Edition no. 9: Part 2

PATHCHAT

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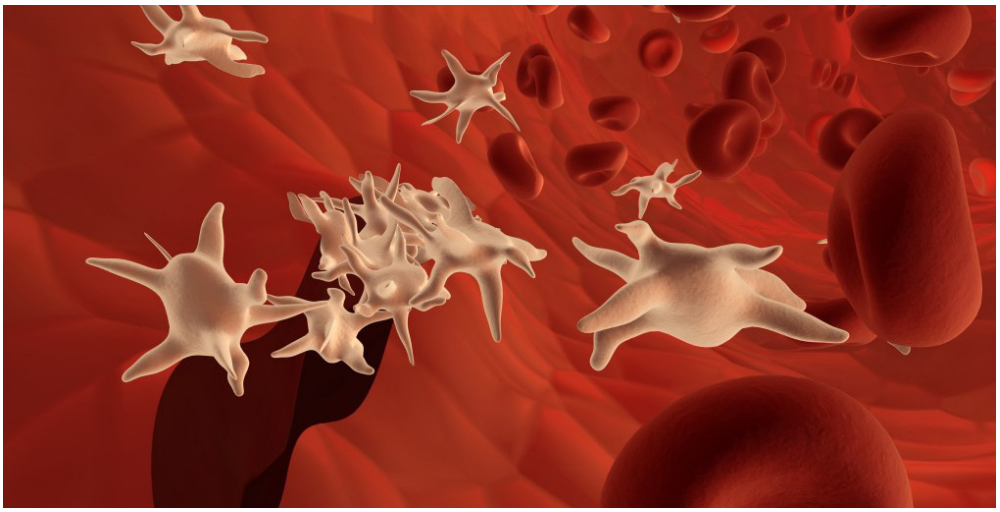
Basic Approach to Abnormal FBC (Part 2):

Platelets and White Blood Cells

PLATELETS

Of note:

- Platelet counts are generally higher in women.
- Persons of African descent show lower platelet counts than those of Caucasian descent.



Thrombocytopenia (see Figure 1)

A pseudo (false) thrombocytopenia, due to either a difficult bleed or ethylenediamine-tetraacetic acid (EDTA)-related platelet clumping, should be excluded by examining a peripheral blood (PB) slide or repeating the platelet count using a sodium citrate tube.

A mild to moderate (75–150 x 10^9/l) incidental thrombocytopenia may occur in healthy women during pregnancy and requires no further investigation.

Once the thrombocytopenia has been confirmed, causes that require urgent treatment should be considered. These include thrombotic thrombocytopenic purpura (TTP)/ hemolytic-uremic syndrome (HUS) and disseminated intravascular coagulation (DIC). Examination of the PB slide (for fragments), lactic acid dehydrogenase (LDH), bilirubin levels, urea and electrolytes (U & E) and DIC screens are recommended. Next, drug-related thrombocytopenia, human immunodeficiency virus (HIV) or other viral infections, auto-immune disease, liver disease and hypersplenism should be considered. A comprehensive drug and alcohol history (including the use of antibiotics, thiazide diuretics, heparin, etc.) should be obtained, and HIV serology, atrial natriuretic factor (ANF) and liver function tests, as well as abdominal ultrasounds performed.

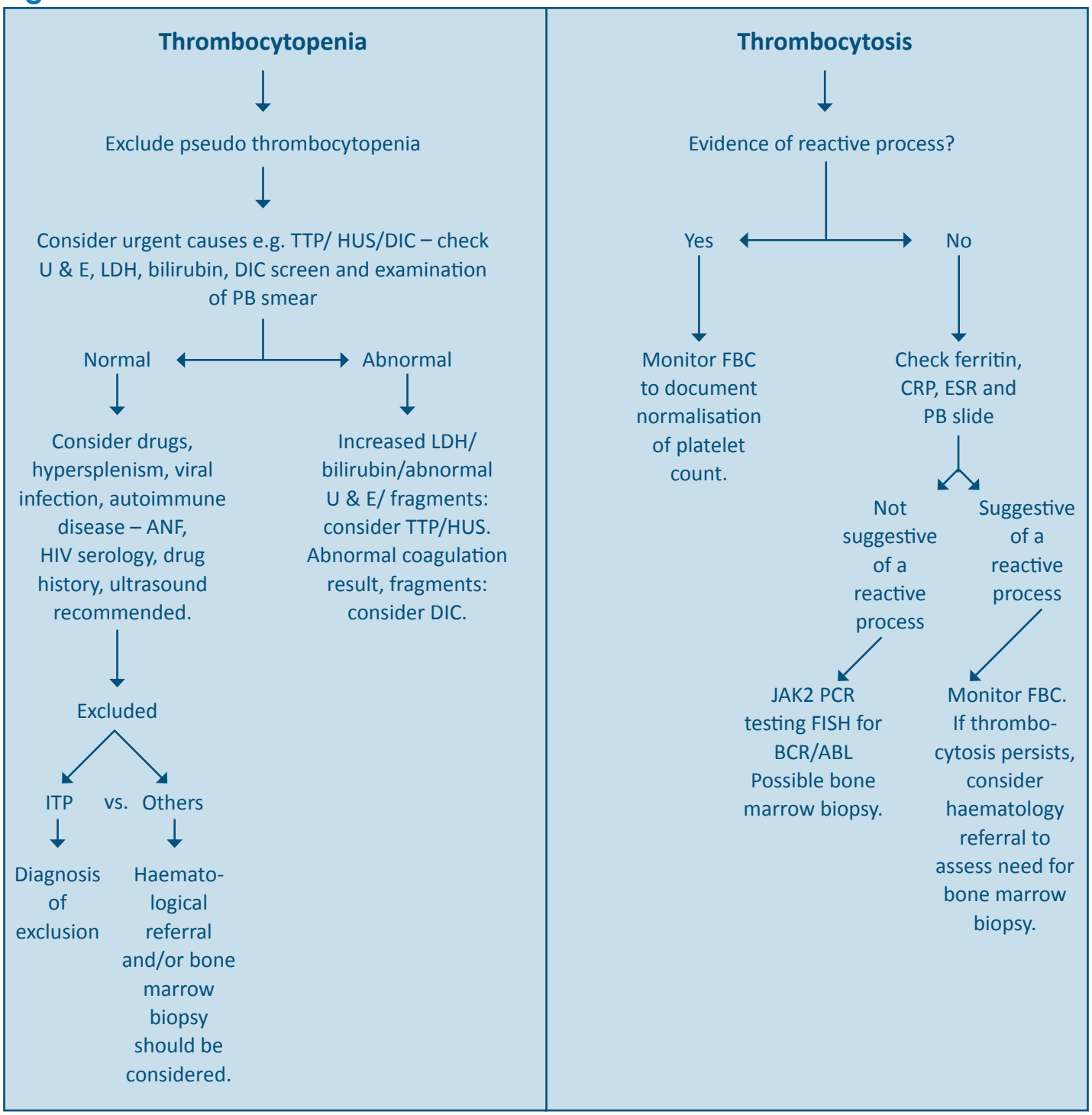
If the above have been excluded, idiopathic thrombocytopenic purpura (ITP) becomes a possibility. If the clinical picture is not consistent with ITP, a bone marrow biopsy should be considered to look for less common disorders such as myelodysplastic syndrome (MDS), lymphoproliferative disease, etc.

Thrombocytosis (see Figure 1)

Thrombocytosis may be either a primary (malignant) or secondary (reactive) process, the former being associated with an increased risk of thrombotic and/or haemorrhagic complications. Common secondary causes include infection, inflammation, pregnancy, iron deficiency, malignancies, post splenectomy. Patient history and examination are generally most helpful in making the distinction between primary and secondary causes. Inflammatory markers and examination of the peripheral blood slide may also assist.

If the above are unhelpful, polymerase chain reaction (PCR) for Janus kinase 2 (JAK2) mutations, fluorescence in situ hybridisation (FISH) for BCR/ABL and possible bone marrow biopsy should be considered.

Figure 1



WHITE BLOOD CELLS

In patients with an abnormal white blood cell count, the type of white blood cells (neutrophil, lymphocyte, monocyte, eosinophila, basophil) affected is important. If indicated, the abnormality should be confirmed on a PB smear.

Of note, persons of African descent show lower white blood cell and neutrophil counts than those of Caucasian descent.

Neutropenia

Neutropenia may be acquired or congenital and is most clinically relevant when severe (<0.5 x 109/l) due to an increased risk for infection. The most frequent causes of acquired neutropenia are drugs and infections (especially viral). Common drugs include antibiotics, NSAIDS, anticonvulsants, antipsychotics, immunosuppressive drugs, etc. However, any drug should be assumed to be a possible cause until proven otherwise. Other less common causes include immune neutropenia, which may be associated with an auto-immune disease, such as systemic lupus erythematosus (SLE) and haematological malignancies, such as MDS.

Evidence of current or recent viral infection should be sought. Any possible offending drug should be stopped and the FBC closely monitored. In persistent moderate (>0.55 x 109/l) neutropenia without an obvious viral (e.g., HIV) or drug cause, further testing may include B12 and folate levels, LFTs and serum protein electrophoresis, ANF and rheumatoid factor (RF) testing. Haematological referral should be considered in patients who are particularly unwell, have a severe neutropenia, lymphadenopathy or hepatosplenomegaly, or if the neutropenia is progressive or persists for longer than six weeks.

Lymphopenia, Monocytopenia and Eosinopenia

Isolated low counts are not usually clinically significant.

Neutrophilia

Neutrophilia may be either reactive or part of a myeloid malignancy. Common causes of a reactive neutrophilia include infection (especially bacterial), inflammation, malignancy, drugs, heavy exercise, pregnancy and smoking. Patient history, a clinical examination and, if necessary, evaluation of the peripheral blood slide will often be all that is required to determine the cause of the neutrophilia and whether further laboratory testing is required. If concerning morphological findings (e.g., blasts, leukoerythroblastic reaction, changes suggestive of chronic myelogenous leukemia (CML)) are noted or if the patient examination and history does not suggest a reactive cause, then further investigation (e.g., FISH for BCR/ABL) and/or haematological referral should be considered.

Lymphocytosis

Review of a peripheral blood slide is recommended as the initial investigative step.

A patient with reactive lymphocytes in an appropriate clinical setting (e.g., atypical lymphocytes in viral infection) should be followed up with a FBC and smear to ensure

resolution of the lymphocyte count once the patient has recovered. A mild lymphocytosis may occur in smokers, post splenectomy and as an acute stress response (e.g., trauma, acute myocardial infarction (AMI)).

Prompt immunophenotypic analysis by flow cytometry is recommended in patients with morphological changes or clinical findings (lymphadenopathy, splenomegaly, hepatomegaly, skin lesions, loss of weight, etc.) that are suggestive of an underlying lymphoproliferative disease.

A lymphocytosis with normal-appearing lymphocytes may be due to chronic lymphocytic leukaemia (CLL). If no worrying clinical features are present, a repeat FBC and smear in 4–6 weeks is recommended. If the lymphocytosis persists, a immunophenotypic analysis should be performed.

Monocytosis

Reactive causes of a monocytosis include chronic infections, inflammatory or granulomatous processes and metastatic cancer. A relative monocytosis may be seen after an AMI or during recovery from chemotherapy or drug-induced neutropenia.

A persistent absolute monocytosis (>1.5 x 109/l) may indicate an underlying myeloproliferative disease and a bone marrow biopsy with cytogenetic studies is usually indicated.

Eosinophilia

The initial step in the investigation of an eosino-philia is to search for secondary causes, for example, parasites, drugs, asthma, allergies, vasculitides or metastatic cancer. A comprehensive medication and toxin history should be obtained and serum immunoglobulin E (IgE), ANF, stool for multiple chemical sensitivity (MCS) and parasites, bilharzia testing and allergy testing are recommended.

If no obvious reactive cause is found, and the eosinophilia is persistent (more than six months) or increasing, the possibility of a primary eosinophilia (e.g., hypereosinophilic syndrome or myeloid malignancy) should be considered. In these patients, a bone marrow biopsy, with appropriate genetic and immunophenotypic testing, is indicated.

In addition to looking for the cause of the eosinophilia, tests to assess for possible eosinophilia-related tissue damage should be considered, for example, chest X-ray (CXR), pulmonary function tests, electrocardiogram (ECG), etc.

Basophilia

Basophilia is a rare finding suggestive of a myeloid malignancy and generally requires examination of the bone marrow and haematological referral.

Lastly:

An abnormal FBC should always be interpreted in light of the underlying clinical environment.

The examination of a PB slide can be of great assistance in determining the cause of an FBC abnormality.

Urgent haematological referral and consultation should be considered in patients with severe cytopenia, pancytopenia, extremely high counts or where the PB morphology is suggestive of a haematological malignancy (e.g., acute leukaemia)