Case Series

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Diagnostic Utility of Megakaryocytic Morphology and Fibrosis Grading in Myeloproliferative Neoplasms: A Series of Five Cases

Pathology Section

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ABSTRACT

Myeloproliferative Neoplasms (MPNs) comprise a heterogeneous group of clonal haematopoietic stem cell disorders characterised by excessive proliferation of one or more myeloid lineages. Despite advances in molecular diagnostics, these entities frequently exhibit overlapping clinical and haematologic features, making accurate classification a diagnostic challenge for pathologists and clinicians alike. This descriptive and educational case series highlights the diagnostic utility of detailed morphologic evaluation, focusing particularly on megakaryocytic morphology and grading of bone marrow fibrosis, in five representative patients encompassing essential thrombocythaemia, prefibrotic primary myelofibrosis, overt primary myelofibrosis, post-polycythaemia vera myelofibrosis, and chronic myeloid leukaemia with secondary fibrosis. Each case underwent a comprehensive diagnostic workup, including complete blood count, peripheral blood smear examination, bone marrow aspiration, and trephine biopsy. Histopathologic evaluation was performed using haematoxylin and eosin, reticulin, and Masson's trichrome stains to assess megakaryocytic clustering, nuclear features, and stromal alterations. Molecular testing for JAK2 V617F, CALR, and MPL mutations, along with cytogenetic studies, was conducted wherever feasible to provide a complementary molecular profile. Detailed morphologic integration allowed precise classification and staging according to both the WHO 2022 and International Consensus Classification (ICC) criteria, correlating histologic patterns with clinical and molecular data. Particular emphasis was placed on distinguishing clonal fibrosis of primary myelofibrosis from secondary, reactive fibrosis seen in chronic myeloid leukaemia, a distinction with significant therapeutic and prognostic implications. This case series underscores the indispensable role of an integrated, multidisciplinary diagnostic approach where morphology, molecular markers, and clinical context converge to achieve accurate diagnosis, refine prognostication, and guide risk-adapted management of MPNs.

Keywords: Bone marrow trephine biopsy, Chronic myeloid leukaemia, Essential thrombocythaemia, Masson's trichrome stain, Overt myelofibrosis, Reticulin stain

INTRODUCTION

The MPNs comprise a heterogeneous group of clonal haematopoietic disorders characterised by chronic proliferation of one or more myeloid lineages and a variable propensity for thrombotic complications, disease progression, and leukaemic transformation. Among these entities, accurate distinction between essential thrombocythaemia, prefibrotic primary myelofibrosis, overt primary myelofibrosis, secondary myelofibrosis, and other myeloid neoplasms remains one of the most challenging tasks in routine haematopathology [1]. Historically, overlapping clinical features, particularly thrombocytosis and splenomegaly, have contributed to diagnostic ambiguity, often leading to misclassification [2]. Morphologic evaluation of bone marrow architecture, megakaryocytic morphology, and assessment of marrow fibrosis using reticulin and trichrome stains have therefore emerged as cornerstone diagnostic tools, forming the backbone of contemporary classification systems [3,4].

With the evolution of diagnostic criteria in the World Health Organisation (WHO) 2022 [5] and ICC [6], greater emphasis has been placed on reproducible histopathologic parameters, particularly megakaryocytic atypia and graded marrow fibrosis, to distinguish biologically distinct MPN entities. This distinction is not merely academic; it carries profound clinical and prognostic implications. Essential thrombocythaemia is generally associated with an indolent course and favourable survival, whereas prefibrotic primary myelofibrosis is increasingly recognised as a more aggressive disease with higher risks of progression to overt myelofibrosis and inferior outcomes [7]. Similarly, overt primary myelofibrosis and secondary myelofibrosis arising from polycythaemia vera are associated with advanced marrow failure and poor prognosis [8], while fibrosis in other myeloid neoplasms, such as chronic myeloid leukaemia, may be reactive and potentially reversible [9]. In this context, meticulous morphologic interpretation remains essential, even in the era of molecular diagnostics.

The present descriptive, educational case series was undertaken to illustrate the diagnostic utility of megakaryocytic morphology and fibrosis grading across the spectrum of MPNs. By presenting five carefully selected cases, including Essential Thrombocythaemia (ET) and prefibrotic Primary Myelofibrosis (PMF), overt PMF, post-polycythaemia vera myelofibrosis, and chronic myeloid leukaemia with fibrosis, we aim to highlight common diagnostic pitfalls, emphasise morphologic distinctions mandated by current classification systems, and demonstrate how accurate histopathologic interpretation directly influences clinical management. This case series thereby illustrates the role of integrating megakaryocytic morphology with fibrosis assessment using special stains in the routine diagnostic evaluation of MPNs.

All cases underwent bone marrow aspiration and trephine biopsy, processed according to standard haematopathology protocols. Trephine biopsy cores were fixed in neutral buffered formalin, decalcified using EDTA, routinely processed, and embedded in paraffin. Histologic evaluation was performed on haematoxylin and eosin-stained sections. Reticulin fibrosis was assessed using the Gomori silver impregnation technique, and collagen deposition was evaluated with Masson's trichrome stain, with vascular walls serving as internal positive controls. Bone marrow fibrosis was graded using the European Consensus Grading System (MF-0 to MF-3), in accordance with WHO 2022 [5] and ICC [6] recommendations.

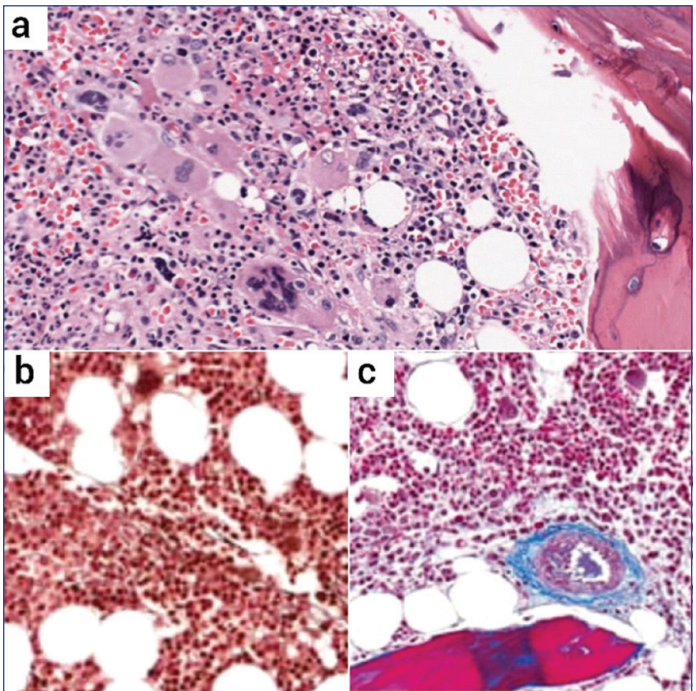
All cases were independently reviewed by two experienced haematopathologists who were blinded to the clinical information, and fibrosis grading was assigned by consensus. Interobserver agreement was high (kappa=0.85), with discrepancies resolved by joint review. Written informed consent was obtained from all patients for the publication of clinical data and images.

CASE SERIES

Case 1

A 45-year-old woman presented with a 6-month history of persistent headache and easy fatigability. She had no significant past medical history and was not on any regular medications. On examination, she had no palpable splenomegaly. Complete blood count revealed isolated thrombocytosis with a platelet count of 950×10^9/L, normal haemoglobin (13.2 g/dL) and leukocyte counts (7.2×10^9/L). Peripheral blood smear showed thrombocytosis with large platelets but no leukoerythroblastosis. Provisional diagnosis of essential thrombocythaemia was considered, with differential diagnosis including prefibrotic primary myelofibrosis and reactive thrombocytosis.

Bone marrow biopsy was normocellular for age and demonstrated proliferation predominantly of the megakaryocytic lineage, with increased numbers of large to giant megakaryocytes showing mature morphology and deeply lobulated, hyperchromatic "staghorn-like" nuclei arranged singly or in loose clusters [Table/Fig-1a]. Granulopoiesis and erythropoiesis were quantitatively and morphologically unremarkable. Reticulin staining revealed scattered fine fibres without intersections, consistent with MF-0 [Table/Fig-1b], and trichrome staining showed no collagen deposition [Table/Fig-1c]. Molecular testing revealed JAK2 V617F mutation positivity. CALR and MPL mutations were not detected. Conventional cytogenetics showed a normal karyotype (46, XX).



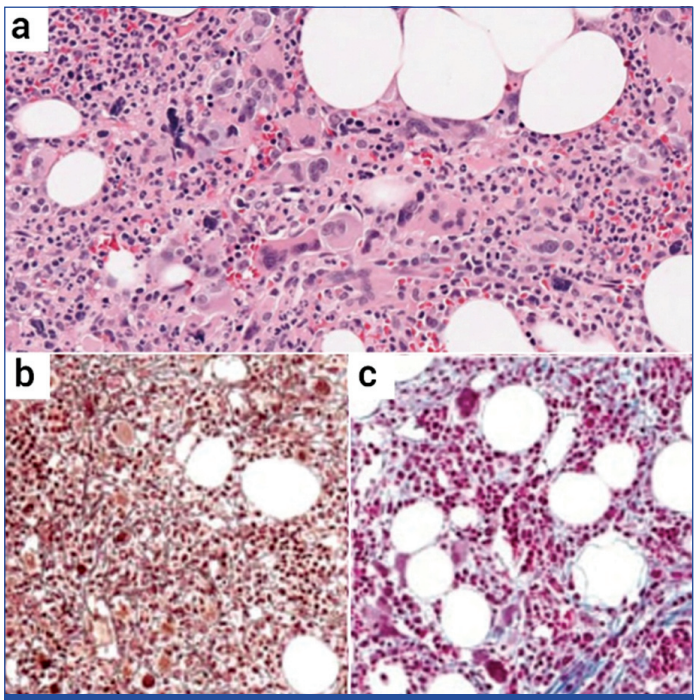
[Table/Fig-1]: Bone marrow findings in essential thrombocythaemia. a) Haematoxylin and eosin-stained section (×400) showing normocellular marrow with increased large to giant megakaryocytes exhibiting mature morphology and deeply lobulated "staghorn-like" nuclei arranged singly and in loose clusters; b) Reticulin stain (×400) demonstrating scattered fine reticulin fibres without intersections, consistent with MF-0 fibrosis; c) Masson's trichrome stain (×400) showing absence of collagen deposition; vascular wall staining serves as an internal positive control.

A diagnosis of essential thrombocythaemia was rendered according to the WHO 2022 and ICC criteria. The patient was treated with hydroxyurea and low-dose aspirin as risk-adapted cytoreductive therapy for 10 months. She achieved a complete haematologic response according to International Working Group-MPNs Research and Treatment (IWG-MRT) criteria and remained clinically stable during further follow-up. During the 24 months of follow-up, platelet counts remained well controlled (280×10^9/L), and the patient was clinically stable without thrombotic or hemorrhagic events, in keeping with the expected clinical course of essential thrombocythaemia.

Case 2

A 58-year-old man presented with a 4-month history of progressive fatigue, abdominal discomfort, and early satiety. He had a history of hypertension controlled with antihypertensive medications. On examination, he had borderline splenomegaly (spleen palpable 2 cm below the costal margin). Complete blood count showed thrombocytosis (platelet count 800×10^9/L) and mild normocytic anaemia (haemoglobin 11.2 g/dL). Peripheral blood smear showed thrombocytosis with some large platelets. A provisional diagnosis of MPN was considered, with a differential diagnosis including essential thrombocythaemia versus prefibrotic primary myelofibrosis.

Bone marrow biopsy demonstrated a hypercellular marrow (80% cellularity) with granulocytic proliferation, relative reduction of erythropoiesis, and increased numbers of atypical megakaryocytes with abnormal nuclear folding, bulbous "cloud-like" nuclei, and dense paratrabecular and perisinusoidal clustering [Table/Fig-2a]. Reticulin staining showed a loose but definite network with frequent intersections corresponding to MF-1 stage of marrow fibrosis [Table/Fig-2b], while trichrome staining revealed no collagen deposition [Table/Fig-2c]. Molecular testing showed CALR exon nine mutation positivity. JAK2 V617F and MPL mutations were negative. Cytogenetic analysis revealed a normal male karyotype (46, XY).



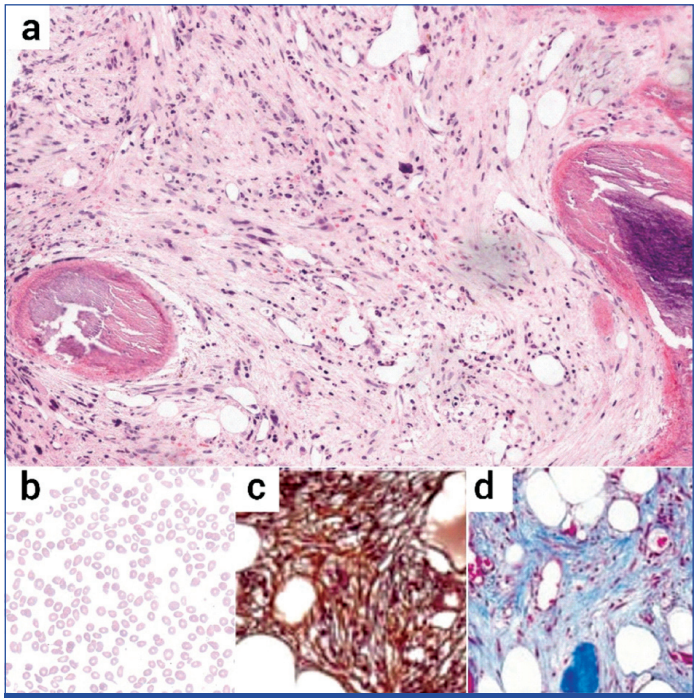
[Table/Fig-2]: Bone marrow findings in prefibrotic primary myelofibrosis: a) Haematoxylin and eosin–stained section (×400) showing hypercellular marrow with granulocytic predominance and clusters of atypical megakaryocytes with bulbous, irregular, "cloud-like" nuclei; b) Reticulin stain (×400) demonstrating a loose but definite reticulin network with frequent intersections, corresponding to MF-1 fibrosis; c) Masson's trichrome stain (×400) showing absence of significant collagen deposition.

These findings supported a diagnosis of prefibrotic/early primary myelofibrosis under the WHO 2022 and ICC criteria. The patient received cytoreductive therapy with hydroxyurea and was monitored closely for 12 months. Progressive anaemia (haemoglobin declining to 9.8 g/dL) and increasing splenomegaly (spleen 5 cm below the costal margin) during 18 months of follow-up indicated disease evolution toward overt myelofibrosis, consistent with the reported clinical behaviour of prefibrotic primary myelofibrosis.

Case 3

A 65-year-old man presented with a 3-month history of constitutional symptoms, including unintentional weight loss (6 kg), night sweats, and worsening fatigue. He also noted early satiety and left upper quadrant fullness. On examination, he had massive splenomegaly (spleen palpable 10 cm below the costal margin). Complete blood count revealed pancytopenia: haemoglobin 8.5 g/dL, white blood cells 3.2×10^9/L, and platelets 85×10^9/L. Peripheral blood smear demonstrated leukoerythroblastosis with numerous teardrop erythrocytes. A provisional diagnosis of overt primary myelofibrosis was considered, with differential diagnosis including post-polycythaemia vera myelofibrosis and other causes of marrow fibrosis.

Bone marrow aspiration resulted in a dry tap. Trephine biopsy revealed a variably hypocellular to moderately cellular marrow with markedly distorted architecture, dilated sinusoids, and clusters of atypical megakaryocytes exhibiting irregular, hyperchromatic, cloud-like nuclei [Table/Fig-3a]. Peripheral blood smear findings correlated with leukoerythroblastosis and numerous teardrop erythrocytes [Table/Fig-3b]. Reticulin staining demonstrated diffuse, dense fibrosis with extensive intersections and coarse bundles corresponding to MF-3 [Table/Fig-3c], and trichrome staining revealed extensive collagen deposition with associated osteosclerosis [Table/Fig-3d]. Molecular testing demonstrated JAK2 V617F mutation positivity. CALR and MPL mutations were negative. Cytogenetics showed a normal male karyotype (46, XY).



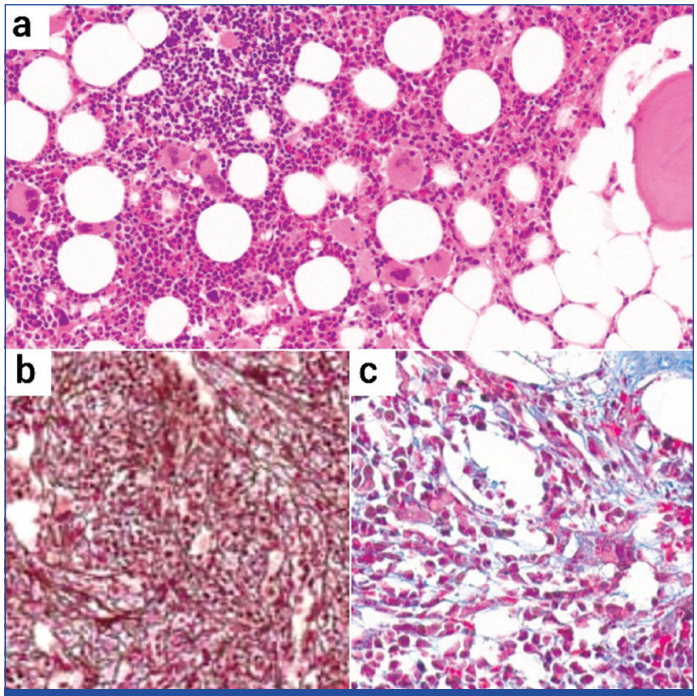
[Table/Fig-3]: Overt primary myelofibrosis with advanced fibrosis; a) Haematoxylin and eosin-stained section (×400) showing markedly distorted marrow architecture with atypical megakaryocyte clusters and associated osteosclerosis; b) Peripheral blood smear (×400) demonstrating leukoerythroblastosis with numerous teardrop erythrocytes; c) Reticulin stain (×400) showing diffuse, dense reticulin fibrosis with extensive intersections and coarse bundles, consistent with MF-3; d) Masson's trichrome stain (×400) highlighting extensive collagen deposition.

A diagnosis of overt primary myelofibrosis was established according to the WHO 2022 and ICC classifications. The patient was managed with supportive care, including transfusion support and symptom-directed therapy. Despite treatment, the disease followed an aggressive course with progressive marrow failure, and the patient showed clinical deterioration over 12 months of follow-up, consistent with the reported clinical course of advanced fibrotic-stage primary myelofibrosis.

Case 4

A 70-year-old woman presented with a 2-month history of worsening fatigue, exertional dyspnoea, early satiety, and left upper quadrant discomfort. She had a 10-year history of JAK2 V617F-positive polycythaemia vera, diagnosed based on elevated haemoglobin (18.5 g/dL), JAK2 V617F mutation positivity, and characteristic bone marrow findings like hypercellularity and panmyelosis. She had been on long-term cytoreductive therapy with hydroxyurea. On examination, she had moderate splenomegaly (spleen palpable 6 cm below costal margin). Complete blood count showed progressive pancytopenia: haemoglobin 9.2 g/dL, white blood cells 4.1×10^9/L and platelets 120×10^9/L. Provisional diagnosis of post-polycythaemia vera myelofibrosis was considered.

Compared with a prior biopsy showing erythroid-predominant hypercellularity typical of polycythaemia vera, the current marrow biopsy demonstrated patchy hypocellularity, architectural distortion, granulocytic predominance, relative erythroid depletion, and increased numbers of pleomorphic, clustered megakaryocytes [Table/Fig-4a]. Reticulin staining showed a diffuse increase in fibres with frequent intersections corresponding to marrow fibrosis stage MF-2 [Table/Fig-4b], and trichrome staining revealed focal collagen deposition [Table/Fig-4c]. Molecular testing continued to show JAK2 V617F mutation positivity. Cytogenetic analysis revealed a normal female karyotype (46, XX).



[Table/Fig-4]: Bone marrow findings in post-polycythaemia vera myelofibrosis; a) Haematoxylin and eosin-stained section (×400) showing architectural distortion with granulocytic predominance, relative erythroid depletion, and pleomorphic, clustered megakaryocytes; b) Reticulin stain (×400) demonstrating diffuse increase in reticulin fibres with frequent intersections, corresponding to MF-2 fibrosis; c) Masson's trichrome stain (×400) showing focal collagen deposition within the marrow stroma.

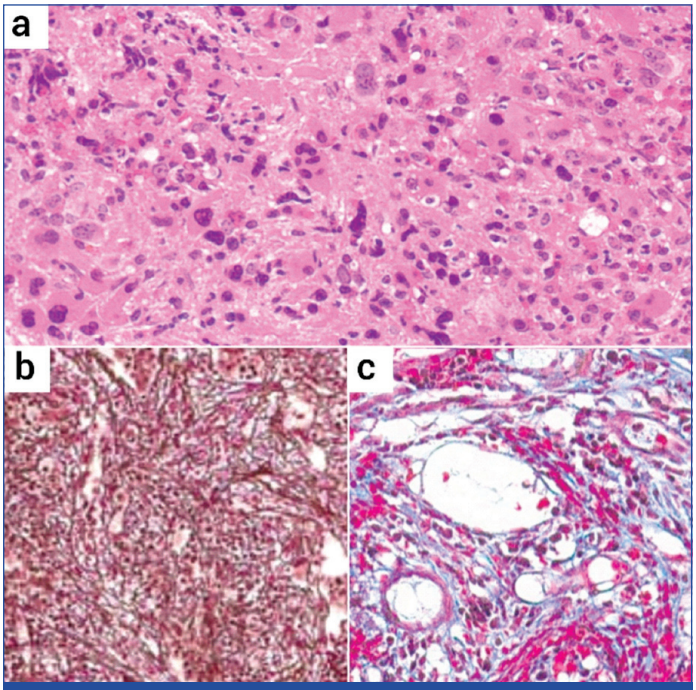
These findings met the WHO 2022 and ICC criteria for post-polycythaemia vera myelofibrosis. Despite ongoing therapy, the patient experienced worsening cytopenias and symptomatic splenomegaly. At 14 months of follow-up, the disease showed continued progression, consistent with the particularly adverse prognosis associated with secondary myelofibrosis arising from polycythaemia vera.

Case 5

A 50-year-old man presented with a 2-week history of fatigue, abdominal fullness, and blurred vision. He had no significant past medical history. On examination, he had mild splenomegaly (spleen palpable 3 cm below costal margin). Complete blood count showed marked leucocytosis (WBC 150×10^9/L) with left shift, basophilia (3%), and mild anaemia (haemoglobin 11.5 g/dL). Platelet count was elevated at 520×10^9/L. Peripheral blood smear showed leucocytosis with myelocytes, metamyelocytes, and basophilia. Provisional diagnosis of chronic myeloid leukaemia was considered,

with differential diagnosis including leukaemoid reaction and other MPNs.

Molecular testing confirmed BCR::ABL1-positive chronic myeloid leukaemia in chronic phase, with a low blast percentage (2%). Bone marrow biopsy was markedly hypercellular (95% cellularity), showing granulocytic proliferation at all stages of maturation, relative suppression of erythropoiesis, and numerous small, hypolobated "dwarf" megakaryocytes [Table/Fig-5a]. Reticulin staining demonstrated moderate to marked fibrosis corresponding to MF-2 [Table/Fig-5b], while trichrome staining was negative or only focally positive [Table/Fig-5c]. Cytogenetic analysis revealed t(9;22) (q34;q11.2) (Philadelphia chromosome) in all 20 metaphases examined.



[Table/Fig-5]: Bone marrow findings in chronic myeloid leukaemia with associated fibrosis; a) Haematoxylin and eosin–stained section (×400) showing markedly hypercellular marrow with granulocytic proliferation and numerous small, hypolobated "dwarf" megakaryocytes; b) Reticulin stain (×400) demonstrating moderate reticulin fibrosis consistent with MF-2; c) Masson's trichrome stain (×400) showing minimal to focal collagen deposition.

A diagnosis of chronic myeloid leukaemia, chronic phase, with associated reticulin fibrosis was rendered. The patient received imatinib mesylate, achieving a complete haematologic response with sustained molecular response on serial quantitative BCR::ABL1 transcript monitoring. A repeat bone marrow biopsy was not clinically indicated due to durable clinical and molecular remission. At 30 months of follow-up, the patient remained in sustained haematologic control with a good prognosis. [Table/Fig-6] presents clinicopathologic summary of cases demonstrating the diagnostic utility of megakaryocytic morphology and fibrosis grading in MPN.

DISCUSSION

This case series emphasises the diagnostic and prognostic value of megakaryocytic morphology and marrow fibrosis grading in the contemporary classification of MPNs. By examining five representative cases spanning essential thrombocythaemia, prefibrotic primary myelofibrosis, overt primary myelofibrosis, post-polycythaemia vera myelofibrosis, and chronic myeloid leukaemia with fibrosis, the series demonstrates how careful histopathologic evaluation resolves clinically overlapping presentations and directly impacts disease classification. The findings are concordant with the WHO 2022 and ICC frameworks, which prioritise reproducible morphologic criteria over clinical surrogates alone in distinguishing biologically distinct MPN entities [10,11].

A recurrent diagnostic pitfall illustrated in this series is the misclassification of prefibrotic primary myelofibrosis as essential thrombocythaemia, particularly in patients presenting with isolated thrombocytosis and minimal splenomegaly. As demonstrated in our prefibrotic PMF case, recognition of characteristic megakaryocytic atypia, bulbous, irregular, "cloud-like" nuclei with dense paratrabecular or perisinusoidal clustering combined with even low-grade reticulin fibrosis (MF-1) is critical for correct diagnosis. Prior clinicopathologic studies have shown that such cases, if misdiagnosed as ET, are associated with underestimation of progression risk and adverse outcomes [12,13]. Conversely, overreliance on fibrosis alone without attention to lineage-specific morphology risks mislabeling reactive or secondary fibrosis as primary myelofibrosis, a diagnostic error exemplified by the chronic myeloid leukaemia case in this series.

Distinguishing clonal MPNs from secondary thrombocytosis, Myelodysplastic/Myeloproliferative (MDS-MPN) overlap syndromes, and reactive marrow fibrosis remains a major diagnostic challenge. Secondary thrombocytosis typically lacks megakaryocytic atypia and preserves normal marrow architecture, while MDS-MPN overlap syndromes demonstrate multilineage dysplasia and distinct clinical contexts. Importantly, marrow fibrosis is not specific to PMF and may represent a reactive, cytokine-mediated process in other myeloid neoplasms [9]. The CML case in this series illustrates that significant reticulin fibrosis may occur in chronic-phase CML and

Case	Entity (WHO 2022 / ICC)	Age/ Sex	Key clinical features	Megakaryocytic Morphology	Fibrosis Grade (Reticulin / Trichrome)	Treatment	Follow-up Duration	Outcome / Prognosis
1	Essential Thrombocythaemia (ET)	45 / F	Isolated thrombocytosis; no splenomegaly	Large to giant, mature megakaryocytes with deeply lobulated "staghorn-like" nuclei; loose clusters	MF-0 / No collagen	Risk-adapted cytoreduction + antiplatelet therapy	24 months	Clinically stable; well-controlled counts; good prognosis
2	Prefibrotic Primary Myelofibrosis (pre-PMF)	58 / M	Thrombocytosis, mild anaemia; borderline splenomegaly	Atypical megakaryocytes with bulbous, irregular "cloud-like" nuclei; dense paratrabecular/perisinusoidal clustering	MF-1 / No collagen	Symptom- and risk-adapted therapy; close monitoring	18 months	Progressive anaemia and splenomegaly; risk of progression to overt MF; reduced survival vs ET
3	Primary Myelofibrosis, Overt Fibrotic Stage	65 / M	Constitutional symptoms, pancytopenia, massive splenomegaly; dry tap	Markedly atypical megakaryocytes with hyperchromatic, irregular nuclei; clustered	MF-3 / Diffuse collagen + osteosclerosis	Supportive and symptom-directed therapy	12 months	Progressive marrow failure; poor prognosis
4	Post–polycythaemia Vera Myelofibrosis (Secondary MF)	70 / F	Long-standing PV; cytopenias, splenomegaly, constitutional symptoms	Pleomorphic, atypical megakaryocytes with clustering; architectural distortion	MF-2 / Focal collagen	Ongoing therapy; supportive care	14 months	Progressive disease; very poor prognosis
5	Chronic Myeloid Leukaemia, Chronic Phase, with Fibrosis	50 / M	Marked leukocytosis, basophilia; mild splenomegaly; BCR::ABL1+	Numerous small hypolobated "dwarf" megakaryocytes	MF-2 / Minimal or absent collagen	Tyrosine kinase inhibitor (imatinib)	30 months	Sustained haematologic control; good prognosis

[Table/Fig-6]: Clinicopathologic summary of cases demonstrating the diagnostic utility of megakaryocytic morphology and fibrosis grading in Myeloproliferative Neoplasms (MPN).

does not negate a favourable prognosis under effective tyrosine kinase inhibitor therapy.

The present cases also reinforce the necessity of dual staining with reticulin and trichrome in routine marrow evaluation. Reticulin staining remains indispensable for identifying early fibrotic changes that define prefibrotic PMF, whereas trichrome staining is essential for detecting collagen deposition, which marks advanced fibrotic-stage disease. In our series, the absence of collagen in prefibrotic PMF and its clear presence in overt primary myelofibrosis and post-polycythaemia vera myelofibrosis underscores the complementary nature of these stains. This distinction is emphasised in the WHO 2022 recommendations, which caution against reliance on reticulin staining alone when staging myelofibrosis [14,15]. Failure to apply both stains risks understaging advanced disease or overstaging early lesions, with direct implications for prognosis and management.

Across the spectrum of cases, fibrosis grade showed a clear association with clinical outcome, reinforcing its role as a surrogate marker of disease biology. Essential thrombocythaemia with MF-0 fibrosis followed an indolent clinical course, whereas increasing fibrosis grades correlated with progressive cytopenias, splenomegaly, and inferior survival. Advanced fibrosis (MF-3) with collagen deposition, as seen in overt primary myelofibrosis, was associated with marrow failure and poor outcome, consistent with its inclusion as an adverse variable in prognostic models such as DIPSS and MIPSS70 [16,17]. Similarly, the presence of MF-2 fibrosis in post-polycythaemia vera myelofibrosis marked disease acceleration and poor prognosis, in keeping with large cohort studies of secondary myelofibrosis [18].

An important teaching point from this series is that marrow fibrosis is not specific to primary myelofibrosis and must always be interpreted within the appropriate morphologic and molecular context. A critical distinction exists between clonal fibrosis and reactive fibrosis. Clonal fibrosis, as seen in primary myelofibrosis and post-polycythaemia vera myelofibrosis, represents an intrinsic component of disease biology driven by abnormal megakaryocyte-derived cytokines and is associated with progressive disease and adverse prognosis [17]. In contrast, reactive fibrosis, as illustrated by the chronic myeloid leukaemia case in this series, is typically cytokine-mediated, potentially reversible, and may regress with effective tyrosine kinase inhibitor therapy without necessarily conferring an adverse prognosis [19-21]. Importantly, significant reticulin fibrosis may also be encountered in other myeloid neoplasms; therefore, recognition of disease-defining features such as granulocytic hyperplasia with dwarf megakaryocytes and BCR::ABL1 positivity is essential to distinguish reactive fibrosis from the clonal fibrosis of primary myelofibrosis and to avoid diagnostic misclassification and inappropriate prognostication [18,22].

In retrospect, this case series underscores the value of early and comprehensive marrow evaluation, particularly in patients with thrombocytosis or evolving cytopenias where clinical features alone are insufficient for precise classification. If repeated, incorporation of systematic molecular correlation and serial marrow biopsies would further strengthen clinicopathologic correlations, particularly in prefibrotic and secondary myelofibrosis, where disease evolution is central to prognosis.

The principal strength of this series lies in its focused, comparative approach, illustrating the full morphologic and fibrotic continuum of MPNs with direct correlation to outcomes. Its emphasis on practical diagnostic challenges enhances its relevance to routine haematopathology practice.

Limitation(s)

Limitations of this study include the small number of cases inherent to a case series design and variability in follow-up duration, which limits direct comparison of long-term outcomes. Uniform molecular genetic data were not available across all cases, as the study was intentionally designed to emphasise the diagnostic utility of megakaryocytic morphology and bone marrow fibrosis grading using reticulin and Masson's trichrome stains, reflecting real-world diagnostic practice where morphologic evaluation remains central. Repeat bone marrow biopsies were not routinely performed during follow-up, particularly in cases with sustained clinical response such as chronic-phase CML; consequently, histopathologic documentation of fibrosis regression was not available in all cases.

Future investigations should prioritise prospective clinicopathologic studies integrating megakaryocytic morphology, standardised fibrosis grading, and molecular profiling across disease stages. Serial marrow evaluation in well-characterised cohorts represents the logical next step to refine diagnostic precision, improve prognostic stratification, and better define the temporal relationship between morphologic progression and clinical outcome in MPNs. Accurate assessment of megakaryocytic morphology combined with dual fibrosis staining remains indispensable for precise classification and prognostication of MPNs.

CONCLUSION(S)

This case series highlights the pivotal role of megakaryocytic morphology combined with reticulin and Masson's trichrome staining in the diagnostic evaluation of MPNs. Reticulin staining is essential for identifying early stromal activation and distinguishing essential thrombocythaemia from prefibrotic primary myelofibrosis, while trichrome staining enables accurate staging of advanced collagen-rich fibrosis in overt and secondary myelofibrosis. Applied using the European Consensus MF grading system within the WHO 2022/ICC frameworks, this integrated approach allows precise classification and prognostication. Clinically, these findings directly support informed, risk-adapted therapeutic decision-making in MPNs.

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