# CASE FIVE

**Short case number: 3_30_5**
**Category: Immune and haemopoietic systems**
**Discipline: Medicine**
**Setting: Hospital Ward**
**Topic: Myeloproliferative disorders_myelofibrosis**

## Case

**You are the medical intern currently working with the haematology team. Margaret Lewis, who is 60 years old presented to her GP recently with a 5-month history of increasing tiredness and weight loss. On examination her GP noted an enlarged spleen. Her FBC has demonstrated an anaemia. She has been referred in by the haematologist for further investigation; the haematologist suspects a myeloproliferative disorder and/or myelofibrosis.**

## Questions

1. Noting her splenomegaly, what are the key features of your history and examination and why?
2. Review the anatomy and function of the spleen and explain the physiological effects of hypersplenism.
3. What are the clinical features of myelofibrosis and hypersplenism and what is the underlying pathophysiology?
4. What investigations are often undertaken in the assessment of myelofibrosis and why?
5. Margaret's condition deteriorates with worsening anaemia and thrombocytopaenia and she requires a splenectomy. What are the problems that can occur post splenectomy?
6. Margaret is subsequently discharged to her GPs care. As part of her ongoing management, what recommendations would you make regarding prophylaxis against infection?

**Suggested reading:**


- Kumar P, Clark ML, editors. Kumar & Clark's Clinical Medicine. 9th edition. Edinburgh: Saunders Elsevier; 2016.
- Colledge NR, Walker BR, Ralston SH, Penman ID, editors. Davidson's Principles and Practice of Medicine. 22nd edition. Edinburgh: Churchill Livingstone; 2014.

## ANSWERS

**Question 1**

**Noting her splenomegaly, what are the key features of your history and examination and why?**

History

- Symptoms of anaemia: weakness, tiredness, dyspnoea, fatigue, postural dizziness.
- Bleeding ( menstrual/gastrointestinal)
- Easy bruising, purpura, thrombotic tendency
- Infection, fever, jaundice
- Lymph gland enlargement,
- Bone pain
- Paraesthesiae ( B 12 deficiency)
- Skin rash
- Weight loss

A full haematological examination should be preformed, in particular looking for signs of malignancy.

- Palpate all draining lymph nodes
- Examine all remaining lymph node groups
- Examine the abdomen, particularly for hepatomegaly and ascites
- Feel the testes
- Preform a rectal examination and pelvic examination
- Examine the lungs and breast and skin for melanoma.

**Question 2**

**Review the anatomy and function of the spleen and explain the physiological effects of hypersplenism.**

The spleen is the largest lymphoid organ in the body and is situated in the left hypochondrium
There are two anatomical components:

- The red pulp, consisting of sinuses lined by endothelial macrophages and cords
- The white pulp, which has a structure similar to lymphoid follicles.

Blood enters via the splenic artery and is delivered to the red and white pulp. During the flow the blood is skimmed, with leucocytes and plasma preferentially passing to white pulp. Some red cells pass rapidly through into the venous system while others are held up in the red pulp.

The spleen is responsible for

- Sequestration and phagocytosis of red cells, or old or abnormal cells
- Extramedullary haemopoiesis
- Production of antibodies – T cells and B cells
- Blood pooling – sequestration of platelets.

Hypersplenism produces:

- Pancytopenia
- Haemolysis due to sequestration and destruction of red cells
- Increased plasma volume.

**Question 3**
**What are the clinical features of myelofibrosis and hypersplenism and what is the underlying pathophysiology?**

Myelofibrosis is a myeloproliferative disorder characterised by:

- progressive fibrosis of the bone marrow
- splenomegaly

Marrow fibrosis is thought to occur as a result of increased secretion of platelet derived growth factor. Loss of marrow capacity results in extramedullary haematopoiesis in the liver, spleen and lymph nodes.

Clinical features of myelofibrosis include:

- usually develops in adults over age 50
- progression is insidious - patients commonly present with fatigue and weakness due to anaemia; or because of abdominal fullness and early satiety due to splenomegaly
- spleen is often massively enlarged
- hepatomegaly occurs in over half of cases

With progressive fibrosis of bone marrow there may be:

- severe anaemia - necessitating transfusion
- bleeding - due to thrombocytopenia
- respiratory pain - due to perisplenitis secondary to splenic infarction
- severe bone pain, especially in the lower legs
- hyperuricaemia and gout - from rapid blood cell turnover
- cachexia

Hypersplenism is an imprecise term commonly used to refer to a clinical state characterised by:

- reduced red blood cells, platelets, and granulocytes in any combination
- splenomegaly of any cause
- an adequately cellular bone marrow - ie. indicating that there is sufficient compensation to cytopenia
- totally or partially correctable by splenectomy

Symptoms include:

- abdominal discomfort
- anaemia
- infection
- bleeding

**Question 4**
**What investigations are often undertaken in the assessment of myelofibrosis and why?**

- Anaemia with leukoerythroblastic features is present. Poikilocytes and red cells with characteristic tear drop forms are seen. The WBC count may be over 100 x $10^9$ /L and the differential WBC may be very similar to that seen in CML.
- The platelet count may be high, but in later stages thrombocytopenia occurs.
- Bone marrow aspiration is often unsuccessful and this gives a clue to the presence of he condition. A bone marrow trephine is necessary to show the markedly increased fibrosis.
- The Philadelphia chromosome is absent; this helps distinguish myelofibrosis from most cases of CML
- A high serum urate
- Low serum folate levels may occur owing to the increased haemopoietic activity.

**Question 5**
**Margaret's condition deteriorates with worsening anaemia and thrombocytopaenia and she requires a splenectomy. What are the problems that can occur post splenectomy?**

Early complications include:

- infection:
    - often subphrenic
- thrombosis:
    - a result of transiently raised platelet levels
    - patients are treated prophylactically with aspirin

Late complications are usually infective:

- asplenic patients are susceptible to rapidly progressive pneumococcal and meningococcal infections
- the risk of infection is reduced by proper prophylaxis

**Question 6**
**Margaret is subsequently discharged to her GPs care. As part of her ongoing management, what recommendations would you make regarding prophylaxis against infection?**

The long term management of asplenic patients aims to minimise the risk of infection.

Prophylaxis has three arms:

- vaccination
- chemoprophylaxis
- general measures

<u>Vaccination</u>

All splenectomised patients and those with functional hyposplenism should receive:

- pneumococcal immunisation

- patients not previously immunised should receive Haemophilus Influenza type b vaccine
- patients not previously immunised should receive Meningococcal Group C conjugate vaccine
- influenza immunisation should be given

Chemoprophylaxsis

Lifelong prophylactic antibiotics should be offered in all cases where a patient has an absent or dysfunctional spleen, especially in the first two years after splenectomy, for all children aged up to 16, and when there is underlying impaired immune function.

A first-line regimen is :

- amoxicillin 250-500 mg daily for adults
- amoxicillin 125mg daily for children 5-14 years old
- amoxicillin 10 mg/kg/d in children under 5 yr of age

General Measures

- carrying a "No Spleen" card which details vaccinations, antibiotic therapy and what action should be taken in case of a flu-like illness
- advice to seek urgent medical attention at early signs of infection in the future, irrespective of prophylaxis
- aspirin prophylaxis against thrombosis is dependent upon the platelet level and should be controlled by a specialist haematologist