SHORT COMMUNICATION

DIFFERENT SHAPES OF MEGAKARYOCYTES IN ESSENTIAL THROMBOCYTHEMIA

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Essential thrombocytopenia is the myeloproliferative neoplasm associated with the JAK2/CALR/MPL mutation. It is characterized by an increase in thrombocytes and abnormal megakaryocytes. WHO established the diagnostic criteria for diagnosing the myeloproliferative disorder, which is the combination of molecular, clinical, and histological findings. The appearance of megakaryocytes on bone marrow biopsy is the distinguishing feature to identify myeloproliferative neoplasm, and this short review would like to emphasize the presentation of megakaryocytes in bone marrow biopsy.

Keywords: Thrombocytopenia; Peripheral smear; Megakaryocytes

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INTRODUCTION

Essential thrombocythemia is one of the three JAK2/ CALR/MPL mutation-associated myeloproliferative disorder secondary to the clonal stem cell aberrations.[1] Essential thrombocythemia overlaps in diagnostic features with polycythaemia vera and myelofibrosis. Hence the morphological features and variation in megakaryocyte' morphology can serve as the distinguishing feature in the diagnosis of a respective myeloproliferative neoplasm.[1–3] This article will emphasize the morphological features of megakaryocytes in essential thrombocythemia.

CASE EXAMPLE

52 years old man with no known co-morbidity presented with incidental findings of persistently raised white blood cells and platelet count. There was no active complaint or B symtoms. He had an episode of hematemesis one year back for which endoscopy was carried out and showed normal findings. Abdominal examination revealed non-tender palpable spleen 6 centimetres below the left costal margin. Complete blood count revealed Haemoglobin: 14.5 g/dl, MCV: 93.1 fl, MCH: 29.9 pg, WBC: 08 X 10^9/L, ANC:4 X 10^9/L, Platelets: 1116 X 10^9/L. The peripheral film revealed increased platelet anisocytosis along with the increased count. Bone marrow aspirate revealed several intensely lobulated megakaryocytic nuclei as well as large pools of platelets. These hyper segmented nuclei were either compact in the arrangement (Figure-1; Leishman stain, 100 X Magnification) or widely spaced (Figure-2; 100 X) sometimes showing abundant cytoplasm (Figure-3; 40 X) as well as in the shape of a stag horn (Figure 4; 40 X). This patient's marrow smears revealed all these variable morphologies of megakaryocytes on microscopy. Bone trephine showed an increased number of large-sized megakaryocytes, which were dispersed in loose clusters (Figure 5, Hematoxylin, and Eosin Stain, 40 X). Reticulin stain revealed a normal pattern of reticulin fibers. JAK2 V617F mutational analysis was positive and Bcr-Abl translocation by PCR was negative.

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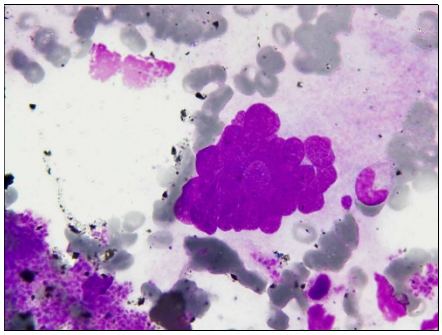

Figure-1: Megakaryocytes with deeply lobulated nuclei in the compact arrangement

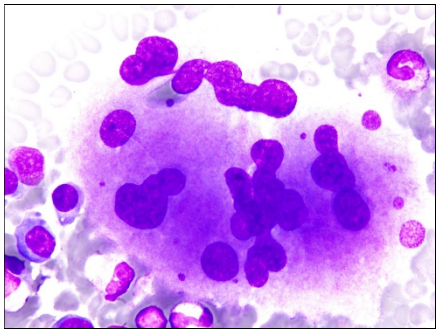

Figure-2: Megakaryocytes with widely spaced hyper segmented nuclei

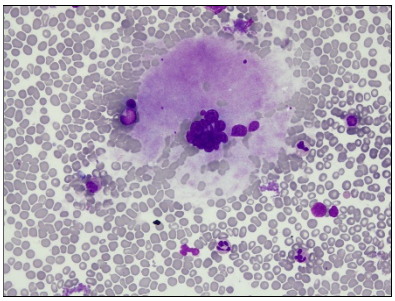

Figure-3: Megakayocytes showing abundant cytoplasm along with hyperlobation of nuclei

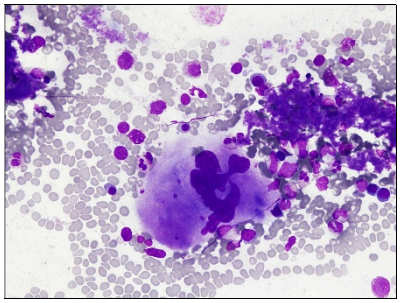

Figure-4: Hyper segmented nuclei in the shape of stag horn

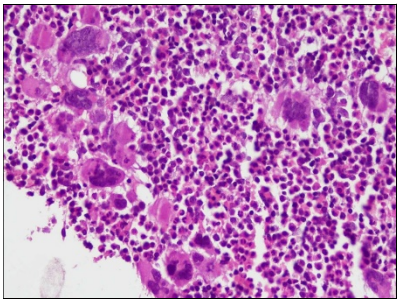

Figure-5: Bone trephine showing an increased number of large-sized megakaryocytes, dispersed in loose clusters

Table-1: 2016 WHO Criteria for Diagnosing Essential Thrombocythemia[3]

Major Criteria	Minor Criteria
Platelets count greater or equal to 450x 10^9/L	Presence of a clonal marker (e.g., abnormal karyotype) or absence of evidence for reactive thrombocytosis
Bone marrow biopsy shows an increase in several megakaryocytes. Megakaryocytes are enlarged, mature with hyper-lobulated nuclei. No significant left shift of neutrophil or erythrocyte production, and minor (grade 1) increase in reticulin fibers(rare)	
Not meeting WHO criteria for BCR-ABL1+ CML, PV, PMF, MDS, or another myeloid neoplasm	
Presence of JAK2, CALR, MPL mutation	

RESULT

It is observed that the histological features particularly megakaryocytes morphology help to identify the exact aetiology and would be valuable in terms of the diagnosis.

DISCUSSION

Essential thrombocythemia is a myeloproliferative neoplasm with an incidence rate of around 1.0–2.5 per 100000 annually.[3] Mutation in any of three genes: JAK2, CALR, or MPL is considered as the main driver to cause any of the myeloproliferative disorders (i.e., Essential thrombocythemia, Polycythaemia Vera, Primary Myelofibrosis). 55–65% of essential thrombocythemia cases have been related to JAK2 mutations, 15–30% have CALR mutation, and 4–8% have MPL mutation.[4]

In 2016 WHO revised the criteria for the diagnosis of ET (Table-1), according to which either all of the major criteria or the first 3 major criteria along with the minor criteria should be met.

The role of megakaryocytes morphology is though controversial in concrete diagnosis but as the clinical features of myeloproliferative neoplasm simulate, megakaryocytes description is indeed a valuable tool in aiding the diagnosis. Hence, bone marrow examination is of prime importance in differentiating essential thrombocytosis from polycythaemia vera and primary myelofibrosis

Trephine biopsy in essential thrombocytosis shows hypercellularity or normal cellularity with an increased number of megakaryocytes and no or little reticulin fibers. Megakaryocytes are in loose clusters in ET, unlike in primary myelofibrosis where dense clustering is present. In addition to it, nuclei of megakaryocytes in ET are either hyper lobulated in the form of staghorn, or compact in the arrangement, or dispersed.[1,5] In the above case, our patient represents all three presentations of nuclei. Furthermore, megakaryocytes in ET have abundant cytoplasm as seen in Figure-3. On the other hand, in polycythaemia vera, bone marrow usually shows normal-sized megakaryocytes with cloud like appearance of nuclei, whereas the primary myelofibrosis pre-fibrotic stage represents normal-sized megakaryocyte distributed in tightly dense clusters with scant cytoplasm, and balloon-shaped/cloud appearance nuclei along with the frequent presence of bare nuclei.[6] A review of trephine by hematopathologist is helpful to confirm and validate the diagnosis of Essential Thrombocythemia.

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