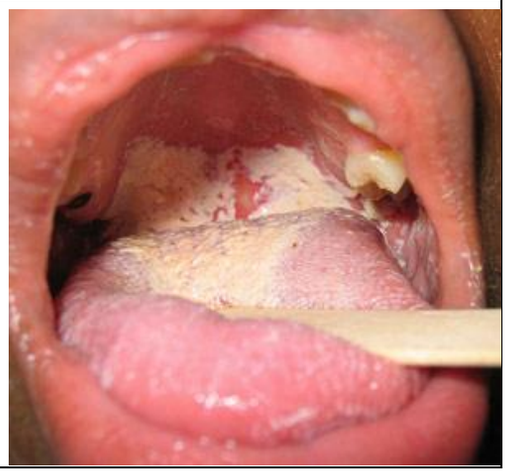
CASE THREE

Short case number: 3_30_3
Category: Immune and haemopoietic systems
Discipline: Medicine
Setting: Hospital Ward
Topic: Anaemia_aplastic [SDL]

Case

You are the medical intern admitting 25 year old Julian Barker, who has been referred to your consultant, via his GP. Julian has been suffering with persistent thrush infections in his mouth and gum bleeds.
A full blood count has revealed that Julian is anaemic, with a low neutrophil and platelet count.



Questions

1. Julian's provisional diagnosis is aplastic anaemia. What is aplastic anaemia?
2. In your assessment of Julian what are the key features of history and examination and why?
3. What clinical features are seen in aplastic anaemia and what is the underlying pathophysiology?
4. What investigation findings are associated with a poor prognosis in aplastic anaemia?
5. As part of Julian's management he requires protective isolation, explain why this is necessary and how it is achieved on a hospital ward.
6. Outline the principles of supportive care in the management of bone marrow failure.
7. Julian becomes increasingly symptomatic due to his anaemia and a blood transfusion is required. Julian's blood group is B positive, explain what this means in terms of the ABO and Rh classification system of blood grouping.
8. You are required to obtain informed consent from Julian for the blood transfusion. Outline the possible immunological and non-immunological complications of blood transfusions.
9. It is important when administering a blood transfusion to ensure that the correct blood is given. Outline the steps that are undertaken to minimise error in the administration of a blood transfusion.

Suggested reading:

- Kumar P, Clark ML, editors. Kumar & Clark's Clinical Medicine. 8th edition. Edinburgh: Saunders Elsevier; 2012.
- Colledge NR, Walker BR, Ralston SH, Penman ID, editors. Davidson's Principles and Practice of Medicine. 22nd edition. Edinburgh: Churchill Livingstone; 2014.
- Australian Red Cross Blood Component Information Booklet 2020 https://transfusion.com.au/system/files/resource_library/Blood_Component_Information_1.pdf

ANSWERS

Question 1
Julian's provisional diagnosis is aplastic anaemia. What is aplastic anaemia?

Aplastic anaemia is a rare condition characterised by anaemia, thrombocytopenia and neutropenia with a hypocellular or acellular bone marrow. Over 70% of cases are idiopathic. Identifiable causes are usually acquired but may be congenital. The underlying cause is identified in less than 30% of cases despite extensive investigation.

Question 2
In your assessment of Julian what are the key features of history and examination and why?

History and examination should be focused on

a) Identifying a possible underlying cause
b) Assessing for the cardinal features of bone marrow failure.

<u>Known acquired causes of aplastic anaemia include:</u>

- drugs:
  - the drug and/or their metabolites may be directly toxic
  - an immune-mediated mechanism may be involved
  - aplasia may develop weeks or months after initiation of treatment, or follow after the drug has been discontinued

- infection:
  - aplasia may develop concurrently with or following a variety of viral infections
  - may be severe following hepatitis C infection and is accompanied by lymphocytopenia and cellular immune deficiency

- rheumatic and immunological disorders

- pregnancy

<u>The cardinal features of severe marrow failure are:</u>

- anaemia - resulting in weakness and fatigue. Usually of slower onset than other features due to the longer survival of red cells compared to platelets and neutrophils, except bleeding is significant.

- bleeding - from mucosa and skin, due to thrombocytopenia. Purpura and petechiae are common. There may be retinal bleeding, sometimes leading to blindness. Spontaneous bleeding indicates severe marrow failure with platelet counts less than 20 x 10^9 per litre.

- bacterial infection - due to neutropenia. Usually with commensal organisms of the skin and GI tract. Recurrent infections in a previously fit person may be a clue.

Septicaemia is a risk in patients with severe neutropenia. Focal signs of infection may be absent, with malaise and fever the only features. Hepatosplenomegaly, lymphadenopathy or bone tenderness are uncommon in aplastic anaemia but are characteristic of bone marrow failure due to leukaemia, myelofibrosis.

Question3
What clinical features are seen in aplastic anaemia (see question 2) and what is the underlying pathophysiology?

Aplastic anaemia may result from defects in haemopoietic stem cells or in the marrow micro-environment. The precise mechanism is often unknown but the ability to correct the defect by bone marrow transplantation suggests that the fault often lies in the stem cells.

Many individuals show evidence of an immune-mediated suppression of haematopoiesis. Cellular mechanisms seem most important. In some individuals T cells produce in vitro suppression of autologous marrow stem cells. Humoral mechanisms may be involved since antibodies to stem cells have been found.

Question 4
What investigation findings are associated with a poor prognosis in aplastic anaemia?

Diagnosis of aplastic anaemia is based upon:

- peripheral blood:
    - neutrophils less than 0.5 x 10^9 per litre
    - platelets less than 20 x 10^9 per litre
    - reticulocyte count corrected for haematocrit less than 1%
- marrow:
    - severe hypocellularity
    - moderate hypocellularity with < 30% of residual cells being haematopoietic

At least two peripheral plus one marrow criteria must be satisfied.

A bad prognosis is associated with the presence of two of the following three features

- neutrophil count <0.5 x 10^9 /L
- Platelet count of <20 x 10^9 /L
- Reticulocyte count of <40 x 10^9 /L

Question 5

As part of Julian's management he requires protective isolation, explain why this is necessary and how it is achieved on a hospital ward.

Rather than isolating the patient to protect others, the patient is the one protected to minimise the risk of acquiring a Multi Resistant Organism risk of acquiring a Multi-MRO).

- Set up Personal Protective Equipment (PPE) trolley outside patient room.
- Trolley should contain gloves, plastic aprons, anti microbial hand gel, protective eye wear & splash resistant masks.
- Place a sign outside the patient's room such as the following to alert staff and visitors.

- Daily room clean to be performed first by the ward PSA.
- Aseptic technique when attending line insertions, line changes, catheter dressings, wound dressings.
- Cleaning of all surfaces every shift.

Question 6

Outline the principles of supportive care in the management of bone marrow failure.

Supportive care includes transfusion of red cells and platelets, and antibiotics.

Question 7

Julian becomes increasingly symptomatic due to his anaemia and a blood transfusion is required. Julian's blood group is B positive, explain what this means in terms of the ABO and Rh classification system of blood grouping.

The ABO group

The four different blood groups are A, B, AB and O. A person's blood group is determined by a pair of genes, one each inherited from their mother and father. Each blood group is identified by its own set of complicated chemical substances - called antigens - located on the surfaces of red blood cells. When a person needs a blood transfusion, it is important that the donated blood matches their particular blood group. A mismatch can cause serious complications. The ABO system of blood grouping involves naturally occurring IgM anti – A and anti B antibodies which are capable of producing rapid and severe intravascular haemolysis of incompatible red cells.

The Rhesus factor

A person's Rhesus type is also determined by a pair of genes, each one inherited from one parent. Blood is either Rh-positive or Rh-negative, depending on whether or not certain molecules are present.

Question 8

You are required to obtain informed consent from Julian for the blood transfusion. Outline the possible immunological and non-immunological complications of blood transfusions.

General Risks:

The commonest causes of transfusion reactions seen at The Royal Children's Hospital are fever, chills, hives and red rashes, these occur in approximately 1% of all blood transfusions. Circulatory overload is a risk for those patients that are already in a high risk group for circulatory overload, for example neonates, cardiac patients.

Transfusion related events:

Adverse reaction	**Risk per unit transfused (unless specified)**
Bacterial sepsis	1: 75,000 for platelets 1: 500,000 for red cells
Haemolytic reactions: Acute Delayed	 1: 12,000 to 77,000 1: 4,000 to 9,000
Anaphylaxis – IgA deficiency	1: 20,000 to 50,000
Fluid overload/cardiac failure	Up to 1% of patients receiving transfusions
TRALI	1: 5,000 to 190,000
Transfusion-associated graft vs host disease	Rare

Reference: ARCBS Blood Component Information Booklet 2009.

In terms of viral safety, Australia has one of the safest blood supplies in the world.

The following outlines risks of transfusion transmitted infection calculated on Australian Red Cross Blood Service (ARCBS) data from 1 January 2007 to 31 December 2008.

- HIV: Approx 1 in 5.4 million
- HCV: Approx 1 in 2.7 million
- HBV: Approx 1 in 739 000

These risks are very small compared to risks of everyday living: chance of being killed in a road accident is about 1 in 10,000.

ABO incompatibility remains one of the most common fatal complications of blood transfusion and most are due to avoidable errors (such as patient/sample identification errors).

Question 9

It is important when administering a blood transfusion to ensure that the correct blood is given. Outline the steps that are undertaken to minimise error in the administration of a blood transfusion.

Always check the identity of the patient:

- When taking sample for blood grouping or crossmatch.
- Before commencing the transfusion.
- In emergency situations a process should be in place for cases where a patient is unable to be identified.

Remember when collecting a pre transfusion blood sample:

- Only one patient should be bled or processed at a time.
- Never pre-label the specimen tubes.
- Check identity by ASKING the patient to state and spell his/her name AND check the wrist band.
- Check the request form and sample match the patient and wrist band.
- Remember to sign the sample and request form.
- The person taking the blood specimen is responsible for ensuring the correct labelling of the specimen.

<u>Transporting blood products:</u>
A common cause of transfusion reactions is the transfusion of an incorrect blood component. This is often due to mistakes when collecting blood components from the hospital blood bank or identification of the patient immediately prior to transfusion.
Hospitals must have a written policy for the collection of blood components and their delivery to the clinical area where the transfusion is to be given.

<u>Administration of Blood:</u>
Safe transfusion practice requires a final patient identity check to be undertaken at the patient's bedside immediately before commencing the administration of the blood component. This is vital

to ensure the right blood is given to the right patient. Transfusions should only be administered where advanced life support measures are available including oxygen, adrenaline and equipment.

Recommended Procedure

- Prior to issue and transfusion, components must be inspected visually.
- The bag/pack is intact- check for pack damage (e.g. cracks or pinholes), tampering or other suggestion that the unit is not suitable for transfusion.
- If there is any evidence of haemolysis, clot formation, abnormal coloration or a significant colour change in the blood bag as compared with the tubing segments (for red cell components), pack damage (e.g. cracks or pinholes).
- If the unit is not suitable for transfusion, it must not be transfused and should be returned to the issuing blood bank or ARCBS for further evaluation.
- The donation or batch number, blood group and component type against the patient blood group, if applicable and the laboratory issue label are all identical.
- Expiry date of the unit has not been exceeded.
- Expiry date of the crossmatch has not been exceeded, if applicable.