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.

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

Essential thrombocytosis

Essential thrombocytosis is another example for 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 is 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. 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 the 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.

**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 a 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:

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

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.
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

[Myelodysplastic Syndrome Guidelines](http://medscape.com) via medscape.com

[Myeloproliferative disorders](http://nih.gov) via nih.gov


[Multiple Myeloma](http://medscape.com) via medscape.com

[Myeloproliferative Neoplasms: A Contemporary Review](http://jamanetwork.com) via jamanetwork.com

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Notes