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Research Article

Morphological Assessment of Megakaryocytes in Bone Marrow Aspirates in Different Hematological Conditions: A Descriptive Observational Study from a Tertiary Care Centre in Jaipur

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ABSTRACT

Background: Megakaryocytes play a pivotal role in thrombopoiesis, and alterations in their morphology provide valuable diagnostic information in a wide spectrum of hematological disorders. Although bone marrow aspiration is routinely performed for the evaluation of cytopenias and hematological malignancies, the diagnostic significance of megakaryocyte morphology across different disease entities remains underexplored.

Methods: A descriptive observational study was conducted in the Department of Pathology, SMS Medical College, Jaipur, including 150 consecutive bone marrow aspiration specimens from patients with various hematological disorders. Bone marrow aspirates were evaluated for marrow cellularity, megakaryocyte number, and qualitative morphological alterations. Morphological abnormalities were categorized as dysplastic, non-dysplastic, or mixed. Clinical findings and hematological diagnoses were correlated with megakaryocyte morphology using appropriate statistical analysis, with a p-value <0.05 considered statistically significant.

Results: Of the 150 cases, 100 (66.7%) were neoplastic and 50 (33.3%) were non-neoplastic disorders. Hypercellular marrow was observed in 55.3% of patients. Altered megakaryocyte morphology was identified in 90.0% of cases, with mixed morphological changes being the most frequent pattern (45.3%). Hypolobulated megakaryocytes (50.0%), immature forms (36.7%), and micromegakaryocytes (35.3%) were the predominant abnormalities. Dysplastic megakaryocyte features were significantly more common in neoplastic disorders than in non-neoplastic disorders (87.0% vs. 48.0%, p<0.001). Megakaryocyte number also demonstrated significant variation across different hematological diagnoses.

Conclusion: Systematic evaluation of megakaryocyte number and morphology during bone marrow aspiration provides important diagnostic information and significantly improves differentiation between reactive and neoplastic hematological disorders. Megakaryocytic assessment should be considered an integral component of routine bone marrow examination.

Keywords: Megakaryocyte, Bone Marrow Aspiration, Hematological Disorders, Dysmegakaryopoiesis, Thrombocytopenia, Bone Marrow Morphology.

INTRODUCTION

Megakaryocytes are highly specialized hematopoietic cells responsible for platelet production and the maintenance of normal hemostasis. (1) They originate from pluripotent hematopoietic stem cells within the bone marrow and undergo a unique maturation process characterized by endomitosis, resulting in large polyploid cells capable of releasing thousands of platelets into the circulation. Thrombopoietin serves as the principal regulator of megakaryocyte proliferation, differentiation, and maturation, while several transcription factors and cytokine-mediated pathways contribute to normal megakaryopoiesis. Because platelet production depends directly on the integrity of megakaryocyte development, abnormalities in

these cells frequently reflect underlying hematological diseases and may provide valuable diagnostic information during bone marrow evaluation.(2,3)

Morphological alterations of megakaryocytes occur in a broad spectrum of hematological disorders and may involve quantitative as well as qualitative abnormalities. Quantitative alterations include increased, decreased, or absent megakaryocytes, whereas qualitative abnormalities comprise dysplastic features such as micromegakaryocytes, hypolobulated nuclei, multinucleation, hypogranular cytoplasm, and bizarre nuclear forms, along with non-dysplastic changes including immature megakaryocytes, emperipolesis, cytoplasmic budding, vacuolization, bare nuclei, giant forms, and hyperlobulated nuclei.(5) Although some of these alterations are characteristic of clonal hematological disorders, others may occur as reactive changes in immune-mediated, nutritional, infectious, or inflammatory conditions. Careful interpretation is therefore essential for accurate diagnosis.(4,6)

Bone marrow aspiration remains one of the most valuable diagnostic procedures in hematology because it allows simultaneous assessment of marrow cellularity, hematopoietic lineage maturation, and megakaryocyte morphology. (8,9) Evaluation of megakaryocytes is particularly useful in patients presenting with thrombocytopenia, thrombocytosis, unexplained cytopenias, leukemias, myelodysplastic syndromes (MDS), myeloproliferative neoplasms (MPNs), aplastic anemia, and various nutritional anemias. In immune thrombocytopenic purpura (ITP), increased numbers of morphologically reactive megakaryocytes generally indicate compensatory platelet production, whereas reduced megakaryocyte numbers are frequently observed in acute leukemias, marrow failure syndromes, and advanced myelodysplastic disorders. Similarly, characteristic dysplastic morphology including micromegakaryocytes and hypolobulated forms serves as an important diagnostic clue in MDS and other clonal myeloid neoplasms.(7)

Several investigators have demonstrated that systematic evaluation of megakaryocyte morphology substantially improves the diagnostic interpretation of bone marrow aspirates. Previous studies have reported considerable variability in megakaryocyte morphology among different hematological disorders; however, most have focused primarily on thrombocytopenic patients or individual disease categories rather than evaluating the complete spectrum of neoplastic and non-neoplastic disorders within a single cohort. Consequently, comparative data describing quantitative and qualitative megakaryocyte alterations across diverse hematological diseases remain relatively limited, particularly in tertiary care settings in developing countries. (10)

Accurate morphological assessment of megakaryocytes has gained additional clinical importance despite advances in molecular diagnostics and immunophenotyping. Although genetic and molecular investigations provide disease-specific information, bone marrow aspiration continues to represent an inexpensive, readily available, and highly informative diagnostic tool, especially in resource-limited healthcare systems. Recognition of characteristic megakaryocyte alterations can facilitate early diagnosis, support disease classification, guide further ancillary investigations, and improve clinical decision-making before advanced molecular studies become available.(15)

MATERIALS AND METHODS

Study Design and Setting

This descriptive observational study was conducted in the Department of Pathology, SMS Medical College and Hospital, Jaipur, Rajasthan. The study was carried out after obtaining approval from the Institutional Ethics Committee over a period of nine months, with an additional two months allocated for data analysis and manuscript preparation.

Study Population

The study included patients with various hematological disorders who underwent bone marrow aspiration as part of their routine diagnostic evaluation. Consecutive eligible bone marrow aspiration specimens received during the study period were included until the required sample size was achieved.

Sample Size

A total of 150 patients were enrolled. The sample size was calculated at a 95% confidence level using an expected prevalence of megakaryocyte morphological alterations of 10.2% and an absolute allowable error of 5%.

Inclusion Criteria

- Bone marrow aspiration specimens with adequate cellularity.
- Patients undergoing bone marrow aspiration for evaluation of hematological disorders.
- Patients providing informed written consent.

Exclusion Criteria

- Patients unwilling to participate.

- Diluted bone marrow aspirates.
- Dry-tap aspirations unsuitable for morphological evaluation.

Bone Marrow Evaluation

Clinical details, complete blood count, and peripheral blood smear findings were recorded before bone marrow examination. Bone marrow aspiration was performed under aseptic precautions using a Salah aspiration needle, predominantly from the posterior iliac crest under local anesthesia. Multiple aspiration smears were prepared immediately, air-dried, and stained using Leishman and May-Grünwald–Giemsa stains according to standard laboratory protocols.

Each bone marrow aspirate was initially evaluated for overall marrow cellularity and categorized as hypercellular, normocellular, or hypocellular. Megakaryocytes were subsequently assessed quantitatively and qualitatively by experienced pathologists using light microscopy.

Megakaryocyte Assessment

Megakaryocyte number was assessed on representative marrow particles over multiple low-power fields and categorized as normal, increased, or decreased according to predefined laboratory criteria.

Morphological evaluation was performed under high-power magnification. Megakaryocyte morphology was classified as normal or altered. Morphological alterations were further categorized into dysplastic, non-dysplastic, or mixed patterns.

The Dysplastic Features Evaluated Included

- Micromegakaryocytes
- Hypolobulated nuclei
- Multiple separated nuclei
- Hypogranular cytoplasm
- Bizarre nuclei

The Non-Dysplastic Alterations Included

- Immature megakaryocytes
- Emperipolesis
- Cytoplasmic budding
- Cytoplasmic vacuolization
- Bare nuclei
- Giant megakaryocytes
- Hyperlobulated nuclei

Cases were finally categorized into neoplastic and non-neoplastic hematological disorders, and megakaryocyte morphology was correlated with the final diagnosis.

Outcome Measures

The primary outcome was the association between megakaryocyte morphology and various hematological disorders.

Secondary outcomes included:

- Distribution of megakaryocyte number among different diseases.
- Frequency of dysplastic and non-dysplastic morphological alterations.
- Association between megakaryocyte morphology and neoplastic versus non-neoplastic disorders.

Statistical Analysis

Data were entered into Microsoft Excel and analyzed using IBM SPSS Statistics version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation (SD), while categorical variables were presented as frequencies and percentages. Comparisons between groups were performed using the Chi-square test or Fisher's exact test, as appropriate. A two-sided p-value <0.05 was considered statistically significant. The findings were summarized using tables to facilitate comparison of demographic characteristics, hematological diagnoses, bone marrow findings, and megakaryocyte morphological alterations.

RESULTS

Table 1. Baseline Demographic and Clinical Characteristics of the Study Participants

Characteristic	Number (%)
Age group (years)	
<20	37 (24.7)
21–40	48 (32.0)
41–60	43 (28.7)
>60	22 (14.6)
Gender	
Male	74 (49.3)
Female	76 (50.7)
Presenting complaint	
Fever	51 (34.0)
Weakness	36 (24.0)

Bleeding manifestations	33 (22.0)
Abdominal pain	9 (6.0)
Pallor	7 (4.7)
Fatigue	5 (3.3)
Weight loss	4 (2.7)
Headache	4 (2.7)
Others	1 (0.6)

Table 2. Distribution of Hematological Disorders Included in the Study

Diagnosis	**n (%)**
Non-neoplastic disorders (n=50)	
Megaloblastic anemia	16 (32.0)
Immune thrombocytopenic purpura	16 (32.0)
Megakaryocytic thrombocytopenia	8 (16.0)
Iron deficiency anemia	8 (16.0)
Dimorphic anemia	2 (4.0)
Neoplastic disorders (n=100)	
Chronic myeloid leukemia	31 (31.0)
Acute leukemia	23 (23.0)
Myelodysplastic syndrome	12 (12.0)
Multiple myeloma	10 (10.0)
Myelofibrosis	7 (7.0)
Myeloproliferative neoplasm	6 (6.0)
Lymphoma	6 (6.0)
Essential thrombocythemia	3 (3.0)
Polycythemia vera	2 (2.0)

Table 3. Bone Marrow Cellularity and Megakaryocyte Number According to Diagnostic Category

Variable	**Non-neoplastic (n=50)**	**Neoplastic (n=100)**	**p-value**
Bone marrow cellularity			
Hypercellular	27	56	<0.001
Normocellular	16	28	
Hypocellular	7	16	
Megakaryocyte number			
Increased	10	39	<0.001
Normal	26	30	
Decreased	14	31	

Table 4. Spectrum of Megakaryocyte Morphological Alterations

Morphological alteration	**n (%)**
Hypolobulated megakaryocytes	75 (50.0)
Immature megakaryocytes	55 (36.7)
Micromegakaryocytes	53 (35.3)
Hyperlobulated nuclei	20 (13.3)
Multiple separated nuclei	20 (13.3)
Bare nuclei	19 (12.7)
Bizarre nuclei	18 (12.0)
Emperipolesis	10 (6.7)
Giant megakaryocytes	10 (6.7)
Hypogranulation	9 (6.0)
Cytoplasmic vacuolization	6 (4.0)

Table 5. Association of Dysplastic Megakaryocyte Morphology with Diagnostic Category

Diagnostic category	**Dysplasia present**	**Dysplasia absent**	**p-value**
Non-neoplastic (n=50)	24	26	<0.001

Neoplastic (n=100)	87	13	

DISCUSSION

The present study evaluated quantitative and qualitative megakaryocyte alterations in bone marrow aspiration smears from patients with a broad spectrum of hematological disorders. Megakaryocyte morphology was abnormal in the majority of cases, and significant associations were observed between megakaryocyte characteristics and the underlying hematological diagnosis. Dysplastic alterations predominated in neoplastic disorders, whereas non-dysplastic changes were more frequently encountered in reactive and non-neoplastic conditions. These findings highlight the important diagnostic role of systematic megakaryocyte evaluation during routine bone marrow examination.

The majority of study participants belonged to the 21–40-year age group, with an almost equal distribution between males and females. Similar age distributions have been reported in previous bone marrow aspiration studies evaluating hematological disorders, although some investigators observed a male predominance and younger age groups among thrombocytopenic patients. Differences in demographic characteristics among studies are likely attributable to variations in patient selection, referral patterns, and disease spectrum. The inclusion of both neoplastic and non-neoplastic disorders in the present study probably contributed to the relatively balanced demographic profile observed.(10,11)

Neoplastic disorders accounted for two-thirds of all cases, with chronic myeloid leukemia representing the most common diagnosis, followed by acute leukemia and myelodysplastic syndrome. In contrast, megaloblastic anemia and immune thrombocytopenic purpura constituted the major non-neoplastic disorders. These observations differ from studies restricted to thrombocytopenic patients, where megaloblastic anemia or immune thrombocytopenia frequently predominated. The broader inclusion criteria employed in the present study provide a more comprehensive overview of megakaryocyte alterations across a wider range of hematological diseases and better reflect the diagnostic workload encountered in tertiary care pathology laboratories.(12,13)

Bone marrow cellularity demonstrated a significant association with the underlying disease category. Hypercellular marrow was the predominant finding, particularly among neoplastic disorders, consistent with increased hematopoietic activity associated with leukemias and myeloproliferative diseases. Similar observations have been reported in previous studies evaluating bone marrow morphology in hematological disorders. Assessment of marrow cellularity remains an essential component of bone marrow interpretation because it provides important information regarding marrow function and assists in differentiating proliferative disorders from marrow failure syndromes.(14)

Megakaryocyte number varied considerably according to the underlying diagnosis. Increased megakaryocyte counts were observed predominantly in immune thrombocytopenic purpura, reflecting compensatory thrombopoiesis secondary to accelerated peripheral platelet destruction. Conversely, acute leukemia and myelodysplastic syndrome frequently demonstrated reduced megakaryocyte numbers because of ineffective hematopoiesis and replacement of normal marrow elements by abnormal hematopoietic cells. These findings agree with previous reports demonstrating disease-specific quantitative alterations in megakaryocytes and reinforce the value of megakaryocyte enumeration during routine marrow examination.(12,13)

Morphological abnormalities were identified in 90% of the study population, emphasizing that megakaryocyte morphology is frequently altered in hematological disorders. Mixed dysplastic and non-dysplastic patterns were the most common overall morphological presentation, indicating that reactive and dysplastic processes may coexist within the same marrow environment. Similar overlapping morphological changes have been described previously, particularly in immune-mediated thrombocytopenia and chronic hematological disorders, highlighting the need for careful interpretation of megakaryocyte morphology in conjunction with clinical and laboratory findings.(14)

Among individual morphological abnormalities, hypolobulated megakaryocytes represented the most frequent finding, followed by immature megakaryocytes and micromegakaryocytes. These abnormalities are well-recognized indicators of disturbed megakaryocyte maturation and have consistently been reported in both clonal and reactive hematological disorders. Previous investigators have similarly

identified hypolobulation and micromegakaryocytes as the most reproducible markers of abnormal megakaryopoiesis. Although these features are highly characteristic of myelodysplastic syndromes, they may also occur in nutritional anemia, immune thrombocytopenia, and other reactive conditions, emphasizing that diagnosis should never rely solely on a single morphological feature.(11,15)

A major finding of the present study was the significantly higher prevalence of dysplastic megakaryocyte morphology in neoplastic disorders compared with non-neoplastic disorders. Nearly nine out of ten neoplastic cases demonstrated dysplastic features, whereas less than half of the non-neoplastic cases exhibited similar changes. These findings support previous observations that dysmegakaryopoiesis represents an important morphological hallmark of clonal hematopoietic diseases, particularly myelodysplastic syndromes and myeloproliferative neoplasms. Nevertheless, occasional dysplastic changes observed in reactive disorders should be interpreted cautiously because isolated morphological abnormalities may not necessarily indicate an underlying clonal disorder.(10,11,15)

CONCLUSION

Megakaryocyte morphology represents an important diagnostic component of routine bone marrow aspiration examination. Significant quantitative and qualitative alterations were observed across various hematological disorders, with dysplastic changes occurring predominantly in neoplastic diseases. Hypolobulated megakaryocytes, immature forms, and micromegakaryocytes were the most frequent abnormalities identified. Comprehensive evaluation of megakaryocyte number and morphology enhances the differentiation of neoplastic and non-neoplastic hematological disorders and should remain an integral part of routine bone marrow reporting, particularly in resource-limited healthcare settings.

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