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Acute Myeloid Leukaemia (AML): The Good, the Bad, and the Ugly

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Abstract

Acute myeloid leukaemia [AML] is a malignant disease of the bone marrow in which hematopoietic precursors are prevented in the early stages of development. Like other malignant tumors, this is due to genetic variation that leads to tumor changes and clonal proliferation. A small number of cases have identified causal factors, such as previous chemotherapy or certain chemical exposures, but most or isolated genetic mutations have no clear causal factors. French Anglo-American [FAB] and the most recent World Health Organization [WHO] classification can help improve the diagnosis and treatment of malignant diseases. Treatment has been achieved through chemotherapy, radiation therapy, and stem cell transplantation.

Keywords: AML, hematopoietic precursors, chemotherapy, radiation therapy, and stem cell transplantation

Introduction

Acute myeloid leukemia (AML) is a malignant disease characterized by an excessive and uncontrolled growth of immature cells (called myeloid blasts) (Nelson, 2018). Frohling et al. also made this point in 2017 who considered it a clonal disease characterized by the accumulation of somatic acquired genetic changes in hematopoietic progenitor cells that alter the normal mechanisms of self-renewal, proliferation and differentiation. The difference between most subtypes of AML and other related blood diseases is the presence of more than 20% blasts in the bone marrow. The underlying pathophysiology of AML includes the arrest of bone marrow cell maturation in the early stages of development. Acute myeloid leukemia is the most common acute leukemia that affects adults. Although acute myeloid leukemia is a relatively rare disease, its incidence increases with age, accounting for approximately 1.2% and 3.5% of cancer deaths in the United States and Nigeria, respectively. The incidence is expected to increase with age as the population increases (Babatunde et al., 2012). Some of the risk factors associated with AML include genetic susceptibility, which has been reported in diseases such as Fanconi anemia and Down syndrome, and then environmental exposure to ionizing radiation and organic

solvents such as benzene (Austin et al. ,2015). The etiology of AML involves several factors, including congenital diseases of the blood system, familial syndromes, environmental exposure, and drug exposure. However, most patients with new-onset AML have no identifiable risk factors. Patients with acute myeloid leukemia have symptoms caused by bone marrow failure, symptoms caused by infiltration of leukemic cells into the organs, or both. The course of time is variable. The diagnosis of AML includes blood tests, bone marrow aspiration and biopsy (final diagnostic test), and genetic abnormality testing. Current standard chemotherapy can be treated with standard therapies. Re-admission is usually required to control the toxic effects of chemotherapy (Marcucci et al., 2016).

Epidemiology of acute myeloid leukemia

Haematological malignancies account for one-fifth of the most common cancers and are the second leading cause of cancer deaths (Siegel et al., 2015). In a 5-year study from 2007 to 2011, leukemia was the fifth most common cause of cancer deaths in men in the United States and the sixth most common cause of cancer deaths in women. In the United Kingdom, hematological malignancies are said to account for 63.2% and 55.7% of men. Female 44.3% (Cohen et al., 2015). In sub-Saharan Africa, it is the third most common malignant tumor in men and the sixth most common malignant tumor in women. Similarly, in Nigeria, it accounts for 17,418.05% of all cancers in Nigeria, ranking third and fifth among men and women respectively (Nwannadi et al., 2013). A study conducted in northern Nigeria showed that the prevalence of males was 19.8%, mainly chronic leukemia (Ochaka et al., 2017). Another study conducted in southwestern Nigeria reported that the prevalence of all male-dominant cancers was 18.05%, mainly NHL (Babatunde et al., 2012). The incidence of acute myeloid leukemia (AML) increases with age; the median age at diagnosis is 63 years. Acute myeloid leukemia accounts for approximately 90% of all acute leukemias in adults, but it is very rare in children (Jemal et al., 2012). The incidence of treatment-related AML (ie, AML caused by previous chemotherapy) is increasing; treatment-related diseases currently account for approximately 10-20% of all AML cases. In addition, compared with women, the incidence of acute myeloid leukemia in men is slightly higher, with a male-to-female ratio of 1.3: (Siegel et al., 2015). In addition, the incidence of AML is related to changes in geographic location. For example, among adults, North America, Europe and Oceania have the highest incidence, as well as Africa, while adult AML is rare. In Asia and Latin America. United States. In contrast, childhood AML is less common in North America and India. This may be due to differences in population genetics and / or environmental factors (Greenlee et al., 2011).

The American Cancer Society (ACS) estimates that 20,240 new cases of AML (11,230 men and 9,010 women) will occur in the United States in 2021 (Cohen et al., 2015). AML is more common in developed countries and more common in whites than in other populations. The prevalence of AML increases with age. The average age of onset is approximately 70 years. However, AML affects all age groups. AML is more common in men than women, especially in elderly patients. This may be because myelodysplastic syndrome (MDS) is more common in men, and advanced MDS often progresses to AML. Some people have suggested that the higher prevalence of male acute myeloid leukemia may be related to occupational exposure. ACS estimates that by 2021, 11,400 people in the United States will die of AML. Among them, it is estimated that there are 6,620 men and 4,780 women (Cohen et al., 2015).

The cause of AML

The cause of AML involves a variety of factors, including blood history, family syndromes, environmental exposure, and drug exposure. However, most patients with new-onset AML do not have any identifiable risk factors. Advanced hematological diseases The most common risk factor for AML is advanced hematological diseases, the most common of which is myelodysplastic syndrome (MDS). MDS is a bone marrow disease of unknown etiology. It most commonly occurs in elderly patients and

manifests as progressive cytopenias that lasts for months or years. Patients with low-risk MDS (for example, MDS with ring sideroblasts) usually do not develop AML, while patients with high-risk MDS (for example, MDS with too many blasts) usually do. Other advanced diseases of the blood system that predispose patients to AML include aplastic anemia and myeloproliferative diseases, especially myelofibrosis (Frohling et al., 2017).

Congenital diseases

Some congenital diseases that predispose patients to AML include Bloom syndrome, Down syndrome, congenital neutropenia, Fanconi anemia, and neurofibromatosis. These patients usually develop AML in childhood; in rare cases, they can appear in adulthood. More subtle genetic diseases, including polymorphisms in the enzymes that metabolize carcinogens, also predispose patients to AML. For example, the polymorphism of NAD (P) H: quinone oxidoreductase (NQO1), an enzyme that metabolizes benzene derivatives, is associated with an increased risk of AML (Allan et al., 2011). The risk of acute myeloid leukemia that occurs after chemotherapy for another disease or of a new acute myeloid leukemia with abnormalities of chromosomes 5, 7, or both is particularly higher. Similarly, glutathione transferase polymorphism is associated with secondary AML after chemotherapy for other malignancies (Allan et al., 2011). Germline mutations of the familial syndrome AML1 gene (RUNX1, CBFA2) occur in familial AML-prone platelet disease, which is an autosomal dominant genetic disease characterized by moderate thrombocytopenia, platelet function defects, and a developmental tendency to the AML. [6] Mutations in CEBPA (a gene encoding CCAAT / α-enhancer binding protein, granulocyte differentiation factor, and members of the bZIP family) have been described in a 3-member family affected by AML (Smith et al., 2014). Holme et al. Studied 27 families with familial MDS / AML. All families have been tested for RUNX1, CEBPA, TERC, TERT, GATA2, TET2 and NPM1 mutations. Five of the 27 families have telomerase mutations (3 TERT, 2 TERC), one has RUNX1 mutation, and four have heterozygous GATA2 mutations (Holme et al., 2012). Gao et al. reviewed GATA2 mutations associated with familial ALMDS (Gao et al., 2014). GATA2 is a key transcription factor for hematopoietic differentiation and lymphatic vessel formation. Germline mutations in GATA2 involve a set of rare complex syndromes with overlapping clinical features of immunodeficiency, lymphedema, and propensity for AML or MDS. With the routine use of the next-generation extended genome in the bone marrow and its confirmation in non-hematopoietic tissues, more patients are diagnosed with germline mutations that make them susceptible to AML. These genes include DDX41, SRP72, ANKRD26 and ETV6 (Guidugli et al., 2017). The classification of myeloid neoplasms and acute leukemia revised by the World Health Organization in 2016 now includes a subtype of "myeloid neoplasms with reproductive susceptibility." Therefore, in order to correctly classify AML patients, these genes must be included in the next-generation panel. Some hereditary cancer syndromes, such as LiFraumeni syndrome, can manifest as leukemia. However, cases of leukemia are less common than solid tumors, which are usually characteristic of these syndromes (Arber et al., 2016).

Environmental exposure

Several studies have shown a relationship between radiation exposure and leukemia. Early radiologists (before proper shielding) are more likely to be found to have leukemia. Patients receiving therapeutic radiotherapy for ankylosing spondylitis have an increased risk of leukemia. Survivors of the Japanese atomic bombing have a significantly higher risk of developing leukemia.
Smokers have a small risk of AML, but it is statistically significant (odds ratio, 1.5) (Brownson et al., 2012). In several studies, smokers have a slightly increased risk of acute myeloid leukemia compared to non-smokers. Exposure to benzene is associated with aplastic anemia and pancytopenia. These patients often develop acute myeloid leukemia. Many of these patients have the erythroleukemia subtype of AML (AMLM6). Exposure to soot, creosote, tanning inks, dyes and solutions, and charcoal

dust are also associated with acute myeloid leukemia (Poynter et al., 2016).

Previous exposure to chemotherapy drugs

As more and more cancer patients survive from primary malignant tumors, more and more patients receive intensive chemotherapy (including bone marrow transplantation [BMT]), due to exposure to chemotherapy drugs, AML. The number of patients has increased. For example, the cumulative incidence of acute leukemia in breast cancer patients receiving adjuvant doxorubicin and cyclophosphamide at 5 years was 0.21% (Smith et al., 2013).

Patients who have been exposed to chemotherapy drugs can be divided into two groups: (a) patients who have been exposed to alkylating agents and (b) patients who have been exposed to topoisomerase II inhibitors. For alkylating agent/radiation exposure, the typical incubation period between drug exposure and acute leukemia is about 35 years, while topoisomerase inhibitors are only 912 months. Patients who have been exposed to alkylating agents, regardless of whether they have received radiotherapy, usually have a stage of myelodysplasia before the development of AML. Cytogenetic testing usually shows 5 and/or 7 (5q or monosomy 7).

Patients who were previously exposed to topoisomerase II inhibitors did not have a stage of myelodysplasia. Cytogenetic testing revealed a translocation involving the 11q23 band. Less commonly, these patients develop other balanced translocation leukemias, such as inversion 16 or t (15; 17) (Andersen et al., 2015).

Pathophysiology of AML

The underlying pathophysiology of AML is the maturation of bone marrow cells in the early stages of development. The mechanism of this stagnation is under investigation, but in many cases it involves the activation or inactivation of genes through chromosomal translocations and other genetic and / or epigenetic abnormalities (Arber et al., 2016). This developmental stagnation leads to two pathological processes. 1. Production Normal blood cells are significantly reduced, leading to varying degrees of anemia, thrombocytopenia, and neutropenia. Second, the rapid proliferation of abnormal myeloblasts, along with their reduced ability to undergo programmed cell death (apoptosis), causes them to accumulate in the bone marrow, blood, and usually the spleen and liver. At the same time, AML is characterized by mutations in genes involved in hematopoiesis. These mutations cause clonal expansion of undifferentiated myeloid precursors (primitive cells) in the peripheral blood and bone marrow, leading to ineffective erythropoiesis and bone marrow failure. Recent studies have also shown that it may be due to a series of recurring genetic changes in hematopoietic stem cells that accumulate with age. In most cases, AML will reappear in previously healthy people. The exact cause of the genetic mutation is unknown, but few risk factors include exposure to radiation, chemotherapy drugs, and smoking. AML can also progress from myelodysplastic disease (MPD), myelodysplastic syndrome (MDS), paroxysmal nocturnal hemoglobinuria, and aplastic anemia. The family causes of gene mutations should also be considered. AML is a highly heterogeneous disease with variable prognosis. It can be caused by genetic mutations, chromosomal translocations, or changes at the molecular level. Approximately 97% of cases have been studied to have genetic mutations. Despite the heterogeneity, they can be divided into favorable, moderate, or unfavorable risk groups based on cytogenetics. The prognosis in these categories varies greatly. Chromosomal translocations t (8; 21), t (15; 17), or inv (16) have a good prognosis, with a 3-year overall survival (OS) of approximately 66%, and 33 in patients younger than 60 years and over 60% Age respectively. People with t (9; 11), monosomy 5 or 7 and normal cytogenetics (CNAML) are at moderate risk. In t (6; 9), inv (3) populations, a high risk of treatment failure and death was observed. Or 11q change. t (8; 21) The presence of cKIT mutations in patients increases the risk of recurrence and reduces OS (Ghiaur et al., 2015).

Symptoms and physical examination

Due to ineffective red blood cell production and bone marrow failure, patients will experience various symptoms, including repeated infections, anemia, easy bruising, excessive bleeding, headaches and bone pain. Depending on the degree of anemia, they may experience general weakness, fatigue, shortness of breath, and chest tightness. Physical examination may reveal bruising, paleness, hepatomegaly, and splenomegaly. Lymphadenopathy is rare. DIC is common in patients with AML. Signs of organ infiltration are not uncommon. They can include enlarged liver and spleen and enlarged lymph nodes. Sometimes a rash occurs due to infiltration of leukemic cells.

Symptoms caused by low blood cell counts

Many of the signs and symptoms of AML are the result of a shortage of normal blood cells, which occurs when leukemic cells crowd out normal hematopoietic cells in the bone marrow. As a result, people do not have enough normal red blood cells, white blood cells, and platelets. These deficiencies appear in blood tests and can also cause symptoms (Ghiaur et al., 2015).

Symptoms of low red blood cell count (anemia)

Red blood cells carry oxygen to all cells in the body. A shortage of red blood cells can lead to:

a. Tiredness (fatigue)
b. Weakness
c. Feeling cold
d. Feeling dizzy or dizzy
e. Headache
f. pale skin grams. Shortness of breath

Symptoms of low white blood cell count

Infection may be due to a shortage of normal white blood cells (leukopenia), especially a shortage of infection-fighting white blood cells called neutrophils (called neutropenia). People with acute myeloid leukemia may get infections that don't seem to go away, or they may get one after another. Fever is usually accompanied by infection. Although AML patients may have a high white blood cell count due to the excessive number of leukemic cells, these cells do not prevent infection like normal white blood cells (Ghiaur et al., 2015).

Low platelet count symptoms

Platelets usually help stop bleeding. A shortage of platelets (called thrombocytopenia) can cause:

a. Bruises (or small red or purple spots) on the skin
B. Excessive bleeding
c. Frequent or severe nosebleeds for
days. Gum bleeding
e. Menorrhagia in women (menstrual bleeding) Symptoms caused by large numbers of leukemia cells

Cancer cells (called blasts) in AML are larger than normal white blood cells and have greater difficulty passing through tiny blood vessels. If the blast cell count is too high, these cells can block blood vessels and make it difficult for normal red blood cells (and oxygen) to reach the tissues. This is called leukocyte stasis. Leukocyte stasis is rare, but it is a medical emergency that must be treated immediately. Some symptoms are similar to stroke symptoms, including:

a. Headache
b. Weakness on one side of the body
c. Slurred
d. Confusion
e. Sleepiness

When the blood vessels in the lungs are affected, people may have difficulty breathing. The blood vessels in the eyes are also affected, resulting in blurred vision and even vision loss.

Bleeding and clotting problems

Patients with a certain type of AML called acute promyelocytic leukemia (APL) may have bleeding and clotting problems. They may have a constant nosebleed or the wound may not stop bleeding. They can also cause lower leg swelling

due to a blood clot called deep vein thrombosis (DVT), or chest pain and shortness of breath due to a blood clot in the lungs called pulmonary embolism or PE (Ghiaur et al., 2015).

Bone or joint pain and abdominal swelling

Some people with AML can cause bone or joint pain due to the accumulation of leukaemic cells in these areas. Leukemic cells can accumulate in the liver and spleen, making them larger. This can be noted by fullness or swelling of the abdomen. The lower ribs usually cover these organs, but when they increase, the doctor can palpate them (Hoffman, 2005).

Spread to the skin and gums

If leukaemia cells spread to the skin, they can cause bumps or spots that look like a normal rash. Tumor-like collections of AML cells under the skin or in other parts of the body are called green tumors, granulocytic sarcomas, or myeloid sarcomas. In rare cases, AML will first appear as a green tumor, with no leukaemic cells in the bone marrow. Certain types of AML can spread to the gums and cause swelling, pain, and bleeding.

Spread to other organs

Leukemia cells rarely spread to other organs. Spread to the brain and spinal cord can cause the following symptoms:

a. Headache
b. Weakness
c. The seizures lasted for
days. Vomiting
E. Balance problems
f. Facial numbness grams. Blurred vision

In rare cases, AML can spread to the eyes, testes, kidneys or other organs.
Swollen lymph nodes

In rare cases, AML can spread to the lymph nodes (bean-sized clusters of immune cells throughout the body), making them larger. The nodes affected on the neck, groin, armpits, or above the collarbone can be felt as lumps under the skin.

Although any of the above symptoms and signs can be caused by AML, they can also be caused by other diseases. Nevertheless, if you have any of these problems, especially if they do not disappear or get worse, be sure to see a doctor so that you can find the cause and treat it if necessary (Hoffman, 2005).

Types of samples used to test for AML

If your doctor thinks you may have leukemia, they will need to examine your blood and bone marrow cell samples to make sure. Other tissue and cell samples may also be collected to help guide treatment.

Blood sample

The blood test is usually the first test to detect leukemia. The blood is drawn from a vein in the arm.

Bone marrow sample

Leukaemia begins in the bone marrow, so checking the bone marrow for leukemia cells is a key part of its detection. The bone marrow sample comes from two tests that are usually performed at the same time, namely, bone marrow aspiration and bone marrow biopsy. The sample is usually taken from the back of the pelvic (hip) bone, but other bones are sometimes used. If only suctioning is done, it can be removed from the breastbone (breastbone).

For bone marrow aspiration, the patient lies on the table (on the side or on the abdomen). The doctor will clean the skin above the buttocks and then numb the area and surface of the bones by injecting a local anesthetic. This can cause a brief tingling or burning sensation. Next, insert a thin, hollow needle into the bone and use a syringe to suck up a small amount of liquid bone marrow. Even with the use of anesthetics, most patients still have some short-term pain when the bone marrow is removed.

A bone marrow biopsy is usually performed immediately after aspiration. Use a larger needle to push down into the bone and remove a small

piece of bone and marrow. This can also cause short-term pain. After the biopsy is completed, pressure will be applied to the area to help prevent bleeding. These bone marrow tests are used to help diagnose leukemia, but can also be repeated later to see if the leukemia responds to treatment (Dohner et al., 2017).

Cerebrospinal fluid (CSF) surrounds the brain and spinal cord. Sometimes AML can spread to the area around the brain and spinal cord. To check for this spread, the doctor can take a sample of cerebrospinal fluid for analysis (a procedure called a lumbar puncture or lumbar puncture). Lumbar puncture is not often used to detect AML unless a person's symptoms may be caused by leukemia cells that have spread to the brain and spinal cord.

For this test, the patient can lie on their side or sit up. The doctor first paralyzes the skin area above the spine in the lower back. Then a small, hollow needle is inserted between the bones of the spine and into the area around the spinal cord to remove some of the fluid. Lumbar puncture is sometimes used to deliver chemotherapy drugs into the cerebrospinal fluid to help prevent or treat the spread of leukemia to the spinal cord and brain (Short et al., 2018).

Laboratory

Tests used to diagnose and classify AML

One or more of the following laboratory tests may be performed on samples to diagnose AML and / or determine specific subtypes of AML.

Complete blood count and peripheral blood smear

A complete blood count (CBC) is a test that measures the number of different cells in the blood, such as red blood cells, white blood cells, and platelets. CBC is usually done with a difference (or difference), which looks at the number of different types of white blood cells. For peripheral blood smears, view the blood sample under a microscope. Changes in the number and appearance of different types of blood cells often help diagnose leukemia.

Most AML patients have too many immature white blood cells and not enough red blood cells or platelets. Many white blood cells can be myeloblasts (generally called primitive cells for short), which are very early forms of hematopoietic cells that are not normally present in the blood. These cells do not function like normal mature white blood cells. These findings may indicate leukemia, but the disease generally cannot be diagnosed without looking at samples of cells from the bone marrow (Dohner et al., 2017).

Blood Chemistry and Clotting Tests

These tests measure the level of certain chemicals in the blood and the ability of blood to clot. These tests are not used to diagnose leukemia, but they can help detect liver or kidney problems, abnormal levels of certain minerals in the blood, or clotting problems.

Routine cell examination under a microscope

A pathologist (a doctor who specializes in laboratory tests) views samples of blood, bone marrow, or cerebrospinal fluid under the microscope, which can be examined by the patient's hematologist / oncologist (one who specializes in laboratory analysis).) Doctor) check for cancer and blood diseases). The doctor will look at the size, shape and other characteristics of the white blood cells in the sample and classify them into specific types. A key factor is whether the cells look mature (like normal blood cells) or immature (they lack the characteristics of normal blood cells). The most immature cells are called myeloblasts (or primitive cells). The percentage of blast cells in the bone marrow or blood is particularly important. It usually requires at least 20% of the original cells in the bone marrow or blood to diagnose AML. (In normal bone marrow, the blast count is 5% or less, and the blood usually does not contain blast cells.) If blast cells are determined (by another test) to have chromosomal changes that only occur in a specific type of AML. AML can be diagnosed even if the percentage of outbreaks does not reach 20%. Sometimes, simply counting and observing cells

is not enough to provide a clear diagnosis. Other laboratory tests can be used to confirm the diagnosis of AML (Dohner et al., 2017).

Cytochemistry

For cytochemical testing, cells are exposed to chemical stains (dyes) that only react with certain types of leukemia cells. These spots can cause color changes visible under a microscope, which can help doctors determine which types of cells are present. For example, a stain can help distinguish AML cells from acute lymphoblastic leukemia (ALL) cells. The staining causes the particles of most AML cells to appear as black dots under the microscope, but it does not cause all cells to discolor (Arber et al., 2017).

Flow cytometry and immunohistochemistry

For flow cytometry and immunocytochemistry, cell samples are treated with antibodies, which are proteins that only adhere to certain proteins in the cell. For immunocytochemistry, cells are then looked at under a microscope to see if antibodies are attached to them (meaning they have these proteins), while for flow cytometry, special machines are used. These tests are used for immunophenotyping: classification of leukemic cells according to the substances (antigens) found on the surface of the leukemic cells. Leukemic cells can have different antigens, depending on the type of cell they started from and their maturity. This information helps classify AML (Arber et al., 2017).

Chromosome tests

These tests examine the chromosomes (long strands of DNA) in the cell. Normal human cells contain 23 pairs of chromosomes, each of which is a certain size and stained in a certain way. Sometimes the cells of acute myeloid leukemia undergo chromosomal changes, which can be seen under a microscope or detected by other tests. Recognizing these changes can help identify certain types of AML and is important for determining the patient's perspective (Arber et al., 2017).

Cytogenetics

In this test, cells are examined under a microscope to see if the chromosomes are abnormal. One disadvantage of this test is that it usually takes about 2 to 3 weeks, because the cells must grow in a laboratory dish for several weeks to see their chromosomes. Cytogenetic test results are written in abbreviations describing chromosomal changes:

A translocation means that parts of two chromosomes have exchanged positions with each other. For example, if chromosomes 8 and 21 have swapped segments, write it as t (8; 21).

An inversion, such as inv (16), means that part of chromosome 16 is now in the reverse order, but is still attached to the chromosome. deletion, for example written as del (7) or 7, means that part of chromosome 7 has been lost.

Add or duplicate, for example +8, means that all or part of chromosome 8 has lost duplicates and there are too many copies in the cell.

Not all chromosomal changes can be seen under the microscope. Other laboratory tests can usually detect these changes.

Fluorescent In Situ Hybridization (FISH)

This test uses special fluorescent dyes attached only to specific genes or specific parts of chromosomes to take a closer look at cellular DNA. FISH can detect chromosomal changes (such as translocations) that are visible under the microscope in standard cytogenetic tests, as well as some small changes that cannot be seen with conventional cytogenetic tests. FISH can be used to find changes in specific genes or parts of chromosomes. It can be used for routine blood or bone marrow samples without the need to grow it first in the laboratory. This means that the results are usually faster than conventional cytogenetic tests (Dohner et al., 2017).

Polymerase Chain Reaction (PCR)

This is a very sensitive test and may also find that some genetic and chromosomal changes are too small to be seen under a microscope. It helps find genetic changes that are only present in a few cells, helping to find a small number of leukemia cells in a sample (for example, after treatment).

At the same time, newer types of laboratory tests can be performed on samples to find specific genes or other changes in leukaemia cells (Arber et al., 2017). Imaging

AML Test Imaging

Uses x-rays, sound waves, magnetic fields, or radioactive particles to create images of the inside of the body. Leukemia does not usually form tumors, so imaging tests are often not helpful for diagnosis. When imaging patients with AML, it is more common to look for infections or other problems, not the leukemia itself. In some cases, if the disease is believed to have spread beyond the bone marrow and blood, imaging tests may be done to help determine the extent of the disease.

X-rays

Routine chest xrays may be done if a lung infection is suspected (Dohner et al., 2017).

Computed tomography (CT) scan

A CT scan uses xrays to make detailed, crosssectional images of the body. This test can help show if any lymph nodes or organs in your body are enlarged. It isn`t usually needed to diagnose AML, but it may be done if your doctor suspects the leukaemia is growing in an organ, like your spleen (NCI, 2018).

CT guided needle biopsy

In some cases, a CT can be used to guide a biopsy needle into a suspected abnormality, such as an abscess. For this procedure, you lie on the CT scanning table while the doctor moves a biopsy needle through the skin and toward the mass. CT scans are repeated until the needle is within the mass. A sample is then removed and sent to the lab to be looked at under a microscope (NCI, 2018).

PET/CT

Some machines combine the CT scan with a PET scan5 (PET/CT scan). For a PET scan, glucose (a form of sugar) containing a radioactive atom is injected into the blood. Because cancer cells in the body grow rapidly, they absorb large amounts of the radioactive sugar. A special camera can then create a picture of areas of radioactivity in the body. With a PET/CT scan, the doctor can compare areas of higher radioactivity on the PET scan with the more detailed appearance of that area on the CT.

Magnetic resonance imaging (MRI) scan

Like CT scans, MRI scans make detailed images of soft tissues in the body. But MRI scans use radio waves and strong magnets instead of xrays. MRI scans are very helpful in looking at the brain and spinal cord, but they are not usually needed in people with AML (NCI, 2018).

Ultrasound

Ultrasound uses sound waves and their echoes to make pictures of internal organs or masses. Ultrasound can be used to look at lymph nodes near the surface of the body or to look inside your abdomen for enlarged lymph nodes or organs such as the liver, spleen, and kidneys. (It can`t be used to look inside the chest because the ribs block the sound waves.) It is sometimes used to help guide a biopsy needle into an enlarged lymph node (NCI, 2018).

Treatment / Management

Individuals who achieve complete remission (CR) with a blast count of less than 5% in the bone marrow after induction therapy tend to have increased survival. Despite induction therapy, there is still minimal residual disease for which consolidation therapy is initiated to prevent any risk of relapse by eliminating the residual disease. Despite many advances, the mainstay of therapy remains a combination of cytarabine based and anthracycline based regimens. For eligible candidates, allogeneic stem cell transplantation should be considered (Andersen et al., 2015).

Induction Therapy

This is a standard of care for younger patients, elderly with low risk of treatmentrelated mortality (TRM), and ones with favorable and intermediaterisk factors. The induction therapy is highly toxic to bone marrow causing pancytopenias and bleeding complications, gastrointestinal system issues, kidney failure due to tumor lysis syndrome, and electrolyte disturbances. It may take up to 1 month for the cell counts to recover, and these patients need aggressive monitoring to manage any complications. Baseline cardiac function should be estimated before initiating the treatment, and the ejection fraction (EF) needs to be monitored carefully, as anthracyclines can cause significant cardiotoxicity.

Various acceptable induction regimens are available. The most common approach, "3 and 7," consists of 3 days of a 15 to 30minute infusion of an anthracycline (idarubicin or daunorubicin) or anthracenedione (mitoxantrone), combined with 100200 mg/m2 of cytarabine (arabinosylcytosine; araC) as a 24hour infusion daily for 7 days. Traditional dosages have been as follows:

- Idarubicin: 12 mg/m 2/d for 3 days
- Daunorubicin: 4590 mg/m 2/d for 3 days
- Mitoxantrone: 12 mg/m 2/d for 3 days

These regimens require adequate cardiac, hepatic, and renal function. On these regimens, approximately 50% of patients achieve remission with one course. Another 1015% of patients enter remission after a second course of therapy.

Improved outcomes have been reported with induction regimens using a higher dose of daunorubicin (90 mg/m2/d for 3 d compared with 45 mg/m2/d). In a study by Fernandez et al in 657 patients younger than 60 years with untreated AML, the complete remission rate with highdose daunorubicin was 70.6%, versus 57.3% with conventionaldose daunorubicin, and overall survival was a median of 23.7 versus 15.7 months, respectively (Fernandez et al., 2014).

Studies have shown greater benefit with higher doses, but toxicities may limit its use. It consists of the "7+3" regimen that includes continuous infusion of cytarabine for seven days along with anthracycline on days 1 to 3. Patients with the refractory disease have shown higher CR and similar overall survival (OS) by using higher doses of cytarabine or by using a combination of fludarabine, cytarabine, and idarubicin. Despite TRM in elderly, chemotherapy has shown to improve the survival rate among the elderly (older than 65 years). Decitabine, a methylating agent, used in the treatment of MDS, has shown improvement in OS in the elderly population. The response should be evaluated by repeating the bone marrow aspirate and biopsy after 2 weeks of initiating the induction therapy. Reinduction can be done with high dose cytarabine or by combining with etoposide if there is persistent evidence of disease. About 60% to 80$\blacksquare$ novo AML will achieve CR with induction therapy. Even before the diagnosis, if APL is suspected, then the treatment should be initiated with alltrans retinoic acid (ATRA), as early use of ATRA decreases the risk of disseminated intravascular coagulation (DIC) and mortality associated with it (Fernandez et al., 2014).

Consolidation Therapy

After achieving CR with induction therapy, consolidation therapy is initiated with high dose cytarabine, called HiDAC and hematopoietic cell transplantation (HCT). They should be monitored for signs or symptoms of acute or chronic graft-versus-host disease (GVHD) (Andersen et al., 2015).

Conclusion

Acute myeloid leukemia remains a rare but fatal malignancy. Despite many advances, the prognosis for this malignant tumor remains very poor. Although advances in supportive care and prognostic risk stratification have optimized established therapies, overall long-term survival rates remain low. Despite significant progress, much remains to be discovered about the exact contribution of these individual mutations to the development of AML.

Chemotherapy is still the mainstay of stem cell transplantation therapy and remains the best hope for cure for many patients with poor cytogenetic risk characteristics. The new targeted therapy is expected to provide effective anti-leukemia activity while reducing the toxicity caused by harmful effects. The key is to prevent further harm to the patient, so a general treatment plan must be developed and implemented.

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