Sistema Socio Sanitario
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MYELODYSPLASTIC SYNDROMES

Epidemiology and pathogenesis

The incidence of myelodysplastic syndromes (MDS) in Europe has been estimated at around 5 cases per 100.000 persons per year. MDS occur predominantly in older patients (usually those older than 60 years), with a median age at diagnosis of approximately 70 years. The disease is due to the acquisition of mutations, leading to the alteration of the hemopoietic stem cell, thus determining a lower production of normal cells (cytopenia), i.e. red cells, white cells and platelets.

Signs and Symptoms

The presentation of the disease is characterized by a reduction of red cells and hemoglobin (anemia) that is responsible for paleness, tiredness, and shortness of breath. Usually, anemia is macrocytic (higher erythrocyte volume). There could be also a decrease of white cells (leukopenia) with a reduction of neutrophils (neutropenia) that could place individuals at increased risk of infection. Thrombocytopenia (low platelet count) might be present and patients may experience cutaneous or mucosal bleedings (petechiae, gingival bleeding, epistaxis) and bleedings from the urinary tract (hematuria) or genital tract (menometrorrhagia) or gastrointestinal tract (melena). MDS are also characterized by an increased risk of progression to acute myeloid leukemia.

Diagnosis

The approach to the diagnosis of MDS should begin with the exclusion of nonmalignant causes of cytopenia. Diagnosis is based on morphologic studies of peripheral blood and bone marrow to evaluate abnormalities of peripheral blood cells and hematopoietic precursors. There are different types of MDS, some of them characterized by one cytopenia (anemia or thrombocytopenia or leukopenia), some with more than one cytopenia, and some with excess of blasts (leukemic cells). Bone marrow biopsy is important to assess marrow cellularity, fibrosis, and topography. Cytogenomic testing (including banding analysis and FISH) is necessary to find out chromosome aberrations. Finally, genetic molecular analysis (small fragments of DNA with specific functions) by PCR allows the identification of distinct mutations affecting epigenetic regulation and chromatin remodeling, splicing factors, transcription, and signal transduction may add prognostic value. In Varese, some patients with this disease are studied with high-throughput sequencing called Next Generation Sequencing (NGS).

Prognosis

Tests described above are necessary to define the disease and the prognosis in every individual patient. The most relevant prognostic factors include bone marrow blasts, specific cytogenetic abnormalities, number, and degree of cytopenia, and presence of specific mutations.

Treatment

Nowadays, MDS therapy is selected based on risk. The goals of therapy are different in low-risk and high-risk patients. Our treatment approach relies on national and international guidelines, i.e. ESMO guidelines i.e. (https://www.annalsofoncology.org), SIE/SIES/GITMO guidelines (https://www.siesonline.it), NCCN (https://jnccn.org/view/journals/jnccn).

In low-risk MDS, the goal is to reduce/abrogate transfusion need and to increase the quality of life. Currently, available drugs for newly diagnosed low-risk MDS include red cell growth factor (erythropoietin), lenalidomide and immunosuppressive therapy. Additionally, luspatercept will be available soon for those patients with MDS with ring sideroblasts, who are not eligible or have lost response to erythropoiesis-stimulating agents. Treatment of high-risk patients is aimed to improve survival. To date, the only currently approved treatments are hypomethylating agents and allogeneic stem cell transplantation. However, the future for MDS patients is promising. In recent years, new emerging strategies for the management of MDS are available in clinical trials such as Roxadustat and Imetelstat for lower-risk MDS and multiple new treatments combinations based on target therapy (antiNEDD-8, antiCD45, antiBcl2) in association with hypomethylating agents for higher-risk MDS. For more information about the hematologic trials available in Varese, please visit the section "Trial Unit" of the Institutional website (https://www.asst-settelaghi.it/ematologia).