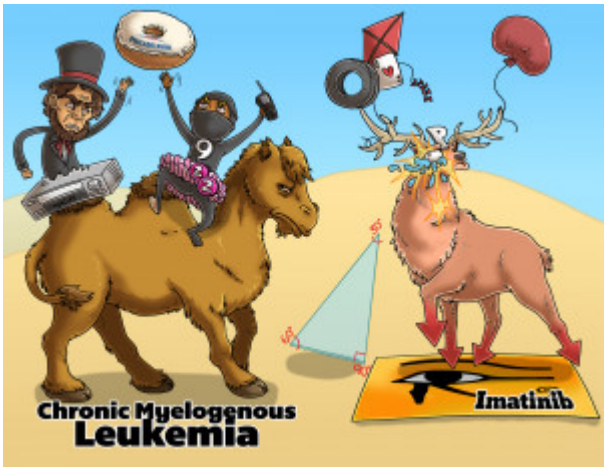
Chronic Myelogenous Leukemia (CML)

Myeloproliferative disorders are characterized by increased production of one or more types of blood cells and are commonly associated with the presence of a mutated constitutively activated tyrosine kinase. Chronic myelogenous leukemia (CML) is a myeloproliferative disorder characterized by the presence of a chimeric BCR-ABL gene derived from portions of the BCR gene on chromosome 22 and the ABL gene on chromosome 9 caused by (9;22) translocation. This is called a Philadelphia chromosome and this gene synthesizes a constitutively active BCR-ABL tyrosine kinase. Activation of this kinase induces pro-growth and pro-survival pathway that are normally turned on by hematopoietic growth factors. For unknown reasons, the BCR-ABL tyrosine kinase preferentially stimulates the proliferation of granulocytic and megakaryocytic progenitors and causes the abnormal release of immature granulocytic forms from the bone marrow into the blood. The bone marrow is typically markedly hypercellular due to the increased numbers of maturing granulocytic precursors. The spleen is also often greatly enlarged as a result of extramedullary hematopoiesis. CML is primarily a disease of adults between the ages 30 and 60. After an average period of 3 years, about half of CML patients enter an accelerated phase of disease, marked by increasing anemia and thrombocytopenia. Within 6 to 12 months, the accelerated phase evolves into a picture that resembles acute leukemia, commonly called a blast crisis. In 70% of blast crises, the blasts are of myeloid origin whereas the remainders are of pre-B cell origin. Understanding the molecular pathogenesis of CML has led to the use of the drug imatinib, which is a specific BCR-ABL inhibitor. Imatinib results in sustained hematologic remission in about 90% of patients with a markedly decreased number of BCR-ABL positive cells in the marrow.



PLAY PICMONIC

Pathophysiology

BCR-ABL

VCR-Abe Lincoln

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9;22 Translocation

(9) Ninja:(22) Double-Tutu

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Philadelphia Chromosome

Philadelphia-cream-cheese

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Signs & Symptoms

Tyrosine Kinase

Tire-kite-ace

CML is characterized by a constitutively active BCR-ABL tyrosine kinase. Activation of this kinase induces pro-growth and pro-survival pathway that are normally turned on by hematopoietic growth factors. For unknown reasons, the BCR-ABL tyrosine kinase preferentially stimulates the proliferation of granulocytic and megakaryocytic progenitors and causes the abnormal release of immature granulocytic forms from the bone marrow into the blood.

Low Alkaline Phosphatase

Down-arrow Elk P

CML is characterized by low alkaline phosphatase levels due to elevated immature granulocytes as opposed to a leukemoid reaction, in which the alkaline phosphatase is normal or elevated.

Splenomegaly

Spleen-balloon

The spleen is often greatly enlarged as a result of extramedullary hematopoiesis. Sometimes the first symptom of disease is a dragging sensation in the abdominal region caused by massive splenomegaly.

Considerations

Blast Crisis

Blast Crying

After an average period of 3 years, about half of CML patients enter an accelerated phase of disease, marked by increasing anemia and thrombocytopenia. When lab work reveals a blast (immature blood cell) count of greater than 30%, the patient is said to be in a blast crisis. On average, this occurs 6-12 months after the accelerated phase. It's important to note that while this phase resembles acute leukemia, they are in fact two separate conditions with unique outcomes and treatments.In 70 percent of blast crises, the blasts are of myeloid origin whereas the remainders are of pre-B cell origin.

Age 30 to 90 Years

30-60-90 Triangle Window

CML is primarily a disease of adults between the ages 30 and 90, with the median age of diagnosis being 60 years of age.

Responds to Imatinib

Eye-mat

Understanding the molecular pathogenesis of CML has led to the use of the drug imatinib, which is a specific BCR-ABL inhibitor. Imatinib results in sustained hematologic remission in about 90% of patients with markedly decreased number of BCR-ABL positive cells in the marrow.