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Acute Myeloid Leukemia

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Facts and Demographics

Acute Myeloid Leukemia, or AML, also known as acute myelogenous leukemia and acute nonlympocytic leukemia (ANLL), is a disease that is estimated to affect 21,380 people in the U.S., killing 10,590 this year alone according to the National Institute of Cancer (NIC, 2017).

AML is a disease of the myeloid cells in the bone marrow. These cells proliferate uncontrollably and lose their ability to differentiate to functioning components of the blood (Sykes et al p. 989).

AML has a 26.6% 5-year survival rate, and 5-10-month survival rate for patients who cannot tolerate the high intensity chemotherapy that is often required for complete remission (Cruz et al p. 53). Relapse rate is reported to be 30% to 40% within the first three years (Cruz et al p. 54).

The disease process is multi-faceted, with many factors that are believed to cause AML, from genetics to environmental exposures (Wang & Bailey, 2016).

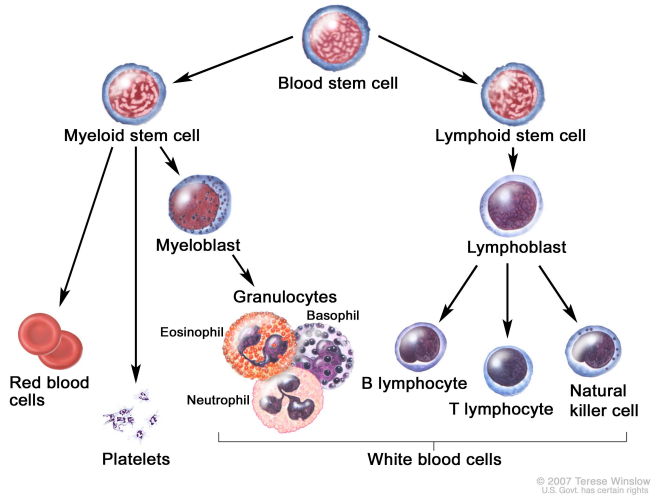

Illustration of differentiation of blood stem cells. Myeloid stem cells differentiate into many different specialized cells, such as red blood cells, platelets, and granulocytes. Figure from the National Cancer Institute (NIH, 2017).

Treatment

The goal of treatment for AML, which can be either a combination of chemotherapy and/or radiation alone, or with a stem cell transplant, is complete remission. Partial remission has shown to have no benefit to survival (www.cancer.gov, 2017).

Treatment is intensive to endure. Patients must first go through chemotherapy and/or radiation to achieve complete remission status, followed by another course of high intensity chemotherapy and/or radiation to prepare for hematopoietic stem cell transplantation (HSCT). Patients receive stem cells from a donor (allogeneic or allo-HSCT) (Mosseso, p. 22).

The goal of HSCT is to have engraftment of the donor cells, which will begin to produce healthy cells. Engraftment of neutrophils can take up to 20 days, and engraftment of platelets can take up to eight weeks (Mosseso, p. 25). The ANC, or absolute neutrophil count must be at least 500/mm^3 for engraftment. Platelet count must be at least 20,000 platelets per microliter for platelet engraftment (Mosseso, p. 25).

Complications

AML patients who receive allo-HSCT have complications related to their body's defense against the foreign cells (Mosseso, p. 23). Immunosuppressive drugs are given to prevent rejection, or patients may receive a combination of immunosuppressive drugs and T cell removal from donor cells (Mosseso, p. 24-25).

Complications also arise from pancytopenia secondary to intensive chemotherapy regimens. Patients are at a high risk for infection and bleeding. They need blood transfusions and antibiotic coverage (WHO, 2014 p. 11). Of note, cardiotoxicity is a potential side effect of the chemotherapies daunorubicin and idarubicin. Central nervous system toxicity is a side effect of cytarabine. Patients can develop severe diarrhea and mucositis secondary to chemotherapy effects as well (WHO, 2014 p. 11).

Graft versus host disease (GVHD) can be a severe chronic or acute process. T cells by the donor activate an immune response in the recipient, which results in an inflammatory response, causing GVHD. Getting the best possible match of major histocompatibility antigens is beneficial in curtailing GVHD (Sairafi et al, p. 1).

Lastly, patients suffer from an enormous amount of emotional and physical stress both during and after treatment. Patients report negative side effects, including both the emotional and financial burden of treatment, as well as long-term effects of treatment (Ghodraty-Jabloo et al, pp. 2037-2041)

Genetic Discoveries

Genetic factors play an important role in both the diagnosis and the treatment of AML. It has been widely accepted that genetic mutations, specifically translocations, have an important impact on disease presentation and treatment (Ohgami & Arber, pp. 122-123).

The average AML genome contains approximately 400 mutations (Link, Wolff & Wolff, p. 409).

Billions of dollars were spent to first map the human genome, something that can be done in four to six weeks now, at a cost of $10,000 to $20,000 (Link, Wolff & Wolff, p. 410).

The first AML genome was mapped in 2008, and since then dozens of mutations have been discovered. (Link, Wolff & Wolff, p. 410). Mutations discovered are not "driver" mutations, in that they do not cause the stem cells to start mutating. Rather they are "background" mutations, in that they can help predict outcomes and relapses (Link, Wolff & Wolff p. 409).
Specific gene mutations, such as the RUNX1-RUNXT1 (10-20% of cases), CBFB-MYH11 (5-10% of cases), PML-RARA (10-20% of cases (Ohgami & Arber pp. 123-124).
Deletions and multiple translocations prove a poor prognosis (Ohgami & Arber p. 124).

The World Health Organization distinguishes AML by the genetic composition of AML. This guides providers to determine the most appropriate plan for patients (Wang & Bailey, p. 1215).

Treatment plans are tailored to the specific type of genetic mutations and abnormalities for improved outcomes (Wang & Bailey, p. 1215).

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