What is MDS?

Myelodysplastic Syndrome (MDS) is a group of disorders in which the bone marrow does not function normally and fails to produce sufficient numbers of healthy blood cells. MDS can occur at any age, but most often develops in patients over the age of 60. MDS is sometimes also called myelodysplasia dysmyelopoiesis, oligoblastic leukemia, smoldering leukemia or preleukemia. In only a minority of cases (up to one third of cases), MDS will progress to acute myeloid leukemia.

MDS is a disease of the bone marrow and blood. In patients with MDS the bone marrow produces too few red blood cells, white blood cells and platelets. To understand MDS it is helpful to know about the normal functions of bone marrow and what healthy blood is. This section first reviews the functions of bone marrow, the composition of blood and finally how blood cells mature and reproduce. This information then provides a background for the description of MDS that follows.

Normal Bone Marrow and Blood Functions

Blood is essential for life. Blood carries oxygen, nutrients, hormones and chemicals to cells throughout the body. It plays an essential part in protecting the body from infection. Blood also helps the body to remove waste and toxins.

All types of blood cells are produced by the bone marrow. The bone marrow is the soft, spongy tissue found in the center of the large bones in the body. Many different cells make up the blood. The three main types of blood cells produced by the bone marrow are red blood cells (RBC), white blood cells (WBC) and platelets.

Red blood cells (erythrocytes, RBC) contain the iron-rich protein hemoglobin that carries oxygen to all tissues of the body. A shortage of RBC is known as anemia. When a person is anemic, they may feel dizzy, shortness of breath, and have headaches because they do not have enough oxygen circulating in their blood.

White blood cells (leukocytes, WBC) are important parts of the body's immune system. They help to prevent and fight infections. There are three main types of WBC: monocytes, granulocytes and lymphocytes, each with an important role in fighting infections.

Platelets (thrombocytes) are small disc-shaped cells that help the blood to clot or stop bleeding when there is an injury. Platelets prevent abnormal or excessive bleeding. If the body's supply of platelets is low a person may bleed or bruise easily.

Blood Cell Growth

The growth and development of normal cells are carefully controlled in the bone marrow to produce the correct numbers of each type of blood cell to keep the body healthy. Although, there are many different types of blood cells, all cells made in the bone marrow start as a single kind of cell called a stem cell. Stem cells make up only a very small proportion of the cells in the bone marrow.

The bone marrow stores stem cells until the body needs a specific type of mature blood cell. Then, by using the stem cells in reserve, the bone marrow can rapidly produce many red cells, white cells or

platelets. As stem cells mature, their features become more and more distinct until the stem cells develop into a specific type of blood cell.

Myelodysplastic Syndromes

Blood cells must be mature to carry out their specific work properly. In MDS the blood cells lose their ability to mature. Under a microscope, the red and white cells show that they have not matured normally. There may also be an increase in the number of these immature blood cells (called blasts). As the disease progresses, the blasts take over the bone marrow and prevent it from making enough normal erythrocytes, WBC and platelets.The mature blood cells that are present may not work properly.

MDS is divided into several types mainly based on the percentage of immature blood cells (blasts) found in the blood and bone marrow. There are five types of myelodysplastic syndromes.

The five types are:

- Refractory anemia (RA) (<5% blasts in bone marrow (BM))
- Refractory anemia with ringed sideroblasts (RAS) (<15% blasts in BM). Very rare in children.
- Refractory anemia with excess blasts (RAEB) (5-20% blasts in BM)
- Refractory anemia with excess blasts in transformation (RAEB-t) (21-30% blasts in BM)
- Juvenile Myelomonocytic Leukemia (JMML) (5-20% blasts and an excess in the blood of the form of WBC called monocyte)

When MDS predominantly affects the white cells, blasts appear in the bone marrow in abnormally large numbers. It is normal to have a small number of blasts (less than 5 percent) in the marrow, but this number may increase to over 5% in MDS patients. This form of MDS is called "refractory anemia with excess blasts" or RAEB. If the blasts become especially numerous this may indicate the event of transformation to acute myeloid leukemia.

Juvenile myelomonocytic leukemia (JMML) has usually been classified as a form of MDS, but is today often considered a separate disease. The hallmark of JMML is an increase in the type of white cells called monocytes. Normally, monocytes circulate throughout the body as a defense against some bacteria infections such as tuberculosis. Monocytes belong to the mature white cells produced in the bone marrow.

Causes and Risk Factors

MDS is very rare in children, less than 4 cases occur annually out of one million children. Most cases of MDS develop in previously healthy children without any known cause. A few children have received radiation therapy or chemotherapy treatments for other diseases (called secondary MDS) and some may have certain uncommon congenital bone marrow disorder. Exposures to toxic chemicals or environmental exposure is not known to cause MDS in children.

Symptoms

A diagnosis of MDS may be made during a regular checkup or routine blood tests. Many patients with MDS have a blood test done because of pallor or symptoms of anemia. Anemia means there are too few red blood cells to carry oxygen to the body, causing patients to feel tired (fatigue) and short of breath.

For many patients, there may be too few white cells to fight infections. They might get infections more easily. Patients may have infections that do not get better after taking antibiotics. A shortage of platelets is commonly found in MDS patients. These patients experience bruising or abnormal bleeding from a small injury (i.e., cut finger) or minor surgical procedure. JMML patients may have other signs of the disease. Their lymph nodes, liver or spleen may enlarge.

Diagnosis

The symptoms of MDS may mimic other common simple or serious illnesses. An accurate diagnosis can only be made by a full evaluation of the blood and bone marrow. A blood test counts each kind of cell in the blood and shows if the marrow is working properly. This test is called a complete blood count (CBC). If the blood test results are not normal, a bone marrow sample may be needed to diagnose the disorder. Bone marrow samples are usually obtained from the iliac crest (hips).

The bone marrow samples are examined under the microscope. Samples are also studied by cytogenetic testing that detects chromosome abnormalities. Information from the cytogenetic test helps to confirm the diagnosis of MDS. Results of these tests take several days to obtain. It is more difficult to diagnose MDS than to diagnose other bone marrow disorders. Therefore the diagnostic process may be delayed and repeated blood and bone marrow samples are often necessary.

Treatment

For all patients with MDS optimal supportive care is essential. This may include transfusions of red blood cells or platelets to control anemia or bleeding. Patients may be more likely to develop infections. The first sign of infection may be a fever. If body temperature exceeds 38.0 C (100.4 F), or if a feeling of chills is experienced, patients should go to their health care provider or hospital immediately, day or night. Broad-spectrum antibiotics are often prescribed for patients to treat infections.

Supportive care is intended to control the consequence of disease, not to eradicate it.

Follow-up appointments on a regular basis are very important to evaluate treatment and disease progression. Frequent physician exams and tests (including sometimes a repeated bone marrow sample) are most important for a successful management of the disease.

Chemotherapy uses cell-killing medications these drugs mostly kill rapidly growing abnormal cells in the bone marrow and blood that are potentially leukemic. Generally, chemotherapy is not useful in childhood MDS with the exception of children with Down syndrome or those with certain cytogenetic abnormalities normally only found in acute myeloid leukemia.

With a few exceptions stem cell transplantation (SCT) is the only curative treatment for children with MDS. SCT uses high doses of chemotherapy and/or radiation therapy to destroy all of the bone marrow (healthy and diseased) in the body. Healthy stem cells from the blood or marrow of another person are given to replace the marrow that was destroyed. The donor may be a relative or an unrelated individual whose tissues are the same or very similar to the stem cell recipient's.