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What are Myeloproliferative Neoplasms (MPN)?

Myeloproliferative Neoplasms (MPNs) refer to a group of rare, chronic blood cancers caused by the excess production of different blood cells by the bone marrow.

MPN is classified into 3 major conditions – Polycythaemia Vera (PV), Essential Thrombocytosis (ET) and Myelofibrosis (MF). These conditions are characterised by increased and abnormal proliferation of bone marrow cells such as white cells, red cells and platelets, which in turn lead to a host of symptoms and complications. These conditions last a long time, are progressive in nature, and may worsen over time.

Polycythaemia Vera (PV)

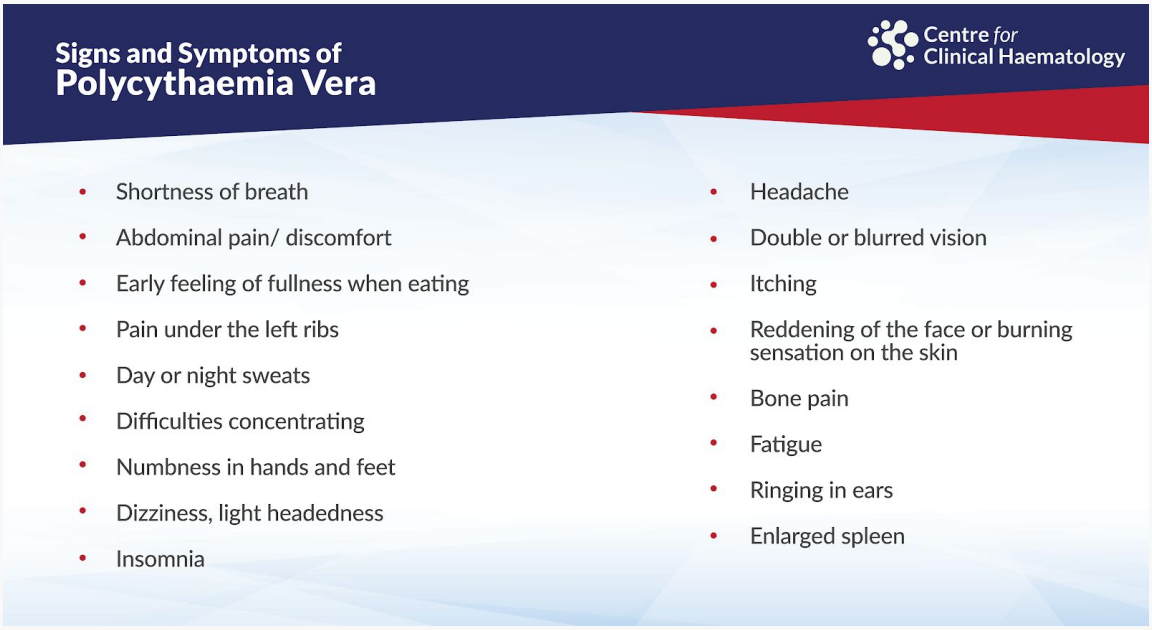
Polycythaemia Vera is a rare, chronic blood disorder in which the patient's bone marrow proliferates by making too many red blood cells causing the blood to be too viscous. Patients with PV are at a higher risk of forming blood clots (thrombosis) because the blood is too 'thick and sticky' which can obstruct the flow of blood through arteries and veins. This may lead to strokes, heart attacks or clots involving other parts of the body such as the leg veins causing DVTs (Deep Vein Thrombosis).

PV is characterised by an increased haemoglobin level. Many patients with PV also have an increased white blood cell count and platelet count. Research has found that almost 97% of patients carry a mutation in a gene (protein) known as Janus Kinase 2 (JAK2). JAK2 usually regulates the production of blood cells in our bone marrow.

PV can happen at any age but is more common after the age of 60 and is more common in men.

Signs & Symptoms

Patients with PV may not experience or show any symptoms initially. Hence, this condition is usually detected during routine tests or screening. As PV progresses, it may present with chronic headaches and flushing of the skin due to the increased haemoglobin level.



Complications

Complications of PV are related to the risk of blood clots, including:

- Leg clots (Deep Vein Thrombosis)
- Lung clots (Pulmonary Embolism)
- Heart attack
- Stroke
- Progression to Leukaemia
- Progression to another MPN (MF)

Prognosis

The prognosis depends on many factors including age, other co-existing illnesses, and the complications that may occur. Blood clots are common and can be serious.

Most patients with PV have a near normal or slightly reduced life expectancy if monitored and treated properly.

About 15% of patients with PV may progress to develop Myelofibrosis (MF). A smaller percentage may progress to develop Acute Myeloid Leukaemia (AML) and the prognosis for this subset of patients may be poorer as these diseases are often resistant to treatment. Our haematologist will monitor your blood and general health regularly to monitor for signs of Leukaemia or Myelofibrosis.

Essential Thrombocythemia (ET)

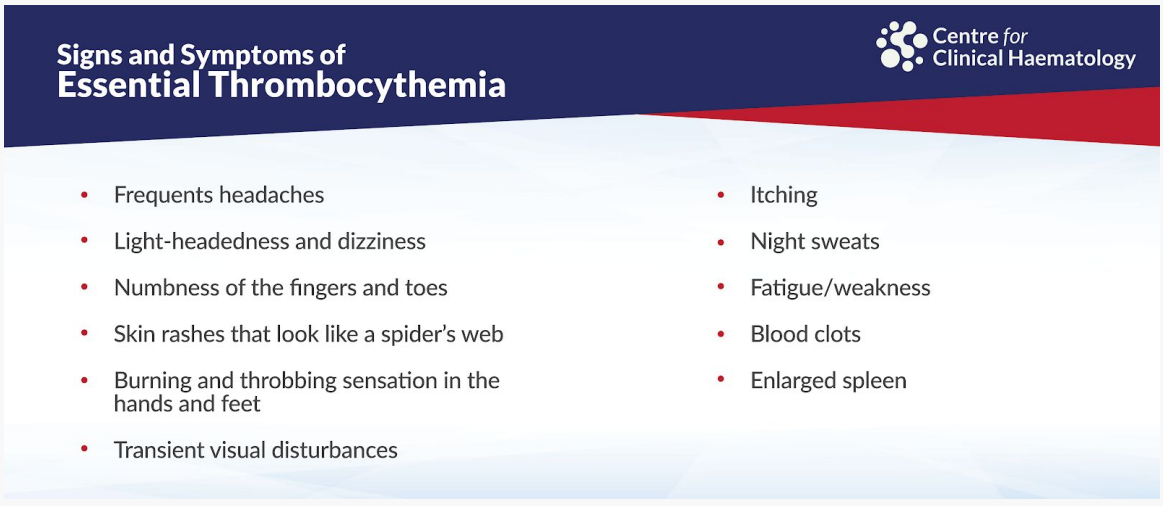
Essential Thrombocythemia is a rare disorder that occurs due to the excessive production of platelets by the bone marrow leading to a high platelet count. The high number of platelets causes the blood to become 'sticky' so people with ET have a high risk of clotting. Less commonly, some patients have bleeding problems because the rapid multiplication of platelets prevents them from developing into mature platelets and hence they do not function properly.

The majority of patients with ET carry mutations in one of 3 recognised genes (or proteins) – Janus Kinase 2 (JAK2), Calreticulin (CALR), and Thrombopoietin receptors (MPL).

ET is slightly more common in women than men. Most people diagnosed with ET are over 60, although in recent years there have been more people under the age of 40 being diagnosed with ET.

Signs & Symptoms

Most patients do not have any symptoms at presentation, and ET is often diagnosed as an incidental finding of a raised platelet count during health screening. Others may present with the following signs and symptoms:



Complications

Complications of ET may include:

- Leg clots (Deep Vein Thrombosis)
- Lung clots (Pulmonary Embolism)
- Heart attack
- Clotting complications
- Pregnancy complications
- Excessive bleeding
- Progression to another MPN, such as Myelofibrosis (MF)
- Progression to Acute Leukaemia

Prognosis

The prognosis depends on a few factors, including age and whether you have other illnesses or complications.

Patients who do not suffer from severe thrombotic (clotting) or bleeding complications can probably expect a near-to-normal lifespan if monitored and treated properly by a haematologist.

Some patients with ET develop Acute Myeloid Leukaemia (AML) or Myelofibrosis (MF) at a late stage of the illness. If this happens, then the outlook can be poorer as these diseases are often resistant to treatment. The haematologist will monitor your blood and general health regularly to monitor for signs of Leukaemia or Myelofibrosis.

Myelofibrosis (MF)

Myelofibrosis is a rare blood cancer caused by the formation of scar tissue in the bone marrow – commonly known as fibrosis. The scar tissue reduces the ability of the bone marrow to form normal blood cells. Patients often present with a high platelet count and a high white cell count but the haemoglobin level is low.

MF may be associated with certain genetic mutations such as the Janus Kinase 2 (JAK2) gene. MF may arise in a background of pre-existing PV or ET, or it can also occur as a primary blood condition (primary MF). It mainly occurs in middle age and older individuals with the average age of diagnosis being 65 years old.

Signs & Symptoms

Some patients are asymptomatic, but most will present with some symptom or sign. Severe fatigue (unrelated to anaemia) is a prominent symptom, occurring in up to 70% of the patients. Abdominal discomfort or fullness is another common symptom, which is described by 30-50% of patients. This occurs due to the enlarged liver and spleen in many patients.

Complications

Complications of MF may include:

- Heart attack
- Stroke
- Leg clots (Deep Vein Thrombosis)
- Infections
- Increased pressure on blood flow to the liver (portal hypertension)
- Bleeding complications
- Progression to Leukaemia

Prognosis

MF is the most advanced subtype of MPN. The prognosis of MF is different for every patient. While some live for many years without developing major symptoms or complications, others may find that their disease progresses more quickly. Factors that influence the prognosis of MF are age, white blood cell count, number of immature cells (blasts and leukaemic cells) in the blood, constitutional symptoms (weight loss, fever, night sweats), low red blood cells, transfusion dependence, low platelet count and abnormal chromosomal analysis.

Patients with MF who progress to leukaemia have a poorer prognosis. Eligible patients may benefit from targeted therapy or chemotherapy to stabilise their disease. Some patients may be cured with a timely stem cell transplantation.

How are MPNs diagnosed?

The diagnosis of MPN is made based on physical signs and symptoms, blood counts, and specific diagnostic tests.

The diagnostic tests that can help to detect MPNs include:

- Routine blood tests such as a full blood count often reveal elevated blood counts
- Specialised molecular tests may be required depending on the suspected type of MPN. Usually tests will be done to screen for the presence of mutations in the JAK2 gene as well as other genes affected in MPNs
- A bone marrow biopsy or aspirate is often performed to confirm the diagnosis of this condition

Treatment of MPNs

The aim of the treatment is to minimise the risk of complications associated with MPN and to improve quality of life.

Antiplatelet therapy
Patients who have a high risk of thrombosis may be advised to use antiplatelet drugs like aspirin to prevent the formation of blood clots.

Venesection
Patients with PV may need venesection. This refers to a procedure where blood is removed from the body to lower the number of red cells.

Transfusion of blood products
Patients having severe symptoms of MPNs are often advised to undergo the transfusion of blood products such as red blood cells and platelets.

Cytoreductive therapy with Hydroxyurea
Cytoreductive therapy with Hydroxyurea is recommended for patients with PV and ET having a high risk of clotting. The treatment includes the use of hydroxyurea, an oral chemotherapeutic agent that can reduce haemoglobin levels and the platelet and white blood cell counts.

Interferon
Interferon is an injectable cytokine that works by normalising the blood counts in patients with PV and ET and in some cases of MF. This treatment is safe and effective even for pregnant women as it is non-teratogenic in nature and does not increase the risk of birth defects.

Targeted therapy with JAK2 inhibitors
JAK2 inhibitors such as Ruxolitinib can be used to treat patients who have developed the complications of MPNs. It can also help to reduce the spleen size and hence alleviates the symptoms caused by an enlarged spleen such as pain under the left ribs and early satiety.

Stem Cell Transplantation
This is the only curative treatment for MF. During a **stem cell transplant**, blood forming stem cells are transferred from a healthy donor to the patient. The decision to pursue stem cell transplant is made by careful consultation with a haematologist specialising in stem cell transplantation.