

Thrombocytopenia

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James talks to Dr Shafqat Inam about thrombocytopenia, or low platelet count, in this podcast.

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About Dr Shafqat Inam

Shafqat Inam is currently a [Haematology](#) registrar at Royal Prince Alfred and Concord Hospitals, and Associate Lecturer at the University of Sydney. He studied medicine at the [University of New South Wales](#) and completed his junior medical officer and basic physician training at Royal Prince Alfred Hospital. Shafqat has a particular interest in research and medical education.

Thrombocytopenia

With Dr Shafqat Inam, Haematology Registrar at Royal Prince Alfred and Concord Hospitals, New South Wales, Australia

Introduction

Thrombocytopenia (low platelet count) is a common finding amongst inpatients and may occur due to a range of factors. It is often picked up incidentally as well as in the context of bleeding. A normal platelet count is $150 - 400 \times 10^9/L$. Degrees of thrombocytopenia: mild $100 - 150 \times 10^9/L$; moderate $50 - 100 \times 10^9/L$; and severe $< 50 \times 10^9/L$. The risk of severe spontaneous bleeding is greatly increased with platelets $< 20 \times 10^9/L$. Evaluation of the patient with thrombocytopenia ought to address both complications from low platelets and the aetiology of the condition.

Case 1

A patient was admitted overnight via the Emergency Department with fever on a background of prosthetic valve, IVDU and alcohol dependence. Their platelet count on admission was $40 (x10^9/L)$.



1. What is your approach to this patient with thrombocytopenia?

- **Consider the potential physiological causes of low platelet count**
 - decreased bone marrow production
 - increased platelet destruction either by consumption or autoimmune process

- sequestration such as in splenomegaly
- **Degree, trend and tempo**
 - mild, moderate or severe
 - chase old blood tests
 - acute vs chronic
- **Key points in history**
 - bone marrow disorders
 - autoimmune disorders
 - recent infections or at risk behaviour (HCV, HBV, HIV)
 - medications including antiplatelets, immunosuppressants and antibiotics
- **Examination**
 - complications (bleeding, thrombosis in HITTS)
 - aetiology (signs of chronic liver disease, lymphadenopathy)

2. What particular medications are associated with thrombocytopenia?

- **Idiosyncratic reactions**
 - penicillins
 - vancomycin
- **Myelosuppressive agents**
 - methotrexate
- **Immune-complex formation**
 - heparin
 - LMWH
- **Antiplatelet agents (do NOT cause low platelet count but inhibit platelet function)**
 - aspirin, clopidogrel (effects can last up to 7 days)
 - NSAIDs

3. What are you looking for in particular on examination?

- **Complications – classically mucocutaneous bleeding (cf. haemophilia)**
 - oral mucosa & gums
 - petechiae & purpura
 - menorrhagia
 - gastro-intestinal bleeding

- CNS bleeding (particularly in context of headstrike)
- Aetiology
 - splenomegaly
 - lymphadenopathy
 - signs of chronic liver disease

4. When are investigations necessary and what should be ordered?

- For patients with an incidental finding of moderate isolated thrombocytopenia tests beyond FBC are not usually required in hospital and can be ordered by a specialist in clinic.
 - This would include:
 - HBV, HCV and HIV serology
 - vitamin B12 and folate
 - autoimmune screen
 - serum EPG
 - bone marrow biopsy (only if significant concern of haematological malignancy)
 - Appropriate to monitor FBC every 2-3 days to observe trend of platelet count until recovering and/or cause has been determined
- If thrombocytopenia is detected in the context of bleeding or there are other blood count abnormalities further investigation in hospital is advised

5. At what level of thrombocytopenia do you begin to worry about significant bleeding and when is transfusion indicated?

- Start to be concerned when $PLT < 50$
 - > 50 , very low chance of spontaneous bleeding
 - for most surgical procedures > 50 is sufficient (except neuroaxial or ocular procedures that usually require > 100)
 - quite worried if $PLT < 20$ (especially < 10)
- Indications for transfusion of platelets
 - $PLT < 50$ with active bleeding
 - $PLT < 20$ and febrile
 - $PLT < 10$ with or without symptoms
 - part of massive transfusion protocol
 - immediately prior to surgical procedures to achieve goal PLT as described above
 - one pool of platelets increases PLT by 25 - 40

- Situations when platelet transfusion is not safe
 - thrombotic thrombocytopenic purpura (TTP)
 - heparin induced thrombotic thrombocytopenia syndrome (HITTS)

Case 2

A 26-year-old female presents to the Emergency Department with petechiae on the shins, ankles and feet. Further history reveals recent easy bruising and menorrhagia. The platelet count is $12 \times 10^9/L$ but WCC and Hb are normal.

6. What is your approach to this patient?

- **Further history**
 - recent viral infection
 - history of haematological issues
 - history of autoimmune conditions
 - recently commenced medications
 - previous blood counts
- **Further examination**
 - oral mucosa looking for wet purpura
- **Most likely differential is idiopathic thrombocytopenic purpura (ITP)**
 - classically in young otherwise well women – may have an autoimmune phenotype (e.g. SLE, rheumatoid arthritis)
 - pathophysiology: autoimmune clearance of platelets
 - often triggered by recent viral illness
 - can follow a chronic course with gradual decline in platelet count
 - treated with immunosuppressants
- **Investigations**
 - EUC and LFTs (largely as baseline before treatment but also screening for any other process)
 - Group & hold given risk of bleeding
 - there is no diagnostic test for ITP – diagnosis based on clinical presentation and exclusion of other causes
 - antiplatelet antibodies were done in the past but shown not to be useful
- **Treatment**
 - Acute
 - corticosteroids – dexamethasone or prednisone (1mg/kg daily for 1-2 weeks then taper)
 - observe as inpatient for short period of time to ensure no severe bleeding

- IVIg (if not responding to corticosteroids)
- no use for platelet transfusion as platelets are rapidly consumed in ITP
- **Long-term**
 - if platelet count remains low may add steroid sparing agents - azathioprine
 - may progress to splenectomy which can be curative for some patients

Case 3

A 72-year-old male is day 8 post elective coronary artery bypass grafting for coronary artery disease. He is on twice daily heparin for DVT prophylaxis. His platelet count has dropped to 80 from 190 pre-op. His left calf is swollen compared to the right.

7. What is your approach to this patient?

- Most likely differential is heparin induced thrombotic thrombocytopenia syndrome (HITTS or HIT) however a full differential should be considered including infection and DIC (check D-Dimer and fibrinogen)
- Pathophysiology of HITTS
 - autoantibody against heparin-platelet factor 4-complex
 - platelets therefore cleared by macrophages leading to thrombocytopenia
 - paradoxically patients are at greater risk of thrombosis
 - mechanism not fully understood however HIT antibodies are thought to be able to activate platelets and hence trigger a clotting cascade
 - HITTS can also occur with LMWH (enoxaparin) although does so at a lower rate

8. How is a diagnosis of HITTS made?

- Largely a clinical diagnosis then confirmed with antibody testing
- Pre-test probability calculated with **4 T's Score**
 - degree of **thrombocytopenia**
 - **timing** relative to heparin exposure
 - presence of **thrombosis**
 - other causes of **thrombocytopenia**
 - each scored 0 to 2

- if total score 0 to 3 - low probability
- 4 or 5 - intermediate probability
- 6 to 8 - high probability
- Although not part of 4 T's Score, patients may develop necrotic skin reaction at site of heparin injections
- Immunological testing warranted if clinical suspicion is high enough (usually intermediate or high probability)
- HITTS is a rare diagnosis and can be life-threatening - must be part of the differential of any patient on heparin with new thrombocytopenia

9. How is HITTS managed?

- Cease heparin if HITTS is suspected
- Consult haematology for advice regarding alternative anticoagulation
- Doppler ultrasound of lower limbs
 - thrombosis can be both venous and arterial
 - most commonly lower limb DVT or PE
 - arterial thrombosis can lead to gangrene

Take home messages

- Thrombocytopenia is common and carries a wide differential which can be narrowed with a focused history
- Complications are usually related to bleeding however paradoxically in some conditions there is an increased risk of thrombosis (e.g. HITTS)
- Important information when seeking haematology advice:
 - history or examination findings of active bleeding
 - history of viral infection, autoimmune conditions, haematological conditions and recent medications
 - previous FBC results

References

- UpToDate: Immune thrombocytopenia (ITP) in adults: Initial treatment and prognosis
- UpToDate: Clinical presentation and diagnosis of heparin-induced thrombocytopenia

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