Malignant Blood Disorders — Myeloproliferative Disorders, Myelodysplastic Disorders and Multiple Myeloma

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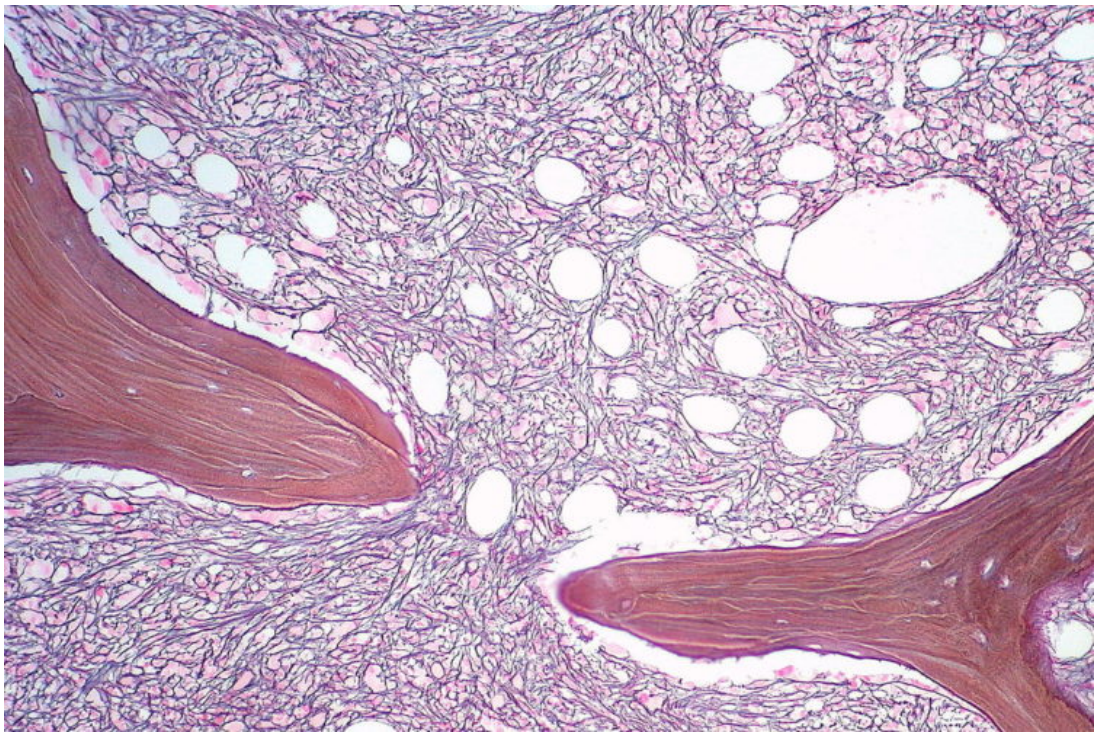
A number of malignant disorders of the blood are characterized by abnormal and uncontrolled growth of certain blood cell types that are associated with prolonged survival even after the establishment of the diagnosis. Myeloproliferative diseases are a collection of disorders of the blood cell lines that are characterized by elevated platelets, white blood cells or red blood cells in the peripheral blood. The myelodysplastic syndromes are quite the opposite as they are characterized by the inability of the bone marrow to produce the normal and different blood cells; hence, can be also defined as bone marrow failure disorders. Myeloma, on the other hand, is a malignant condition of the plasma cells that is characterized by uncontrolled activation, proliferation and the production of abnormal antibodies.



Myeloproliferative Disorders

Different disease processes have been implicated with **elevated platelets counts, white blood cells or red blood cells**. While, in some cases, a pure cell line is affected,

usually the condition can affect **multiple cell lines**.

Polycythemia vera

Patients with **polycythemia vera** present with elevated red blood cells in particular, but other cell lines can also be affected. Patients with polycythemia vera usually carry the **genetic mutation JAK2V617F**. They usually have no symptoms at the time of diagnosis; hence, the diagnosis is usually incidental.

Once the disease progresses, patients can complain of **fatigue**, **dyspnea**, **itching**, **nosebleeds**, **headaches,** and **thrombotic arterial disease**. They can also develop **splenomegaly** and can complain of **abdominal pain** or **distension**.

Men are more likely to be affected by polycythemia vera, patients are usually **older than 60** years of age and a **previous history of exposure to radiation** can be elicited in a significant number of cases.

Phlebotomy can be used to lower the iron load associated with an elevated red blood cell count. **Hydroxyurea** can be used to lower the number of red blood cells. **Aspirin** and **antihistamines** have been used to lower itchiness.

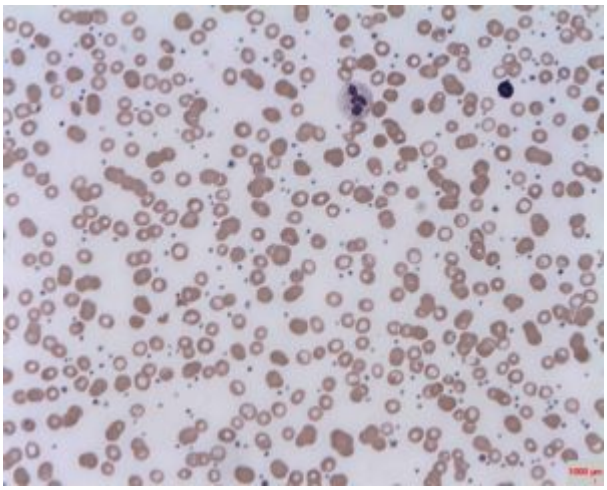


Image: "Thrombocytosis is the presence of abnormally high platelet counts." by Erhabor Osaro (Associate Professor) – Own work. License: CC BY-SA 3.0

Complications of polycythemia vera include blood cancer, bleeding and clotting disorders. It has no cure, however, medications cn control the progression of the disease.

Essential thrombocytosis

Essential thrombocytosis is another example of the myeloproliferative disorders where the main cell line affected is the one responsible for the production of platelets. Such patients are usually at an exquisitely high risk of **thrombotic events,** such as strokes and acute ischemic heart disease. Patients can also complain of **headaches**.

Again, the **elderly** are more likely to develop the condition. Essential thrombocytosis is the only form of myeloproliferative disorders that are **not associated with splenomegaly**. Treatment is usually symptomatic and tailored against the thrombotic complications.

Essential thrombocytosis may mimic secondary thrombocytosis, primary myelofibrosis, polycythemia vera, and chronic myelogenous leukemia. Complications of essential thrombocytosis include stroke, heart attack, and bleeding disorders. The median survival of the patients with essential thrombocytosis is 20 years.

Idiopathic myelofibrosis

Idiopathic myelofibrosis is a condition that is characterized by **too much collagen production in the bone marrow**. In contrast to the other forms of myeloproliferative disorders, patients with myelofibrosis have a **reduced number of different blood cell lines**.

Patients can develop **anemia**, **weight loss and fever** due to opportunistic infections and are at an increased risk of **bleeding complications**. Exposure to **benzene** and **toluene** has been linked to an increased risk of myelofibrosis.

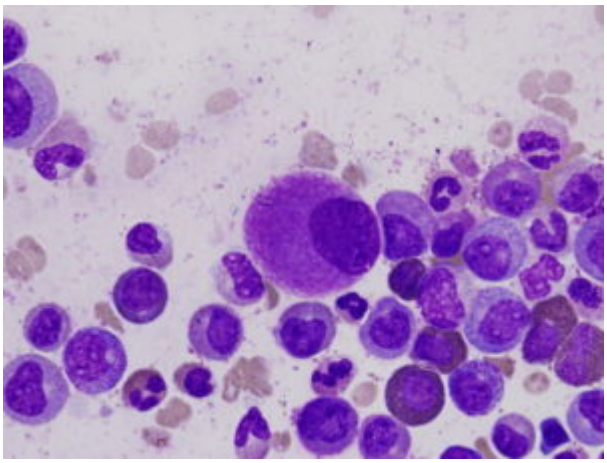


Image: "A small, hypolobated megakaryocyte in a bone marrow aspirate, typical of chronic myelogenous leukemia." by Difu Wu – Own work. License: CC BY-SA 3.0

Chronic myelogenous leukemia

Chronic myelogenous leukemia (**CML**) is the last form of myeloproliferative disease of interest to us in this discussion. CML is characterized by **elevated granulocytes**.

Patients present with **fatigue**, **weight loss**, **fever** and **night sweats**, **joint pain**, **dyspnea** and an increased tendency to **opportunistic infections**. Patients with CML can also have **splenomegaly**.

Patients with the **Philadelphia chromosome** are at an increased risk of developing CML. In contrast to the other forms of myeloproliferative disorders, patients with CML are relatively younger, **45 to 50 years** of age.

Exposure to radiation is a possible risk factor for patients who are not carriers of the Philadelphia chromosome. Treatment for CML cannot be covered in this topic, but it includes **chemotherapy**, **biologic therapy**, **stem-cell transplantation,** and **donor lymphocyte infusion**. Imatinib, cyclophosphamide, and cytarabine are possible chemotherapeutic options for CML.

Complications of CML include fatigue, muscle cramps, myelosuppression, and pancytopenia. Prognosis of CML is variable depending upon several factors.

Myelodysplastic Disorders

Myelodysplastic disorders (**MDS**) are characterized by **hypercellular bone marrow** and **peripheral cytopenias**. The bone marrow is infiltrated by **abnormal stem cells** that are incapable of maturation and production of the different cell-lines found in the blood such as red blood cells, thrombocytes, and white blood cells. It is important to notice that the bone marrow is **usually hypercellular** in contrast to the hypocellular bone marrow of anaplastic anemia.

The **hematopoietic stem cell population** might be injured because of a **viral infection**, **radiation exposure** or **cytotoxic chemotherapy** for another condition. Patients who develop the disorder, without previous exposure to chemotherapy or radiation, are considered as having a **primary myelodysplastic disorder**.

Symptoms of myelodysplastic disorders include **anemia**, **thrombocytopenia** and a **history of recurrent infections**. Patients can present with **heart failure**, **recurrent bleeding complications**, **fever** and **night sweats**.

The current **World Health Organization classifications of myelodysplastic disorders** can be summarized as in the table below:

Classification	Important features of blood	Important features of bone marrow
MDS with single lineage dysplasia	single cytopenias	dysplasia > 10 % of a single cell line with < 5 % blasts
MDS with ring sideroblasts	anemia	evidence for erythroid precursors with ring sideroblasts > 15 %
MDS with multi-lineage dysplasia	multiple cytopenias	dysplasia > 10 % in multiple cell lines with or without sideroblasts and with < 5 % blasts
MDS with excess blasts-1	similar to MDS with multi-lineage dysplasia but with 5—9 % blasts	
MDS with excess blasts-2	similar to MDS with multi-lineage dysplasia but with 10—19 % blasts	
MDS-unclassified	cytopenia of any cell line	no or minimal dysplasia but with characteristic MDS cytogenetics
MDS with isolated deletion of 5q	anemia with normal or elevated platelets count	erythroid dysplasia with isolated deletion of 5q and < 5 % blasts

Multiple Myeloma

Myeloma is a **form of plasma cell cancer** that can be either isolated to a single tumorous growth, called **plasmacytoma** or multiple tumorous growths as is the case with multiple myeloma. The most common location for the **abnormal growth and tumor formation of plasma cells** is in the **bone**.

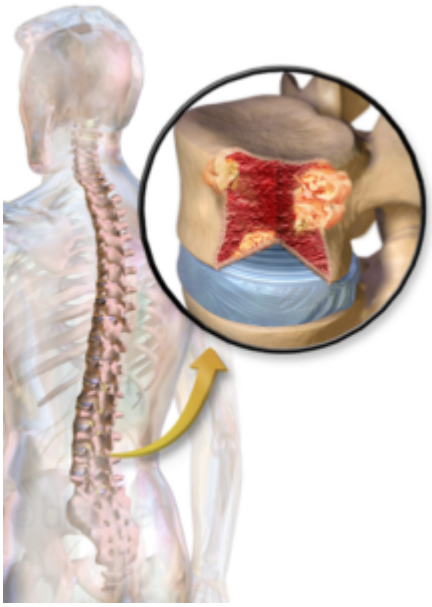


Image: “Multiple Myeloma.” by Blausen Medical Communications, Inc. – Donated via OTRS, see ticket for details. License: CC BY 3.0

Myeloma risk increases with age, is more common among **men**, can be linked to previous **exposure to radiation** and some patients show a **family history** of the disease. Patients who have had a previous history of **monoclonal gammopathy** of undetermined significance are at an increased risk of developing multiple myeloma.

Patient’s semiology can be related to **bone problems** or **blood-related symptoms**. Patients can have weak and fragile bones, increased risk of broken bones, and bone pain. Patients can also develop **systemic symptoms,** such as weight loss, loss of appetite and constipation.

Constipation is believed to be related to **elevated blood calcium levels**, which happens in patients with multiple myeloma. Patients can also develop **anemia**, or **opportunistic infections**.

Patients with multiple myeloma can have **low red blood cell count**, **elevated monoclonal antibodies**, **elevated light-chain proteins,** and **elevated beta-2 microglobulin**.

A **bone marrow biopsy** reveals elevated counts of plasma cells in the bone marrow. Bone x-rays and magnetic resonance imaging can reveal the **tumors**.

Treatment for multiple myeloma includes **chemotherapy**, **biologic therapy** and **stem cell transplantation** in case of bone marrow failure. Patients usually survive between 7 to 10 years after the diagnosis.

Differential diagnoses of MM

1. Metastatic bone disease
2. Lymphoma

Survival of the patients with MM ranges from one year to ten years. Five-year relative survival of the patients with MM is 46.6%.

References

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