran University of Medical Sciences, Imam Khomeini Hospital Complex (Approval Code: IR.TUMS.IKHC.REC.1402.404). All procedures were conducted in accordance with the ethical standards of the institutional and national research committees and with the Declaration of Helsinki. Written informed consent was obtained from all participants prior to inclusion in the study.

Consent for publication

Not applicable.

Data availability

The datasets used in this study can be found in online repositories, the name of which can be found in the article. Other data presented in this study are available on request from the corresponding authors.

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