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Review

Imaging features of myeloproliferative neoplasms

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Myeloproliferative neoplasms (MPNs) are a heterogeneous group of haematological disorders including polycythaemia vera (PV), essential thrombocythaemia (ET), primary myelofibrosis (PMF), and chronic myeloid leukaemia (CML). These disorders show large overlap in genetic and clinical presentations, and can have many different imaging manifestations. Unusual thromboses, embolic events throughout the systemic or pulmonary vasculature, or osseous findings can often be clues to the underlying disease. There is limited literature about the imaging features of these disorders, and this may result in under-diagnosis. Multiple treatments are available for symptom control, and the development of multiple new pharmacological inhibitors has significantly improved morbidity and prognosis. Knowledge of these conditions may enable the radiologist to suggest an MPN as a possible underlying cause for certain imaging findings, particularly unexplained splanchnic venous thrombosis, i.e. in the absence of chronic liver disease or pancreatitis. The aim of the present review is to outline using examples the different categories of MPN and illustrate the variety of radiological findings associated with these diseases.

Background

Myeloproliferative neoplasms (MPNs) are a related group of haematological malignancies including polycythaemia vera (PV), essential thrombocythaemia (ET), primary myelofibrosis (PMF), and chronic myeloid leukaemia (CML). MPNs are characterised by clonal proliferation of stem and progenitor cells resulting in increased mature cells of one or more blood cell lineages. The pattern of these changes in the full blood count together with other clinical features, bone marrow histology, and molecular testing allow confirmation of the specific diagnosis (Table 1).[1]

The discovery of the Philadelphia (Ph) chromosome in CML over 50 years ago was instrumental in providing evidence for the genetic basis of cancer. The presence of this t(9;22)(q34;q11) translocation between the *BCR* and *ABL1* genes must be confirmed to make a diagnosis of CML.[1] More recently, the identification of additional specific genetic aberrations has allowed more reliable diagnosis and classification of the Ph-negative MPNs. Almost all PV patients have a mutation in the *JAK2* gene,[2] most often a V617F mutation, or occasionally a mutation in exon 12 of the gene,[3] while the majority of patients with ET and PMF have a mutation in the *JAK2*, *CALR*[4,5] or (least commonly) *MPL* genes.[6] These mutations have numerous effects on intracellular signalling, but in particular, they result in

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Table 1
Clinical and epidemiological features of myeloproliferative neoplasms.

MPN	Epidemiology	Clinical features	Laboratory features	Genetic basis	Management
ET	Incidence: 1.5–2.0/100,000 Median age 50–55 years F:M 2:1	Thrombosis Bleeding Headaches	Plt > 450×10/l Normal iron levels and CRP Megakaryocytic hyperplasia/atypia in marrow	*JAK2* (55%) *CALR* (25%) *MPL* (5%)	Aspirin Hydroxycarbamide Anagrelide Interferon-α
PV	Incidence: 2.0–3.0/100,000 Median age 55–60 years F:M 1:1.2	Thrombosis Neurological Sx Pruritus Plethora Splenomegaly	High haematocrit: >0.52 in men >0.48 in women Bone marrow pan myelosis	*JAK2* (>95%)	Aspirin Venesection Hydroxycarbamide Interferon alpha Ruxolitinib
PMF	Incidence: 0.5–1.5/100,000 Median age 50–60 years F:M 1:1	Splenomegaly Extra-medullary haematopoiesis Constitutional symptoms Cytopenias	Cytopenias Leuco-erythroblastic blood film Tear drop red cells Increased bone marrow fibrosis	*JAK2* (55%) *CALR* (30%) *MPL* (5%)	Blood transfusion Ruxolitinib Splenectomy Allogeneic stem cell transplant
CML	Incidence: 1.5–2.0/100,000 Median age 50–60 years F:M 1:1.4	Splenomegaly Bleeding Anaemia Constitutional symptoms	Leucocytosis 20–200×10^9/l Full spectrum of normally maturing granulocytes in peripheral blood	*BCR-ABL1* (100%)	Imatinib Second generation inhibitors (e.g., dasatinib, nilotinib) Allogeneic stem cell transplantation

PV, polycythaemia vera; ET, essential thrombocythaemia; PMF, primary myelofibrosis; CML, chronic myeloid leukaemia; Plt, Sx.

constitutive activation of *JAK*/*STAT* growth pathways that leads to unregulated cell proliferation and contributes to the clinical phenotypes observed.[7–10]

A proportion of patients with MPNs are diagnosed incidentally after examination of a full blood count and/or peripheral blood film performed for other clinical reasons.[11] Patients with an MPN diagnosis may present with thrombosis, bleeding, splenomegaly, or extramedullary haematopoiesis. Moreover patients occasionally present with these features, especially splanchnic thrombosis, in the absence of a pre-existing MPN diagnosis or blood count abnormality, but molecular testing may then confirm the presence of a *JAK2* mutation and hence an underlying MPN.[12] It is therefore important for radiologists to be familiar with these conditions so that they can raise the possibility of occult MPN in this clinical context. In a meta-analysis that included almost 2000 patients with Budd–Chiari syndrome or portal vein thrombosis, 17% and 15% of patients, respectively, had a *JAK2* V617F mutation in the absence of typical blood count findings of an MPN.[13] Other typical symptoms of PV and ET include headaches, gout, pruritus, small vessel symptoms such as erythromelalgia (burning pains in the fingers or toes), and pregnancy complications such as recurrent miscarriage. PMF and CML may also be associated with constitutional symptoms and symptomatic cytopenias (especially anaemia).

Imaging findings

Thrombosis

ET and PV both predispose to thrombotic events, which can present in an unusual fashion (Figs 1–3). Guidelines have been published regarding the appropriate investigation of atypical thrombosis.[14] In the brain, arterial thrombi can occur as well as dural sinus thrombosis.[15] The splanchnic

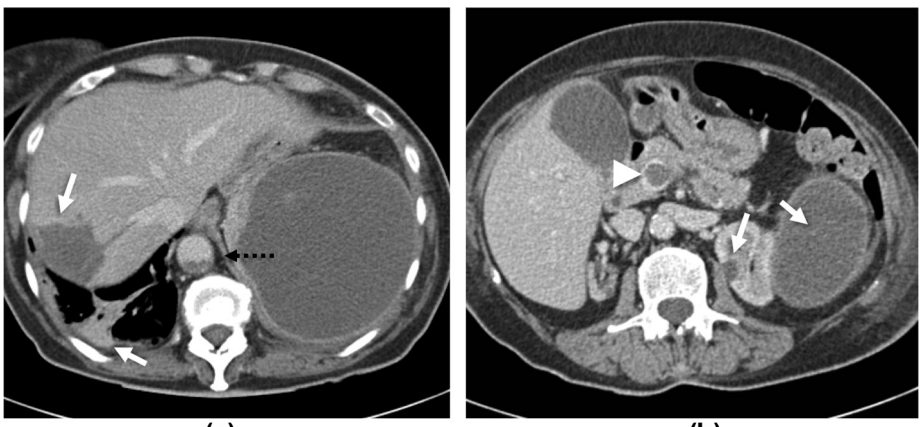

Figure 1 Axial contrast-enhanced CT image of a 71-year-old man with PV. There are infarcts in the kidneys, liver, right lung, and spleen (white arrows). The case demonstrates systemic arterial thromboembolism (visceral infarcts and mural thrombus in the aorta, black arrow), portal venous thrombus (white arrow head), and systemic venous thrombus (iliofemoral thrombus, leading to PE and pulmonary infarct).

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