Evaluation of Thrombocytopenia

Thrombocytopenia is defined as a platelet count of less than 150 x 10^9/L. The relevance of thrombocytopenia in an individual patient depends upon the clinical presentation. Thrombocytopenia is associated with a defect in primary haemostasis. However, although clinically significant spontaneous bleeding does not occur until the platelet count is less than 10-20 x 10^9/L, the presence of thrombocytopenia can aggravate surgical or traumatic bleeding, or prevent the administration of effective medical treatment for some conditions e.g. cancer chemotherapy.

In hospitalised patients, thrombocytopenia appears relatively frequently on the background of a multi-system disorder with multiple aetiologies or pathophysiologic mechanisms. Conversely, in the outpatient or primary care setting, thrombocytopenia is often isolated and asymptomatic, and diagnosis of the specific cause may be more straightforward (Table 1).

Table 1: Common causes of thrombocytopenia in a primary care setting

Primary immune thrombocytopenia (ITP)
Drug-induced thrombocytopenia (DITP)
Infections: HIV, HCV, CMV, other recent viral infection
Connective tissue disorders: SLE, rheumatoid arthritis, antiphospholipid syndrome
Myelodysplastic syndrome (MDS)
Congenital thrombocytopenia

Mechanisms of thrombocytopenia

The major mechanisms for thrombocytopenia are decreased production, and increased destruction of platelets. Typical examples of decreased production are bone marrow failure syndromes (e.g. myelodysplastic syndrome, chemotherapy induced thrombocytopenia), whereas increased destruction is seen in conditions such as ITP. A less common mechanism is platelet sequestration, seen in congestive splenomegaly due to portal hypertension.

Importance of history taking and physical examination

Aspects of particular importance in the medical history include: the presence of a family history of thrombocytopenia; the time course of the thrombocytopenia or of any associated bleeding manifestations; specific disease history e.g. autoimmune disorders; pregnancy status in premenopausal women; recent medications and vaccinations; recent travel; ingestion of alcohol and/or quinine containing beverages; and risk factors for retroviral infections and viral hepatitis.

Physical examination should focus on the location and severity of any bleeding manifestations, and other abnormalities that can assist in diagnosing of the cause of the thrombocytopenia, such as the presence of organomegaly. Patients with thrombocytopenia typically experience mucocutaneous bleeding. In comparison, the presence of joint or extensive soft tissue bleeding suggests the presence of a coagulation or clotting factor disorder.

Isolated thrombocytopenia

In this context, isolated thrombocytopenia is defined as a low platelet count in the absence of any abnormality in the red blood cell and white blood cell lineages, and no signs or symptoms of systemic illness.

A low platelet count during a routine evaluation in an otherwise asymptomatic person is a relatively common reason for referral to hospital outpatient clinics by general practitioners. Isolated thrombocytopenia has a limited differential diagnosis (Table 1). The two most prevalent aetiologies are primary immune thrombocytopenia (ITP) and drug-induced thrombocytopenia (DITP).

Primary Immune Thrombocytopenia (ITP)

Although ITP is the most common cause of isolated thrombocytopenia, there are no investigative tests sensitive or specific enough to confirm this diagnosis, which remains one of exclusion. There is no consensus on the set of investigations to perform, and practice varies greatly not only from country to country but also from centre to centre within the same country. A suggested evaluation protocol is to follow the recommendations set forth in the International Consensus Report on the Investigation and Management of ITP (Table 2). An ultrasound of the abdomen (to rule out the occasional initial manifestations of chronic liver disease with hypersplenism, and the presence of enlarged abdominal-pelvic lymph nodes), and a chest radiograph (to exclude silent mediastinal lymphadenopathy and silent tuberculosis) could also be requested.

Antiplatelet antibody assays are not very sensitive, although their specificity approaches 90%. The role of bone marrow biopsy remains controversial.

Table 2: Basic laboratory evaluation of patients with suspected ITP

Full blood count
Peripheral blood film
Bone marrow examination (in patients older than 60 years)
Quantitative Ig level measurement
Blood group (Rh)
Direct antiglobulin test
Helicobacter pylori
HIV
HCV

Drug Induced Thrombocytopenia (DITP)

Patients with DITP usually present with moderate to marked thrombocytopenia and bleeding manifestations of varying degrees of severity. The decrease in the platelet count typically occurs within 2 to 3 days of the patient taking a drug that has been taken previously, or 1 to 3 weeks after commencing a new drug. When the drug is stopped, the thrombocytopenia usually resolves in 5 to 10 days after drug withdrawal.
Clinically, DITP can be easily confused with ITP. Accurate history taking can help in the diagnostic process. In particular, if the patient has taken a medication for the first time, a diagnosis of DITP should be considered.

DITP should also be suspected when patients have recurrent episodes of thrombocytopenia with prompt recovery. Sometimes the diagnosis is particularly challenging because the substance causing the thrombocytopenia is not a drug but a food or beverage, such as walnuts, cow's milk, cranberry juice, tonic water (contains quinine), and certain herbal remedies.

Thrombocytopenia in pregnancy

Platelet counts of < 150 x 10^9/L have been reported in 6-15% of women at the end of pregnancy, but counts < 100 x 10^9/L are observed in only 1% of pregnant women. The most common causes of thrombocytopenia are gestational thrombocytopenia (GT, 70%), preeclampsia (21%), and ITP (3%).

GT is seen in the mid-second to third trimesters of pregnancy. There is no clearly defined minimum value of the platelet count in GT but counts < 70 x 10^9/L should raise suspicion of an alternative diagnosis. To support a diagnosis of GT, the woman should have no past history of thrombocytopenia (except during a previous pregnancy), and the thrombocytopenia should resolve spontaneously within 1 to 2 weeks after delivery.

ITP occurs in 1-2 in 1000 pregnancies but is the most common cause of isolated thrombocytopenia in the first and early second trimesters. Approximately one third of cases are first diagnosed during pregnancy, whereas two thirds are in patients with pre-existing disease. Differentiating ITP from GT is clinically important because pregnancies in women with ITP can be complicated by severe neonatal thrombocytopenia in 9 to 15% of cases, with a risk of neonatal intracranial haemorrhage of 1 to 2%. In women with no history of ITP, platelet counts below 100 x 10^9/L early in pregnancy and declining as gestation progresses are more consistent with ITP than GT. The situation becomes more complicated if a low platelet count is detected during the third trimester. There is a problematic platelet count range between 50 and 70 x 10^9/L in which the diagnosis remains uncertain. Whenever the platelet count is < 50 x 10^9/L in the absence of obstetric complications such as preeclampsia, the diagnosis should be ITP by default. As always in medical practice, laboratory results need to be interpreted in the clinical context.

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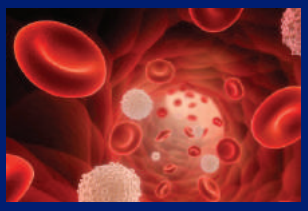

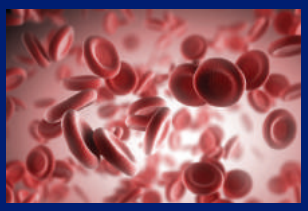

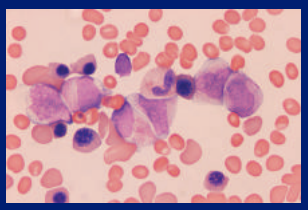

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