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Case Report

A Patient with Altered Sensorium and Splenic Abscess Diagnosed to Be a Case of Myeloproliferative Disease: A Case Report

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Abstract

About 1.0 to 2.5 individuals per 100000 have essential thrombocytosis every year. The prevalence was seen mostly in females and was reported to be 38 to 57 per 100000 between 2008 and 2010. The incidence increases with age and most of the patients presents in age group of 50 and 60. A middle-aged male patient came with the complain of dragging sensation due to massive splenomegaly without any constitutional symptoms except that there was acute onset of altered sensorium since 1 day. Ultrasound was suggestive of massive splenomegaly with splenic abscess. Later he was diagnosed to be the case of hematological disorder i.e Myeloproliferative disorder.

Keywords: ***thrombocytosis, splenic abscess, myeloproliferative disorders***

Introduction

Essential thrombocytosis is also known as essential thrombocythemia (ET). This is one of the myeloproliferative neoplasms and was included among other myeloproliferative disorders like polycythemia vera, primary myelofibrosis and essential polycythemia [1,2].

The WHO has following diagnostic criteria for ETT [3]. These includes Major and Minor criteria when all 4 of major or first 3 and the minor ones are fulfilled.

Major criteria

1. Platelet count ≥ 450,000/microlitre
2. The bone marrow biopsy shows proliferation, mainly of the megakaryocytic lineage, with an increase in the number of enlarged, mature megakaryocytes with hyper loculated nuclei. No significant increase or left shift in neutrophil granulopoiesis or erythropoiesis is present, and there is very rarely a minor increase in reticulin fibers.
3. Not meeting criteria for BCRABL1+CML, PCV, myelofibrosis, MDS, or other myeloid neolplasms
4. + JAK2, CALR, or MPL

Minor criteria

1. Presence of a clonal marker
2. Absence of evidence of reactive thrombocytosis.

There are subtle difference between the British Society of Hematology (BSH) 2014 diagnostic criteria [4] and the WHO 2016 diagnostic criteria an important distinction being that a bone marrow is not necessary (although recommended) for a diagnosis of ET by the BSH criteria with an appropriate pathogenic mutation and the absence of any alternative myeloid malignancy being sufficient [5].

BSH (2014 Modification of 2010 Criteria)[1]	
A1	Sustained platelet count ≥ 450 × 10^9/L
A2	Presence of an acquired pathogenic mutation (JAK2/CALR/MPL)
A3	No other myeloid malignancy
A4	No reactive cause for thrombocytosis and normal iron stores
A5	Bone marrow aspirate and trephine biopsy showing increased megakaryocyte numbers displaying a spectrum of morphology with predominant large megakaryocytes with hyperlobated nuclei and abundant cytoplasm. Reticulin is generally not increased (grades 0–2/4 or grade 0/3)
Diagnosis requires A1-A3 or A1 + A3-A5	

The majority of patients with essential thrombocytosis have mutations in one of the three genes: Janus Kinase 2 (JAK2), calreticulin (CALR) or myeloproliferative leukemia virus oncogene (MPL) [5]. Rare cases involve mutations in the thrombopoietin gene

(THPO), which are associated with autosomal dominant hereditary thrombocytosis and somatic mutations in tet methylcytosine dioxygenase 2 (TET 2) [6]. These genes are known as "driver mutations" due to their role in developing myeloproliferative neoplasm [7].

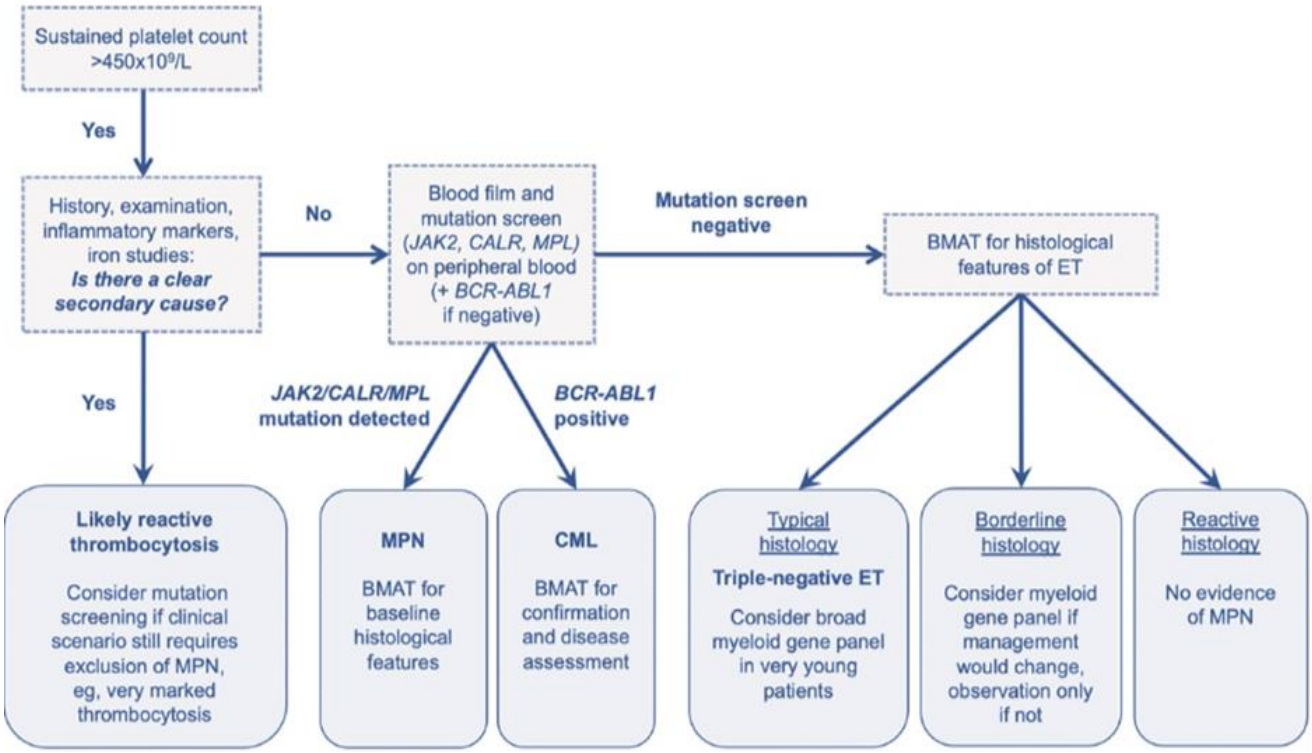
Reports shows decrease in von Willebrand ristocetin cofactor activity and high molecular weight von Willebrand factor multimers [8,9]. Several reports show patients with an acquired deficiency of antithrombin III, protein C, protein S [10].

Thrombocytosis is divided into two groups: Primary and secondary/reactive [11]

Primary thrombocytosis, especially essential thrombocythemia and polycythemia vera, have an increased risk of thrombosis and bleeding compared to secondary thrombocytosis [12].

80 to 90 % of thrombocytosis patients are having secondary causes [13].

Extreme thrombocytosis may rarely result in thrombotic events such as acute myocardial infarction, mesenteric vein thrombosis and pulmonary embolism [14].



Diagnostic pathway for essential thrombocythemia. BM = bone marrow; BMAT = bone marrow aspirate and trephine; CML = chronic myeloid leukemia; ET = essential thrombocythemia; MPN = myeloproliferative neoplasm.

Source

Low-Risk Essential Thrombocythemia: A Comprehensive Review

HemaSphere5(2): e521, February 2021.

Age < 60 years has been associated with a reduced rate of leukemic transformation and myelofibrosis when compared with those over the age of 60, although given the long survival of younger patients, the lifetime risks may be comparable [15,16].

Spurious thrombocytosis is characterised by the presence of non-platelet structures in the peripheral blood which are counted as platelets by the automated counters used in modern complete blood counts. A variety of such structures are needle like cryoglobulin crystals [17], cytoplasmic fragments of circulating leukemic cells [18], bacteria [19] and red blood cell microvesicles following massive burn injury [20] are examples of structures mimicking platelets.

Vascular complications, such as arterial and venous thrombosis, are the leading causes of morbidity and mortality in patients with ET (essential thrombocythemia) [21.22].

Thrombosis is a common complication associated with essential thrombocythemia [21,22], with an estimated incidence of around 14% after 10 years, [23] and a prevalence of 10% to 35% at the time of diagnosis [24]. Microvascular complications like erythromelalgia, migraine and paresthesia are also observed. In some extreme cases of thrombocytosis (platelet count>1000×10^9/l). Bleeding in such cases is typically due to an acquired von Willebrand syndrome(aVWS). The mechanism of aVWS is not entirely clear but is believed to be due to loss of high molecular weight multimers of von Willebrand factor through increased proteolysis by ADAMTS13 and/or increased vWF adsorption onto the surface of platelets [25,26]. Bleeding appears to be dependent on platelet count.

Case Report

A male patient, 60 year old came to the emergency for the main complain of altered sensorium since 1 day. Subsequently he gave the history of left sided dragging sensation or heaviness without any tenderness. He had h/o left sided hemiplegia few months back which resolved itself. He was hypertensive and Diabetic since > 1 and half years. He had no h/o fever, weakness or pain. Old documents were suggestive of splenic abscess for which he was took treatment several times but it recurred. He had h/o chronic cystitis and umbilical hernia along with mild prostatomegaly. There was no H/o any addiction or any c/o seizures, hypoglycemia, abnormal body movements, headache, syncope, chest pain, erythromelagia, acrocyanosis and visual changes.

On examination, BP was 166/98 mmHg, Pulse 82/ minute, regular, Spo2 was 98%, RBS 198 mg/dl. GCS was E4 V1 M6. On abdominal examination, there was 7 cm spleen enlargement below the costal margin, liver was 2 cm enlarged. There was no tenderness present.

Urinary infection was present. Patient was kept on antibiotics, Hydroxyurea 500 mg OD, anti-platelet (tab Ecosprin-AV 75/20) and anti-diabetics,

Following investigations were done-

Hb 14.50 gm/dl

TLC 13.61 × 10^3 /µl 16.08 × 10^3 /µl

Polymorph 85%, lymphocyte 9%, eosinophil 1%, monocyte 4%, basophil 1%

Platelet count 10.22× 10^3 /µl, 13.33 × 10^3 /µl, 1647× 10^3 /µl ↑↑, 1226 × 10^3 /µl, 1107 × 10^3 /µl

MCV 80.70 fl

MCH 24.70 pg

MCHC 30.60 g/dl

RDW-CV 18.3 %

HCT 47.4%

PT/INR 16.30/1.28

Urine routine shows turbid consistency, protein 2+, blood +++, WBC 0-1/HPF, RBC 30-60/HPF,

Urine c/s normal,

Serum calcium(ionic) 1.13 mmol/l

Serum potassium 5.14 mmol/l

Serum sodium 136 mmol/l

Serum urea 42.44mg/dl

Serum creatinine 1.23 mg/dl, 1.51

Anti HCV -ve

HBsAg -ve

HIV -ve

HBA1C 9.9%

HSCRP 55.62 mg/l

Serum uric acid 6.05 mg/dl

Serum Bilirubin(T) 0.61 mg/dl, SGOT 57.20 U/L, SGPT 54.77 U/L serum Alk. Phosphatase 306.80 U/L

Serum Albumin 4.19 g/dl

Serum protein (T) 8.14 gm%

Serum Ferritin 200 ng/ml

Serum Iron 98 mcg/dl

Ultrasound whole abdomen

1. 1st report

Liver GB, CBD, Portal vein, pancreas, kidney normal.

Spleen enlarged in size (~15.39cm) with shows heteroechoic lesion at mid and lower pole of the spleen (measuring ~ 14.12 ×10.57 ×9.06 cm), volume 708 cc s/o Splenic abscess.

Herniation of small bowel loops is noted in anterior abdominal wall in umbilical region through in a defect (measuring ~ 16 ×15 mm) s/o umbilical hernia.

2. 2nd report

Liver GB, CBD, Portal vein, pancreas, normal.

Spleen enlarged eith hypoechoic lesion 68.4 × 62 × 42.1 mm = 93.57cc with organised collection without internal vascularity seen s/o abscess.

Anterior abdominal wall defect of size 17.2 mm in umbilicus region. Sac containing omental fat which is reducible.

Urinary Bladder Partially distended, UB wall is irregularly thickened and trabeculated.

Prostate enlarged in size (44.8 × 41.0 × 37.7 mm= 36.23 gms)

Impression: Mild splenomegaly with splenic abscess, umbilical hernia, chronic cystitis, Benign prostate enlargement

3. 3rd report

Liver enlarged with 19.4 cm with hypoechoic echotexture.

GB, CBD, Pancreas, Kidney normal

Spleen is enlarged in size 17.6 cm with a cystic area of size 4.7 × 4.6 cm. volume 47 ml seen at upper part of spleen with another cystic area of size 13.1 × 12.3 cm volume 1.10 litre seen at mid and lower part of spleen.

Cystitis+++

Impression: No ascites, left pleural effusion (minimal)

Umbilical Hernia + with gap of 18.2 mm

Moderate hepatomegaly

Splenomegaly (17.6 cm) with a cystic area of 4.7 × 4.6 cm. volume 47 ml seen at upper part of spleen with another cystic area of size 13.1 × 12.3 cm volume 1.10 litre.

B/L pyelonephritis with right hydronephrosis(mild) (left>right)

Cystitis +++, PVR 91 mls(significant)

Prostate enlargement++

4. 4th report

Liver normal (~12.6cm), GB, CBD, Pancreas, kidney normal.

Spleen: Entire splenic parenchyma is replaced by heterogeneously hypoechoic lesion with largest measuring~ 7.8 ×7.8 × 7.8 cm with liquefiable content within, likely splenic abscess.

Bone Marrow Aspiration And Biopsy
Cellularity proportion 26 % Blast 00 promyelocyte 00 Myelocyte 02% Metamyelocyte 05 % Neutrophil + band: 58% eosinophil 02% Basophil 00 Monocyte 00

HEMATOLOGY REPORT

SITE : Bone marrow

GROSS : **Clinical Details:**

Indication: ? Myeloproliferative Neoplasm
Clinical details: Thrombocytosis with splenic abscess and left flank pain for 2 months.
Anatomic site of aspirate/biopsy: Right posterior superior iliac crest

Specimen types:
Peripheral blood smear
Bone marrow aspiration
Bone marrow core (trephine) biopsy
Bone marrow core touch preparation (imprint)

Macroscopic:
Number of cores: One
Aggregate length: 1.6 cm

MICROSCOPIC : **1) Peripheral blood smear (BMC-31/24):**

Hb	RBC		WBC		Platelet	Others
13.0g/dl	Count:	5.1(10^6)/ul	Count:	11.2(10^3)/ul	1026.0 (10^3/ul)	No haemoparas or atypical cells seen.
	MCV:	80.1fl	Neutrophil:	77%		
	MCH:	25.4pg	Lymphocytes:	17 %		
	MCHC:	31.7g/dl	Monocytes:	05 %		
	RDW-CV:	17.8%	Eosinophil:	01%		
	Reticulocyte count	2.1	Basophil:	00		

Comment on PBS: **RBC:** Predominantly normocytic normochromic cells. **WBC:** Neutrophil leucocytosis. **Platelets:** Severe thrombocytosis, moderate anisocytosis, few giant and large platelets along with frequent platelet clumps are noted.

Aspirate Morphology:

2)Bone marrow aspiration (BMA-31/24): Particulate marrow and adequate for evaluation

Cellularity: Hypercellular for age

Erythroid series	Myeloid series	Lymphocytes
Cellularity: Adequate **Maturation:** Normoblastic	**Cellularity:** Adequate **Maturation:** Evident	**Cellularity:** Within normal limits.

HEMATOLOGY REPORT

Cellularity Proportion: 26%	Blast: 00 Promyelocyte: 00 Myelocyte: 02% Metamyelocyte: 05% Neutrophil + band: 58% Eosinophil: 02% Basophil: 00 Monocyte: 00	**Cellularity Proportion:** 06% **Morphology:** Normal **Plasma Cells** **Cellularity:** Within normal limits. **Cellularity Proportion:** 01% **Morphology:** Normal
Megakaryocytic Series:		
Cellularity: Increased **Morphology:** Loose, small and large clustered megakarocytes are noted. These cells are large sized, having deeply lobated nuclei and abundant amount of eosinophilic cytoplasm.		
Myeloid: Erythroid Ratio: 2.5:1		
Others: No atypical cells, granulomas or haemoparasites seen.		

Cyto-chemical stain:

Perl's stain for iron stores: Adequate, Grade 3 (Modified Gale's Criteria). No ring sideroblasts are noted.

COMMENT :

- **HYPERCELLULAR MARROW WITH TRILINEAGE HAEMATOPOIESIS WITH GRANULOCYTI HYPERPLASIA AND INCREASED MEGAKARYOPOIESIS.**
- **POSSIBILITY OF MYELOPROLIFERATIVE NEOPLASM (ESSENTIAL THROMBOCYTHEMIA) IS SUGGESTED.**

NOTE : *Reflex mutational analysis for **JAK2/CALR/MPL** is advised for confirmation/further characterization.*

Jak 2 V617f Test – +Ve, Detected (Pcr Qualitative)

Discussion

The symptoms are due to microvascular inflammation, platelet aggregation and arteriolar microthrombi formation [27,28] and are more common in ET than PV, with some vasomotor symptoms present in 29–40% of ET patients at presentation [29-31]. In present case, patient had c/o left sided hemiplegia few months back.

The frequency of erythromelalgia, the most common vasomotor complication of PV and ET, is not directly correlated with higher platelet counts, and in fact, vasomotor symptoms are essentially never present in reactive thrombocytosis. These facts underlie the important role that qualitative platelet abnormalities [28] and increased thromboxane-induced platelet activation [32] play in causing vasomotor symptoms, as erythromelalgia has been described in patients with relatively normal platelet counts in a multitude of nonhematologic conditions [33]. The lack of specificity of these symptoms makes estimating prevalence difficult, but the typical prompt response of ET-related vasomotor symptoms to aspirin can be a useful diagnostic as well as therapeutic intervention.

The incidence of macrovascular thrombotic complications at diagnosis varies between 11% to 25% in ET and 12% to 39% in PV [34-38]. Arterial thrombosis ie the frequent type of complications. Stroke or transient ischemic attack in the cerebrovascular circulation is the most common site of arterial thrombotic disease, followed by the coronary arteries and peripheral vasculature [39,40]. The present case had H/o transient ischemic attack and CVA.

In patients with ET, there is a higher occurrence of arterial thrombotic events compared to polycythemia vera (PV), and around 40% of thrombotic events are venous in nature [41]. In younger patients, > 50% of venous thrombotic events happens to occur in such locations like splanchnic veins and cerebral sinuses [42-44].

Given the frequency of thrombotic events in these unusual locations, strong consideration should be given to evaluation for occult Ph- MPN in any patient presenting with splanchnic or cerebral sinus thrombosis. Case series have reported that 23-51% of patients suffering from splanchnic thrombosis without any other risk factors can be diagnosed with an underlying Ph- MPN at the time of thrombosis [45,46], and JAK2V617F mutations have been demonstrated in a number of such patients, many of which only met full criteria for a Ph- MPN later in their course [47,48].

As per various epidemiological studies, age plays an important role as a risk factor for thrombosis in the general population [49].

Conclusion

In patients with thrombocytosis, and > 60 years, various non specific clinical situations can be the presentation. In a patient with syncopal attacks and evidence of thrombosis, specially with splenomegaly and hepatomegaly, a proper approach is must to exclude various causes of thrombocytosis like primary or secondary/reactive. In diagnostic dilemna, JAK2 status must be investigated with bone marrow biopsy. High risk groups must be recognised early and timely intervention with antiplatelet and cytoreductive therapy is given.

Ethical Approval

The ethical approval was not required as patient's identity was not disclosed.

Conflicts of Interest

The authors declare that there is no conflicts of interest.

Author's Contribution

Jyoti Verma did the plan of manuscript preparation, investigations and management, Upendra have contribution in interdepartmental references and timely as required inward management and Inderjeet have contribution in literature review, sampling and collection of reports. Tejaswani have contribution in collection of reports and sampling. Sumit have done the written references and sampling.

Data Availability Statement

Data will be made available on request to the corresponding author (Jyoti Verma).

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