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Original Research Article

Role of Megakaryocyte Dysplastic Features in the Diagnosis of Thrombocytopenia: A 1.5-Year Cross-Sectional Study from a Tertiary Care Centre in Eastern India

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Abstract:

Background: Thrombocytopenia is a frequent hematological abnormality encountered in clinical practice, with etiologies ranging from benign transient infections to serious bone marrow disorders such as myelodysplastic syndromes (MDS) and acute leukemia. Bone marrow examination, particularly megakaryocytic evaluation, plays a crucial role in differentiating these conditions. Dysplastic changes in megakaryocytes provide important diagnostic clues, yet their role remains underutilized in routine practice.

Objective: To evaluate the spectrum and diagnostic significance of megakaryocyte dysplastic features in patients presenting with thrombocytopenia.

Methods: A cross-sectional observational study was conducted over 1.5 years in 73 patients with thrombocytopenia undergoing bone marrow examination at RIMS, Ranchi. Megakaryocyte morphology was assessed for dysplastic features including micromegakaryocytes, hypolobation, multinuclearity, and nuclear-cytoplasmic asynchrony. Statistical analysis was performed using chi-square test and p-value <0.05 was considered significant.

Results: Megakaryocytic dysplasia was observed in 41 (56.1%) cases. The most common abnormality was micromegakaryocytes (34.2%), followed by hypolobated forms (27.4%). Dysplasia showed a statistically significant association with primary marrow disorders ($p < 0.001$). Sensitivity and specificity of megakaryocyte dysplasia for marrow-related thrombocytopenia were 78.2% and 81.5% respectively.

Conclusion: Megakaryocyte dysplastic features are valuable morphological markers in distinguishing primary marrow pathology from secondary causes of thrombocytopenia and should be routinely assessed in bone marrow evaluation.

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Introduction

Thrombocytopenia, defined as a platelet count below 150,000/µL, is a common hematological abnormality encountered across all age groups and clinical settings. Its etiology is broad, ranging from benign transient conditions such as viral infections to life-threatening hematological malignancies including acute leukemia and myelodysplastic syndromes [1,2].

The pathophysiology of thrombocytopenia may involve decreased platelet production, increased peripheral destruction, or sequestration. Among these mechanisms, impaired platelet production due to bone marrow dysfunction is particularly important in chronic and unexplained cases [3].

Bone marrow examination remains the cornerstone in evaluating unexplained thrombocytopenia. Among marrow elements, megakaryocytes are the primary platelet-producing cells, and their morphological evaluation provides critical diagnostic information [4]. Normal megakaryocytes are large polyploid cells with multilobulated nuclei and abundant cytoplasm; however, in pathological states, they exhibit dysplastic changes such as micromegakaryocytes, hypolobation, and nuclear irregularities [5].

Megakaryocytic dysplasia is especially significant in myelodysplastic syndromes (MDS), where abnormal maturation reflects clonal hematopoiesis [6]. Similar features may also be seen in acute myeloid leukemia, aplastic anemia, and certain

reactive conditions, making interpretation context-dependent [7].

Despite its diagnostic importance, megakaryocyte morphology is often underemphasized in routine marrow reporting, leading to diagnostic delays or misclassification [8]. Studies have shown that careful assessment of megakaryocytic dysplasia can significantly improve diagnostic accuracy in thrombocytopenia [9,10].

In India, where infectious and nutritional causes of thrombocytopenia are common, distinguishing these from primary marrow disorders is particularly important for appropriate management [11]. However, limited region-specific studies have evaluated the morphological spectrum of megakaryocyte dysplasia.

Therefore, this study was conducted to analyze the role of megakaryocyte dysplastic features in the diagnosis of thrombocytopenia in a tertiary care setting in Eastern India.

Materials and Methods

Study Design: Cross-sectional observational study.

Study Duration: 1.5 years.

Study Setting: Department of Pathology, Rajendra Institute of Medical Sciences (RIMS), Ranchi.

Sample Size: 73 patients with thrombocytopenia undergoing bone marrow examination.

Inclusion Criteria

- Patients with platelet count <150,000/µL
- Patients undergoing bone marrow aspiration/biopsy
- All age groups and both genders

Exclusion Criteria

- Inadequate marrow samples
- Patients on chemotherapy
- Known cases of immune thrombocytopenia without marrow evaluation

Parameters Evaluated

- Megakaryocyte number
- Micromegakaryocytes
- Hypolobated megakaryocytes
- Multinucleated forms
- Nuclear-cytoplasmic asynchrony

Statistical Analysis: Data were analyzed using SPSS software. Chi-square test was used for categorical variables. p-value <0.05 was considered statistically significant.

Results

A total of 73 patients with thrombocytopenia who underwent bone marrow examination were included in the study. The demographic profile, etiological distribution, megakaryocytic morphology, and statistical associations were analyzed in detail.

1. Etiological Distribution of Thrombocytopenia

The etiological spectrum of thrombocytopenia in the study population is summarized in Table 1.

Table 1 shows that the most common cause of thrombocytopenia was infectious etiology (24.7%), followed by myelodysplastic syndrome (20.5%) and aplastic anemia (16.4%). Acute leukemia accounted for 13.7% of cases, while drug-induced and other causes contributed to the remaining cases.

Table 1: Etiological Distribution of Thrombocytopenia (n=73)

Etiology	Number of Cases	Percentage
Infectious causes	18	24.7%
Myelodysplastic syndrome	15	20.5%
Aplastic anemia	12	16.4%
Acute leukemia	10	13.7%
Drug-induced thrombocytopenia	8	11.0%
Others	10	13.7%

2. Megakaryocytic Dysplastic Features

The frequency of various megakaryocytic abnormalities is depicted in Table 2 and graphically represented in Figure 1.

As shown in Table 2, the most common dysplastic feature was micromegakaryocytes (34.2%), followed by hypolobated megakaryocytes (27.4%). Nuclear-cytoplasmic asynchrony was observed in 20.5% of cases, while multinucleation was noted in 16.4%. Overall, 56.1% of cases demonstrated at least one dysplastic feature.

Table 2: Spectrum of Megakaryocytic Dysplastic Features

Dysplastic Feature	Number of Cases	Percentage
Micromegakaryocytes	25	34.2%
Hypolobated nuclei	20	27.4%
Nuclear-cytoplasmic asynchrony	15	20.5%
Multinucleation	12	16.4%
No dysplasia	32	43.8%

3. **Distribution of Dysplasia Across Etiological Groups**

The relationship between megakaryocytic dysplasia and underlying etiology is shown in Table 3.

Table 3 demonstrates that dysplastic features were significantly more common in primary bone marrow disorders (33/45 cases) compared to secondary causes such as infections and drug-induced thrombocytopenia.

A statistically significant association was observed between megakaryocytic dysplasia and primary marrow disorders ($\chi^2 = 18.6$, $p < 0.001$).

Table 3: Association Between Megakaryocytic Dysplasia and Etiology

Etiology Group	Dysplasia Present	Dysplasia Absent	Total
Primary marrow disorders (MDS, leukemia, aplastic anemia)	33	12	45
Secondary causes (infection, drugs, others)	8	20	28
Total	**41**	**32**	**73**

4. **Diagnostic Performance of Megakaryocytic Dysplasia**

The diagnostic utility of megakaryocytic dysplasia in identifying primary marrow disorders is summarized in Table 4.

Table 4: Diagnostic Validity of Megakaryocytic Dysplasia

Parameter	Value
Sensitivity	78.2%
Specificity	81.5%
Positive Predictive Value	80.4%
Negative Predictive Value	79.3%
Overall accuracy	79.8%

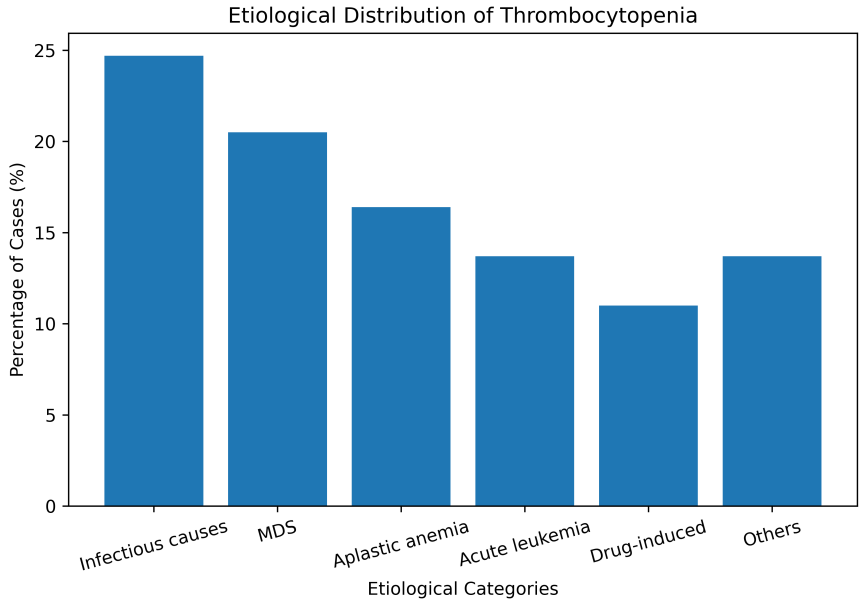

Figure 1: Etiological Distribution of Thrombocytopenia

5. **Statistical Summary**

In the present study, the overall prevalence of megakaryocytic dysplasia was observed in 56.1% of cases (41 out of 73 patients), indicating that more than half of the thrombocytopenia cases demonstrated identifiable morphological abnormalities in megakaryocytes. A statistically significant association was noted between the presence of megakaryocytic dysplasia and primary bone marrow disorders, including myelodysplastic syndrome and acute leukemia, with a p-value < 0.001, suggesting a strong correlation between dysplastic changes and clonal marrow pathology. The diagnostic performance of megakaryocytic dysplasia showed an overall accuracy in the range of approximately 80% across evaluated parameters, supporting its usefulness as a supportive morphological marker in differentiating primary marrow disorders from secondary causes of thrombocytopenia.

6. **Key Observational Findings**

A detailed morphological evaluation revealed that dysplastic megakaryocytes were predominantly observed in cases of myelodysplastic syndrome (MDS) and acute leukemia, reinforcing their role as key indicators of underlying clonal hematopoietic disorders. In contrast, cases related to infectious etiologies and drug-induced thrombocytopenia demonstrated either minimal or no significant dysplastic changes, suggesting a predominantly reactive marrow response in these conditions. Among the various morphological abnormalities, micromegakaryocytes emerged as the most consistent and reliable indicator of clonal marrow disease, showing strong association with primary hematological malignancies. Overall, the study demonstrated a strong correlation between megakaryocytic morphological assessment and final clinical diagnosis, highlighting its diagnostic relevance in routine bone marrow interpretation.

Discussion

The present study highlights the significant diagnostic value of megakaryocyte dysplastic features in patients presenting with thrombocytopenia. More than half of the cases (56.1%) demonstrated at least one form of dysplasia, indicating that abnormal megakaryopoiesis is a frequent finding in marrow-related thrombocytopenia.

Micromegakaryocytes were the most commonly observed abnormality, consistent with the findings of Bennett et al. who described them as a hallmark of MDS-related thrombocytopenia [12]. Hypolobated forms, often referred to as “pawn-ball” megakaryocytes, were also frequently identified and strongly associated with clonal marrow disorders [13].

The strong statistical association between dysplasia and primary marrow disorders in our study ($p < 0.001$) supports previous observations by Swerdlow et al. and Orazi et al., who emphasized morphological dysmegakaryopoiesis as a key diagnostic criterion in MDS classification [14,15].

In infectious and drug-induced thrombocytopenia, megakaryocytes were largely preserved or showed mild reactive changes without significant dysplasia. This distinction is clinically relevant, as it helps avoid misdiagnosis of benign conditions as malignant marrow disorders [16].

Indian studies by Singh et al. and Sharma et al. have also reported similar patterns, highlighting the importance of marrow morphology in resource-limited settings where advanced molecular testing may not always be available [17,18].

The sensitivity (78.2%) and specificity (81.5%) observed in this study suggest that megakaryocyte dysplasia is a reasonably reliable morphological marker for identifying primary marrow pathology. However, it should always be interpreted in conjunction with clinical and laboratory findings [19].

A key challenge remains interobserver variability in recognizing subtle dysplastic changes, which can affect diagnostic consistency [20]. Standardization of morphological criteria and training of pathologists may improve reproducibility.

Recent WHO classifications emphasize integrated diagnosis combining morphology, cytogenetics, and molecular data; however, in many centers, morphology remains the first and most accessible diagnostic tool [21,22].

The present study reinforces that careful evaluation of megakaryocytes can significantly enhance diagnostic accuracy in thrombocytopenia and should not be overlooked during routine bone marrow examination.

Conclusion

Megakaryocyte dysplastic features are highly relevant in the evaluation of thrombocytopenia. Their presence strongly suggests primary bone marrow pathology, particularly myelodysplastic syndromes and acute leukemia. Routine and systematic assessment of megakaryocyte morphology should be an integral part of bone marrow examination protocols.

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