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Clinicopathological Profile of Patients with Myeloproliferative Neoplasms presenting with Nonabdominal Vein Thrombotic Event

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INTRODUCTION

- Myeloproliferative neoplasms (MPNs) are marked by the clonal proliferation of abnormal hematopoietic stem or progenitor cells and involve thrombohemorrhagic complications.
- Risk factors impacting MPNs include modifiable factors such as age, hyperlipidemia, hypertension, and diabetes, as well as disease-related factors like leucocytosis and erythrocytosis. (1,2)
- Approximately 20% of MPN cases present with thrombosis and risk persists. More common is splanchnic thrombosis, other sites also involved.
- Polycythemia vera patients have highest incidence (3.5 events per 100 person-years)(3) followed by essential thrombocythemia and primary myelofibrosis patients with slightly lower rates (2.5 events per 100 person-years).(4)

AIM

- We aim to study the clinical and laboratory factors and its association with thrombosis in patient with MPN.
- To study the various subtypes of MPN and its association with thrombosis type.
- To study the treatment landscape among those with thrombosis.

METHOD

- It is a cross-sectional observational study
- Inclusion criteria
  - Age>18 years
  - Diagnosed case of either arterial or venous thrombosis and myeloproliferative neoplasm including molecular and bone marrow findings
- Exclusion criteria
  - Abdominal vein thrombosis
- Clinical parameters : Following data was collected: age at presentation and diagnosis of thrombosis, subtype of MPN, driver mutation, spleen size, any cardiovascular risk factors, type and site of thrombosis, temporal relation between the even and diagnosis of MPN, therapy received for thrombosis and for MPN and outcome.
- Thrombosis was defined with radiological evidence of arterial or venous thrombosis.
- Statistics: Data were presented using median/range and percentage. MS Excel 2016 was used for analysis.

RESULTS

- Over 36 months, 31 events of non abdominal vein thrombosis occurred in total 29 cases of myeloproliferative neoplasms.
- The median age of diagnosis was 43 years (18-70 years).
- PV was the most common MPN complicated with thrombosis followed by ET and PMF.
- PV had 50% arterial and 50% venous events as compared to ET where around 87.5% patients had a venous thrombosis.
- Around 23(79.4%) patient had diagnosis of thrombosis preceding the diagnosis of MPN whereas only 3 (10.3%) patient were previously
- diagnosed with MPN when presenting with a thrombotic event whereas 3(10.3%) patient had diagnosis of MPN during investigation for acute thrombotic event.
- In those with MPN being diagnosed after thrombotic event, the median time interval between a thrombotic event and diagnosis of MPN was 6 months (0 – 120 months).
- Hypertension was the most common additional cardiovascular risk factor.
- Treatment of the acute episode involved anticoagulant and antiplatelet agent along with management of MPN.
- Long term complications was seen in 4 patient with 3 being post thrombotic syndrome for DVT and one patient had chronic thromboembolism associated pulmonary hypertension.

Figure 1. Distribution of thrombotic events

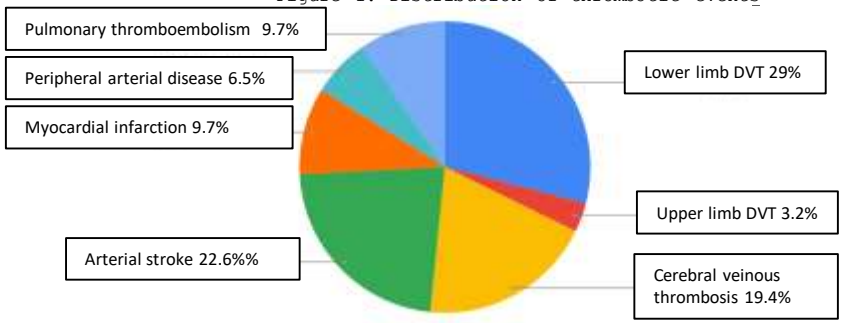


Table 1. Baseline characteristics of patients with myeloproliferative neoplasm

Age in years	43 (18-70)
Gender Male Female	 18(58.4%) 12(41.4%)
Median body mass index	22(14.9-30)
Type of MPN •PV •ET •PMF •Post PV- MF •MPN-U	 18(62.1%) 8(27.6%) 2(6.9%%) 1(3.4%) 0
Mutation status •JAK2 V617F •CALR •MPL •Triple Negative •Not available	 21(72.4%) 4(13.8%) 0 2(6.9%) 2(6.9%)
Splenomegaly	15(58.6%)
Cardiovascular risk factors	10(34.5%)
Baseline hematological parameters •Hb(gm/dl) •WBC(cells/ul) •Platelets($(10^3$/ul))	 16.2(7.4-21.4) 10900(6550-39730) 470(77-1882)
LDH (mg/dl)	321 (123-351)

PV- polycythemia vera, ET - essential thrombocytosis, PMF- primary myelofibrosis ,JAK - janus kinase, CALR - calreticulin, MPL - myeloproliferative leukemia virus oncogene, Hb - hemoglobin, WBC - white blood cells, LDH - lactate dehydrogenase.

Table 2. Clinical features and treatment landscape of thrombosis in MPN

Thrombosis •Arterial •Venous	 11(37.9%) 18(62.1%)
Site of Thrombosis (total events-31) •UL DVT •LL DVT •PE •MI •CVA •CVT •PAD	 1(3.2%) 9(29%) 3(9.7%) 3(9.7%) 7(22.6%) 6(19.4%) 2(6.4%)
Timing of diagnosis of MPN •At the same time •After diagnosis of a thrombotic event •Before thrombotic event	 3(10.3%) 23(79.6%) 3(10.3%)
Treatment of MPN Phlebotomy with aspirin Phlebotomy with aspirin and hydroxyurea Only aspirin Hydroxyurea with aspirin Danazol and thalidomide	 2(6.9%) 13(44.8%) 2(6.9%) 11(37.9%) 1(3.4%) `
Treatment of thrombotic events Anticoagulant •DOAC •VKA •LMWH Antiplatelet Combination of DOAC and Antiplatelet	 5(17.2%) 8(27.6%) 3(10.3%) 11(37.9%) 2(6.9%)

DVT – Deep vein thrombosis, PE – pulmonary embolism, MI – myocardial infarction, CVA- cerebrovascular accident, CVT- cerebral venous thrombosis, PAD – Peripheral artery disease, MPN – Myeloproliferative neoplasms, DOAC – direct oral anticoagulants, VKA – Vitamin K antagonists, LMWH – low molecular weight heparin

CONCLUSIONS

- Thrombosis contributes to morbidity in patient with MPN.
- Early suspicion of MPN followed by adequate molecular workup helps in prognostication and management of the disease
- JAK2 mutational study in patient presenting with unprovoked thrombosis or thrombosis at unusual age and site should be considered.

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