Clinical Reviews

The patient with Acute Thrombocytopenia

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Abstract

A wide variety of conditions can present with acute thrombocytopenia, ranging from those that are relatively benign and self-limiting to those that require urgent therapeutic intervention. Initial decision-making relies on a good history and the results of some simple investigations. Although a precise diagnosis of the underlying cause might often not be possible in the acute setting, supportive treatments should be provided to all patients. This article describes a practical approach to the diagnosis and initial management of patients presenting with acute thrombocytopenia, with the aid of a case vignette.

Keywords

Thrombocytopenia, evaluation, management.

Learning points

- Clinicians should be vigilant of major bleeding (e.g. intracranial, intra-abdominal) in all patients with severe thrombocytopenia.
- Thrombotic microangiopathy should be suspected in patients with thrombocytopenia, haemolytic anaemia, fragmented red cells on the peripheral blood film and elevated lactate dehydrogenase.
- Thrombotic microangiopathy with normal coagulation screen should be presumed to be due to thrombotic thrombocytopenic purpura (TTP); early plasmapheresis significantly reduces mortality
- A detailed drug history is important because discontinuation of the offending drug usually leads to resolution of the thrombocytopenia.
- Sepsis is a major risk factor and a common cause of acute thrombocytopenia.
- Tropical infections like malaria and dengue should be considered in all returning travellers presenting with fever and thrombocytopenia.
- Intravenous pulse methylprednisolone and intravenous immunoglobulin (IV Ig) should be considered in patients with suspected immune mediated thrombocytopenia, who are bleeding.

A 27-year old woman presents to the acute medical unit with a two-day history of purpura in both legs.

Her records reveal that she was diagnosed with systemic lupus erythematosus (SLE) at the age of 16 on the basis of her clinical symptoms that included inflammatory joint pains and photosensitive skin rashes, lymphopenia, mild thrombocytopenia, positive anti-nuclear antibody (ANA), elevated anti-double stranded DNA and low levels of complement proteins C3 and C4. Anti-phospholipid antibodies were all negative. She has never had overt internal organ involvement. Her current medications include prednisolone 5 mg/day, hydroxychloroquine 300 mg/day and vitamin D 1000 units/day.

Her full blood count, checked by her general practitioner in the morning, had shown haemoglobin 108 gm/L, white cell count 4.4 x 109/L and platelet count 16 x 109/L. Two months earlier, her haemoglobin was 109 gm/L, white cell count was 4.3 x109/L and platelet count 104 x 109/L.

How should this problem be approached?

The striking abnormality in the *acute drop* in her platelet count. A recent drop in the platelet count is more concerning than a chronically low platelet count that is stable.

There are four key questions:

- Is the thrombocytopenia geniune?
- Is the patient bleeding?
- What is the underlying cause of the thrombocytopenia?
- How active is her lupus in the rest of the organ systems?

I. Is the thrombocytopenia genuine?

Artefactual or pseudo-thrombocytopenia may result if the platelet count is checked with an EDTA (ethylene diamine tetra acetic acid) sample, as is routine in most laboratories. The apparent lowering of the platelet count results from *in-vitro* platelet clumping, thus preventing all the platelets from being counted. Platelet clumping is caused by platelet glycoproteins IIB/IIIA antibodies, which develop because of EDTA-induced conformational change in the platelet glycoproteins.[1]

If artefactual thrombocytopenia is suspected, the laboratory will ask to repeat the blood count with a citrate sample and check the peripheral blood film for platelet clumping.[2]

The thrombocytopenia in this patient is unlikely to be artefactual, as she has already presented with purpura and her platelet count has declined quite dramatically.

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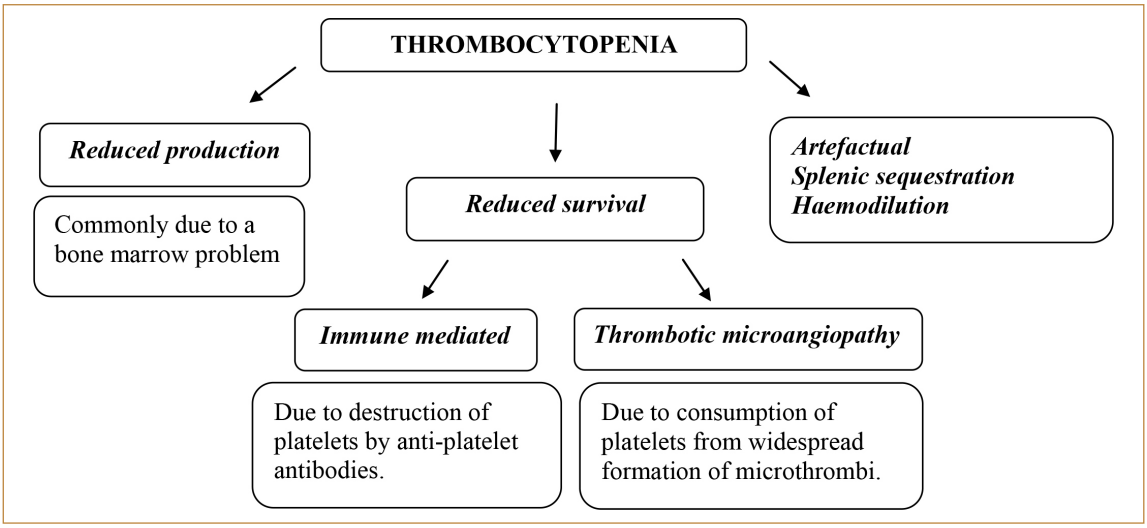

Figure 1. Classification of the underlying causes of thrombocytopenia

II. Is the patient bleeding?

Although thrombocytopenia is defined as a platelet count below 150 x 10^9/L, patients seldom bleed *spontaneously* unless the platelet count drops to below 10-20 x 10^9/L.[3] The threshold, however, may be higher in patients with associated coagulation abnormality or qualitative platelet defect. Risk of bleeding increases with advancing age. One meta-analysis of 17 studies estimated the age-adjusted rate of bleeding, with platelet counts persistently below 30 x 10^9/L, as 0.4%, 1.2% and 13% per patient per year for those younger than 40, 40-60, and older than 60 years old, respectively.[4]

Bleeding due to thrombocytopenia generally occurs into the skin or mucous membranes. Cutaneous bleeding manifests as purpura, echymosis or petechiae, and mucous membrane bleeding as epistaxis, gum bleeding, haematuria or menorrhagia. Major bleeding (e.g. intracranial or intra-abdominal bleeding) is uncommon, but a careful gastrointestinal and neurological history and examination is required. Fundoscopy is also important because retinal haemorrhage can predict intracranial bleeding; bleeding in the region of the macula, although rare, can cause blindness. According to one systematic review of 118 studies (n = 10,908 patients), the weighted proportions were 1.4% (95% CI 0.9 to 2.1%) for intracranial bleeding and 9.6% (95% CI 4.1 to 17.1%) for severe non-intracranial bleeding in adult patients.[5]

There is no history of epistaxis, bleeding gums, haemoptysis, haematemesis, melena, rectal bleeding, haematuria or vaginal bleeding. She is conscious, alert and oriented. There are no focal neurological symptoms or abdominal pain. Her oxygen saturation is 98% on room air, temperature 37C, pulse 84/min, blood pressure 120/80 mm Hg and respiratory rate 16/min. Fundoscopy is unremarkable. There is evidence of purpura affecting both legs.

III. What is the underlying cause of the thrombocytopenia?

In this case it is important to consider all possible underlying causes and not just those related to SLE.[6-8]

True thrombocytopenia, in general, may result from ***reduced bone marrow production and/or reduced platelet survival***. Reduced platelet survival could be secondary to immune mediated peripheral destruction *or* increased platelet consumption due to thrombotic microangiopathy (Figure 1). Less common mechanisms include ***splenic sequestration*** (caused by redistribution of platelets from the circulating pool to the splenic pool, as in patients with long-standing splenomegaly) and ***haemodilution*** (due to administration of large amount of platelet-free fluids like colloids or crystalloids in patients who have suffered a massive haemorrhage).

From a practical perspective, the key underlying diagnoses that one should consider in the emergency setting are listed in Box 1 and discussed in detail below. Pregnant women may present with thrombocytopenia,[9] usually during the latter half of pregnancy; this is not discussed further in this article, but all pregnant patients with significant thrombocytopaenia should be discussed urgently with the obstetric and haematology team.

Box 1: Important underlying causes of thrombocytopenia to consider in the emergency setting

- Thrombotic microangiopathy
- Infections (e.g. sepsis, malaria, dengue)
- Alcohol or drug induced thrombocytopenia
- Bone marrow failure (e.g. acute leukemia)
- Immune mediated thrombocytopenia

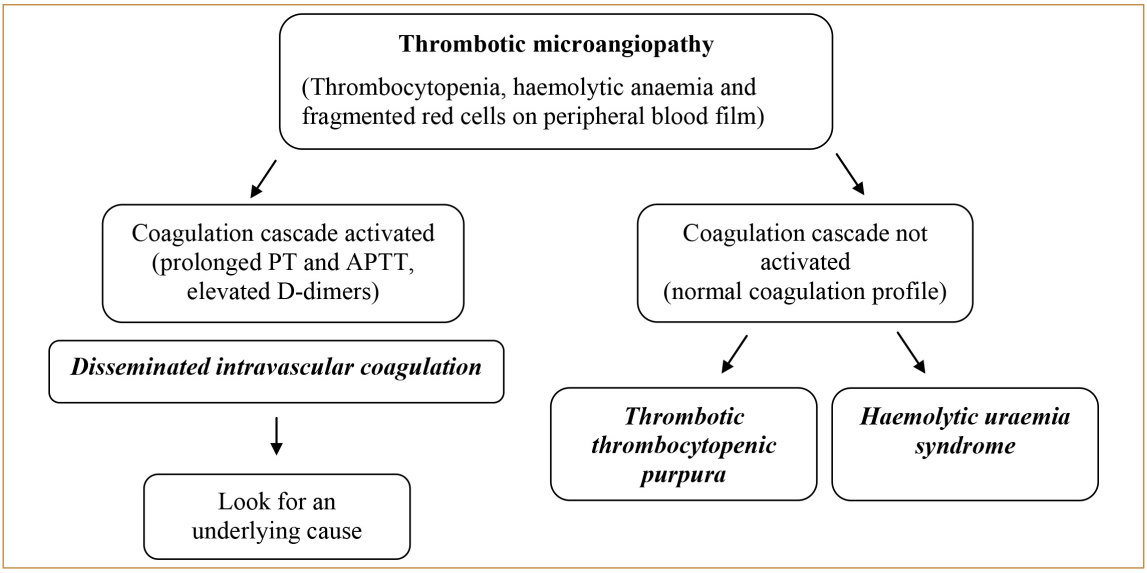

Figure 2. The three most common causes of thrombotic microangiopathy

Thrombotic microangiopathy

Thrombotic microangiopathy (TMA)[10-12] refers to the widespread formation of microthrombi in the circulation, which may lead to tissue ischemia. TMA is characterised by:

- ***Thrombocytopenia,*** which occurs because the platelets are used up for the formation of microthrombi.
- ***Microangiopathic haemolytic anaemia (MAHA),*** which occurs because the red cells become fragmented when they try to pass the microthrombi.
- ***Fragmented red cells in the peripheral blood film:*** at least two fragmented red cells should be present in one high power field. It should be noted that fragmented red cells may not be present for the first 2-3 days after onset.
- ***Elevated serum LDH and reticulocyte count*** (due to haemolysis) with negative Direct Anti-globulin test (as the haemolysis is non-immune mediated). The LDH elevation results from haemolysis and tissue ischemia.[12]

TMA could be broadly classified into two types (Figure 2) depending on whether [a] the coagulation system is activated and [b] the microthrombi contain platelets and red cells in a fibrin mesh *or* just platelets alone.

The key to activating the coagulation cascade, as in patients with ***disseminated intravascular coagulation*** (DIC), is the release of tissue factor by various insults such as infection, trauma, burns, snake venom, dead foetus or amniotic fluid embolism.[13] Because clotting factors are used up in the process, laboratory findings of DIC include prolongation of prothrombin time (PT), activated partial thromboplastin time (APTT) and thrombin time (TT), with low fibrinogen and elevated D-dimers.

Several conditions are associated with the formation of platelet thrombi, and the common factor is the presence of increased amounts of von Willebrand factor (vWF).[13] vWF helps with platelet aggregation during the process of formation of the primary haemostatic plug, and is mainly secreted in response to endothelial injury. A small amount of vWF is also secreted continuously at basal levels (i.e. even when there is no need to form a haemostatic plug) in the form of ultra-large multimers, but inappropriate platelet aggregation is prevented because the protease enzyme ADAMTS13 (acronym for A Disintegrin And Metalloproteinase with a ThromboSpondin type 1 motif, member 13) keeps breaking these multimers into smaller units. Thus, platelet thrombi can form because of increased production of ultra large vWF multimers *or* reduced ADAMTS13 activity.

Thrombotic thrombocytopenic purpura (TTP) occurs because of [a] ADAMTS13 mutations causing hereditary deficiency of ADAMTS13 activity *or* [b] the development of IgG autoantibodies that inhibit ADAMTS13 activity (the latter is the mechanism in patients with SLE).

The classical pentad of TTP comprises:

- thrombocytopenia,
- MAHA
- Fever
- central nervous system (CNS) dysfunction
- acute kidney injury (AKI).

CNS dysfunction and AKI occur because of microthrombi occluding the high shear capillaries and arterioles in the brain and kidney, but are rare. Mortality of untreated TTP is > 90%, but reduced

to < 20% with plasma exchange therapy.[15] Hence, in practice, the presence of thrombocytopenia and MAHA in the absence of an alternative cause is considered sufficient for a diagnosis of TTP so that treatment could be commenced promptly.[12]

Increased release of vWF can be triggered by the Shiga toxin produced by E coli 0157:H7 (typical or diarrhoea (+) ***haemolytic uraemia syndrome***),[16] a dysregulated complement system (atypical or diarrhoea (-) haemolytic uraemia syndrome),[17] activation of the renin-angiotensin-aldosterone system (***malignant hypertension***)[18] or release of bioactive substances from the oxidatively stressed placenta (***pre-eclamptic toxaemia***),[19] ***cancers***, especially mucin producing adenocarcinomas, ***acute pancreatitis***, ***bone marrow transplantation*** and ***drugs*** such quinine, mitomycin, gemcitabine, clopidogrel and ticlopidine.

Alcohol or drug induced thrombocytopenic purpura

A variety of drugs are known to cause thrombocytopenia.[20-21] Discontinuation of the offending drug usually leads to resolution of the thrombocytopenia, although this can sometimes take several weeks. A comprehensive database of drugs reported to cause thrombocytopenia is available at www.ouhsc.edu/platelets. The history should also include a detailed enquiry about alcohol consumption, as it is a common cause of thrombocytopenia. Some foods, beverages, tonic water and vaccines can also cause thrombocytopenia.[21]

Mechanisms of drug induced thrombocytopenia include reduced production (e.g. cytotoxic therapy suppressing the bone marrow) or increased destruction (e.g. the offending drug binds to the platelet glycoprotein, and the drug-glycoprotein complex elicits an antibody response).

Heparin induced thrombocytopenia (HIT) is an important condition to consider; key features are outlined in Box 2.

Box 2: Heparin induced thrombocytopenia[22]

- Heparin induced thrombocytopenia (HIT) usually occurs due to the development of antibodies against the complex of heparin and platelet factor 4.
- It typically manifests about 5-14 days after commencement of heparin (there is a lag time, as the antibodies are IgG), but it can occur earlier if the patient was exposed to heparin in the previous three months (even a heparin flush or a heparin coated catheter).
- HIT is characterised by arterial and venous thrombosis, skin necrosis and thrombocytopenia.
- HIT is ten time more likely with unfractionated heparin than with low molecular weight heparin.
- The likelihood of HIT can be predicted by the 4T score (calculators are available online) which includes[1] degree of Thrombocytopenia,[2] Timing of the decline in platelet count,[3] presence of Thrombosis and[4] the probability of other causes of Thrombocytopenia.
- If suspected, the heparin should be discontinued and a haematologist's advice sought immediately.
- A milder form, otherwise known as type I HIT, is also recognised (the immunologically mediated form discussed above is also known as type II HIT). It is due to a non-immunological interaction between the heparin and the platelets, leading to platelet clumping.

Thrombocytopenia due to infection

Sepsis should be considered in all patients with an acute thrombocytopenia [23]. Studies evaluating thrombocytopenia in patients with sepsis have reported an incidence ranging from 22% to 58%. Thrombocytopenia has been shown to be an independent predictor of mortality in patients with sepsis. Clinicians should be aware that patients with thrombocytopenia and an underlying infection often have multi-organ dysfunction.

Several infections like malaria (usually *Plasmodium vivax* or *falciparum*), dengue, meningococcaemia, leptospirosis, Zika virus infection, human immunodeficiency virus (HIV), hepatitis C, infectious mononucleosis, cytomegalovirus infection and Helicobacter pylori have been reported to cause thrombocytopenia. Clinicians should consider testing for HIV and hepatitis C in all patients with unexplained thrombocytopenia.[24] Mechanisms of infection related thrombocytopenia include reduced production, increased destruction or splenic sequestration (as in malaria).

Malaria and dengue should be suspected in returning travellers and those living in mosquito prevalent areas, who present with fever.[25-26] If confirmed, the advice of a specialist in infectious diseases or tropical medicine should be sought.

Bone marrow failure

A problem with the production of platelets by the bone marrow is more likely if the other cell lines are also affected. Some underlying causes include bone marrow infiltration by haematological or metastatic cancers, aplastic anaemia, myelofibrosis, vitamin B_{12} and folate deficiency, haemophagocytic lymphohistiocytosis, infections and drugs.

Some pointers that suggest an underlying cause include recent ingestion of a drug that could potentially cause bone marrow toxicity, the finding of lymphadenopathy or hepatosplenomegaly, presence of leukemic blasts or tear drop cells in the peripheral blood film, and low serum vitamin B_{12} or folate.

Haemophagocytic lymphohistiocytosis (HLH), although very rare, deserves special mention, as it can be rapidly fatal if not recognised and treated early.[27] As the term implies, it is characterised by phagocytosis of erythrocytes, leucocytes and

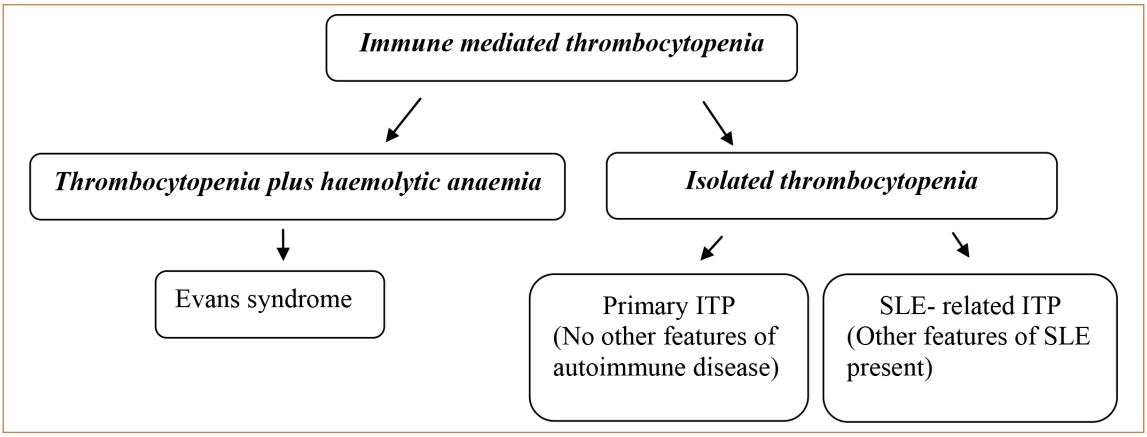

Figure 3. Classification of immune mediated thrombocytopenia

platelets by activated macrophages. Activation and proliferation of lymphocytes and macrophages could be secondary to infection, autoimmune diseases like juvenile idiopathic arthritis, Adult onset Still's disease or SLE, cancers and lymphoma. Features of HLH include:

- Cytopenia involving all three cell lines (due to the haemophagocytosis)
- Etremely high serum ferritin (produced by the activated macrophages)
- Reduced serum fibrinogen (plasminogen activator produced by the activated macrophages breaks down the fibrin; fibrinogen levels fall, as it is used up for the formation of fibrin)
- Falling ESR (as the fibrinogen helps with erythrocyte sedimentation)
- Elevated serum triglycerides (tumour necrosis factor-α produced by the macrophages inhibits lipoprotein lipase, thus preventing lipolysis of triglycerides)
- Hepatitis (this is almost universal, and is the result of cytokine induced inflammation).

Evidence of haemophagocytosis could be sought in the bone marrow, lymph node or liver, but its absence would not help to rule out HLH. If HLH is confirmed or suspected, it is important to look for an underling cause such as infection, autoimmune disease, solid cancer or lymphoma.

Immune mediated thrombocytopenic purpura (ITP)

Immune mediated thrombocytopenic purpura (ITP) is mediated by anti-platelet antibodies, the usual target antigens being platelet membrane glycoproteins. It is a diagnosis of exclusion. Hence, the aetiology should be presumed to be immune mediated only if no other cause is found.[28] (Figure 3 and Box 3)

ITP can occur in patients with other features of SLE (SLE-associated ITP) *or* without any other features of autoimmune disease (primary-ITP). One retrospective analysis found a positive anti-nuclear antibody (ANA) in a titre of > or = 1/80 in a third of patients with primary-ITP.[29] However, a positive ANA alone, in the absence of other clinical manifestations, should not lead to a diagnosis of SLE-associated ITP.[30] SLE-associated ITP can be severe and present acutely, usually with evidence of active disease in the other organ systems, but it responds well to corticosteroids.[6]

The occurrence of autoimmune haemolytic anaemia (AIHA) and ITP, either simultaneously or sequentially, is known as Evans syndrome.[31] It is characterised by [a] features of haemolysis such as elevated reticulocyte count, unconjugated hyperbilirubinemia, elevated LDH and decreased haptoglobin, [b] positive Direct Antiglobulin test, and [c] presence of spherocytes on the peripheral blood film.

Case Progression

Our patient feels well except for the purpura in her legs. She reports no recent symptoms of infection and hasn't travelled abroad in the last two years. Her only medications include prednisolone, vitamin D and hydroxychloroquine. She does not take any 'over the counter' medications. She says she has never smoked and always been teetotal. She has been married for five years, but never been pregnant. Her last menstrual period was two weeks ago. She uses the intra-uterine device for contraception.

Physical examination is completely unremarkable except for the purpura. There is no evidence of hepatosplenomegaly or lymphadenopathy. Cardiovascular and respiratory examination is unremarkable, her abdomen is soft and non-tender, and there is no focal neurology.

Her initial blood test results are as follows:

Peripheral blood film: There is no evidence of platelet clumping, fragmented red cells, spherocytes or blast cells.

Reticulocyte count: 0.8% (0.5 – 1.5%)

Lactate dehydrogenase: 310 U/litre (240-480 U/litre)

Box 3. Summary of initial investigations to request for patients with thrombocytopenia

In all patients	
Peripheral blood film	To look for fragmented red cells (MAHA), spherocytes (immune mediated haemolysis), tear drop cells (myelofibrosis) or blast cells (acute leukemia).
Lactate dehydrogenase, reticulocyte count	Elevation may suggest haemolysis, which is a component of thrombotic microangiopathy.
Coagulation profile (including PT, APTT, fibrinogen and D-dimers)	Abnormal coagulation is suggestive of DIC and makes TTP less likely.
Liver enzymes	Elevated transaminases may be due to HELLP syndrome, malaria, sepsis, hepatitis or drugs.
Renal panel	Acute kidney injury is more suggestive of HUS than TTP.
Anti-nuclear antibody	Screening test for systemic lupus erythematosus.
In some patients (depending on presentation)	
Stool cultures and serology for E coli 0157: H7	For patients with diarrhoea and suspected HUS
Cultures of blood or other specimens	For suspected DIC, TTP or infection related thrombocytopenia.
Screening tests for malaria, dengue, EBV, CMV, HIV, hepatitis C and Helicobacter pylori	
Pregnancy test	In all pre-menopausal women
Serum B_{12} and folate	
Platelet dependent factor-4 antibodies	For suspected heparin induced thrombocytopenia
ADAMTS13 activity assay	Plasmapheresis should be begun urgently in patients with suspected TTP even before the results are available.
Anti-nuclear antibody	For suspected immune mediated thrombocytopenia
IgG and IgM cardiolipin antibodies, IgG and IgM β2-glycoprotein antibodies and lupus anticoagulant	To screen for anti-phospholipid syndrome
Ferritin, triglycerides and ESR	For suspected HLH

MAHA: macroangiopathic haemolytic anaemia, PT: prothrombin time, APTT: activated partial thromboplastin time, DIC: disseminated intravascular coagulation, TTP: thrombotic thrombocytopenic purpura, HUS: haemolytic uraemia syndrome, HELLP: haemolysis, elevated liver enzymes and low platelets, EBV: Ebstein Barr virus, CMV: cytomegalovirus, HIV: human immunodeficiency virus, HLH: haemophagocytic lymphohistiocytosis.

Prothrombin time: 12 seconds (11-14 seconds)

Activated partial thromboplastin time: 30 seconds (25-35 seconds)

Bilirubin: 8 mmol/L (5-17 mmol/L)

Aspartate aminotransferase: 22 U/L (18-40 U/L)

Alanine aminotransferase: 32 U/L (17-63 U/L)

Creatinine: 78 µmol/L (70-120 µmol/L)

Urine pregnancy test: negative.

Her presentation is not in keeping with splenic sequestration or haemodilution. Pregnancy related thrombocytopenia can be excluded based on the date of her last menstrual period and the negative urine pregnancy test. She is not receiving any drugs or 'over the counter' preparations that are known to cause thrombocytopenia. Tropical infections like malaria and dengue are unlikely because of the negative travel history. Bone marrow failure and HLH are also unlikely because of the stable white cell count and haemoglobin. Thrombotic microangiopathy can be excluded because of the stable haemoglobin, absence of fragmented red cells on the peripheral blood film, and the normal reticulocyte count and LDH. Thus, her thrombocytopenia is most likely immune mediated, possibly related to her SLE itself.

IV. How active is her lupus in the rest of the organ systems?

Patients with lupus and acute thrombocytopenia often have evidence of active disease in the rest of the organ systems, particularly neuropsychiatric and renal.[32-34] A careful history and examination is essential along with early involvement of the patient's rheumatologist or other relevant specialist team, depending on the organ system involved.

She does not complain of joint pains, skin rashes, mouth ulcers or hair loss. She feels tired, but this has been no worse recently. Her weight has been steady. There are no neurological, psychiatric, cardiac, respiratory or gastrointestinal symptoms suggestive of lupus flare. Her urinalysis is normal, with no evidence of proteinuria, haematuria or active sediments. Her erythrocyte sedimentation rate is 33 mm/ hour (was 31 mm/

hour three months ago), C3 level is 60 mg/dl (83-193 mg/dl), C4 is 12 mg/dl (15-57 mg/dl) and double stranded DNA is 76 IU/ml (negative result < 25 IU/ml).

There is no clinical evidence of lupus in the rest of her organ systems. Hence, management should focus on the thrombocytopenia alone, but with continued close monitoring for involvement of other organ systems. There is evidence of serological activity, with elevated double stranded DNA (although not new) and low complement levels.

Principles of Initial Management

The following general principles apply to the acute management of all patients with thrombocytopenia:

- Patients with platelet counts < 30 x 10^9/L, those who are bleeding and those with specific diagnoses such as TTP or bone marrow failure should be discussed with the haematologist urgently.
- Patients with haemodynamic instability should be managed in a critical care or HDU setting.
- The indications for **platelet transfusions** are summarised in Box 4.[35]

Platelet transfusions may exacerbate the underlying problem in conditions such as TTP, HUS, HIT, DIC (when thrombosis predominates) and ITP, and so should be avoided in such patients unless there is evidence of life threatening haemorrhage.

- Aspirin or non-steroidal anti-inflammatories should be discontinued; intramuscular injections and unnecessary procedures be avoided (unless platelet cover is provided).
- In hypertensive patients, the blood pressure should be gradually lowered in order to reduce the risk of intracranial bleeding.
- A proton pump inhibitor should be considered in patients at risk of upper GI bleeding.
- Tranexamic acid is an anti-fibrinolytic agent that can reduce bleeding by stabilising clots that have already formed.[36] Both oral and intravenous formulations are available. It is contraindicated in patients with haematuria (because of the risk of clot retention), severe renal impairment and consumption coagulopathies.

Box 4. Indications for platelet transfusion (the 10K, 20K and 50K triggers)

Platelet count < 10	Prophylactic platelet transfusion should be considered, as there is an increased risk of spontaneous bleeding.
Platelet count < 20	In patients with sepsis.
Platelet count < 50	In patients with GI bleeding, and before procedures (e.g. lumbar puncture, central line insertion, endoscopy).

* Bleeding is unlikely if the platelet count is > 50, unless the patient is taken for intracranial surgery or there is a qualitative platelet defect.

Specific management

For patients with suspected TTP, the advice of a haematologist should be sought urgently so that plasmapheresis could be considered.[10-12, 37-39]

Plasmapheresis probably works by removing the ADAMTS13 antibodies and providing the protease to help break down the polymers of vWF. There is no evidence that plasmapheresis is useful for patients with HUS. Hence, plasmapheresis can be discontinued in patients with positive stool cultures or serology for E coli 0157: H7.[39-40]

If DIC is a possibility, the underlying cause should be treated.[41]

Those who are bleeding may require red cell and platelet transfusion, fresh frozen plasma to replenish the coagulation factors, and cryoprecipitate to replenish the fibrinogen.

All medications that are potentially likely to cause thrombocytopenia should be discontinued.[20] Alcohol induced thrombocytopenia generally improves within one week of abstinence.

It should also be borne in mind that drugs can cause immune mediated thrombocytopenia, the management of which may include corticosteroids and intravenous immunoglobulin (IV Ig) if the patient is bleeding.

For patients with suspected immune mediated thrombocytopenia, the aim of treatment is to reduce the risk of bleeding.

High dose corticosteroids, usually oral prednisolone, starting with 0.5 to 1 mg/ kg body weight, are the first line of treatment [42] [8]. Pulse intravenous methylprednisolone is not superior to oral high dose prednisolone, and may be associated with increased risk of infection or avascular necrosis. IV Ig should be added in patients who are actively bleeding and those in whom a rapid rise in platelet count is desired. The response to either corticosteroids or IV Ig is good in the short-term, but not sustained in the long-term in a vast majority of patients.

Case Outcome

She is screened for HIV and hepatitis C, as they are associated with immune thrombocytopenia. There was no evidence of hepatitis B at the time of diagnosis of her lupus more than 10 years ago, but her hepatitis B status is checked again in anticipation of commencing immunosuppressive therapy. She is referred to the haematologist and her rheumatologist.

The dose of her oral prednisolone is increased up to 0.5 mg/ kg/day, as the platelet count stays between 12-16 x 10^9/L over the next three days. Platelet transfusion is not considered, as the platelet count is between 10-20, with no clear evidence of sepsis or major bleeding. Her platelet count gradually improves over the next two weeks.

Conflicts of interest

None.

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