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Acute Lymphocytic Leukemia New Prognosis Factors

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Short Communication

Chronic Lymphocytic Leukemia

It is the most common adult leukemia in the western world. Its complexity has increased as a result of the advent of new biological agents, the identification of molecular predictive markers and the introduction of more sensitive and sophisticated techniques evaluate minimal residual disease. The western world, CLL accounts for almost 25% of all leukemias and 1.3% of all cancers. Its incidence is substantially lower among Asian people and higher among Ashkenazi Jews. It is estimated that its incidence will continue its upward trend. It affects mainly elderly people, (more than 70% are> 65 years, the median age at diagnosis is 72 years). Men and white people are more frequently affected than women and other races.

Etiology

It is thought that there is a genetic predisposition for CLL, with a higher prevalence among relatives of patients with sporadic CLL, and there are 6 known single nucleotide polymorphisms that confer an increased risk of developing CLL. The frequency of CLL increases progressively with age, suggesting that also persistent exposure to an antigen of aging itself or not may be a predisposing factor. It is emphasized that, among patients with hepatitis C, the incidence of CLL is significantly higher than in the general population. Although people living on farms or exposed to Agent Orange are at greater risk of developing LLC and sun exposure protects their start, it has never been proven.

Clinical Presentation

Patients with CLL have varied clinical presentations. The majority are asymptomatic and the CLL is diagnosed only by an incidental finding of lymphocytosis in a hemogram, which may be accompanied, to a variable degree, with anemia and / or thrombocytopenia. In some cases, patients may also have palpable lymphadenopathy and / or hepatosplenomegaly, which in rare cases may cause symptoms secondary to local compression.

Extranodal and/or extramedullary presentations are rare, with the involvement of the skin and the central nervous system being more frequent. A minority of patients will present constitutional symptoms, such as persistent fever, night sweats, and/or involuntary weight loss, while fatigue is a common symptom. Finally, CLL can be diagnosed as a consequence of the appearance of clinical signs and symptoms secondary to its complications and not due to its direct participation, including autoimmune diseases, infections or second cancers.

Diagnosis

Bone marrow biopsy is not necessary to diagnose CLL, but it can be done when there is anemia and/or thrombocytopenia. The diagnosis of CLL requires the presence of at least 5 × 109 / B lymphocytes in the peripheral blood and of a clonal population of B cells, detected by flow cytometry, positive for the restriction of light chains (kappa or lambda), CD5 , CD23, CD79b and, the expression of immunoglobulin and, the expression of surface immunoglobulin and low levels of CD20D. Rarely, CLL cells may have a defined atypical morphology, such as more than 15% of cells with cleft nuclei and/or lymphoplasmacytoid features, and an atypical immunophenotype, with a modified Matutes score of <4 (based on the atypical expression of CD5, CD23, FMC7, surface immunoglobulin, CD22, and/or CD79b); this entity is sometimes called an atypical or variant LLC. The main entities that should be included in the differential diagnosis of CLL are mantle cell lymphoma (MCL), splenic marginal zone lymphoma, and prolymphocytic B-cell leukemia

Treatment

Not all patients with CLL require treatment at the time of diagnosis, and most can undergo active surveillance for many years before requiring treatment. The indications are based mainly on 3 elements: symptoms, complete blood count and findings of the physical examination.

Indications to start the treatment of chronic lymphatic leukemia Therapeutic indications

a) Progressive constitutional symptoms

b) Progressive failure of the bone marrow: anemia and / or thrombocytopenia

c) Progressive lymphadenopathies (at least 10 cm)

d) Progressive hepatomegaly or splenomegaly

e) Progressive lymphocytosis (doubling time <6 months)

f) Autoimmune hemolytic anemia refractory to steroids and/ or immunological thrombocytope- nia

g) The constitutional symptoms, defined as persistent and unexplained fever (temperature> 38°C) and/or weight loss (> 10% of the base weight in the course of less than 6 months) and/or severe night sweats, may represent a first indication for treatment.

Progressive lymphocytosis, hemoglobin <10 g / dl or a platelet count <100 × n 109 / l represent another indication for treatment. It is emphasized that, instead of the absolute number of lymphocytes, the guidelines recommend the duplication of lymphocytes over time (rapid dupli- cation is when it occurs in less than 6 months). On the other hand, in the presence of anemia and/ or thrombocytopenia, an autoimmune etiology should always be ruled out, and only refractory autoimmune hemolytic anemia and/ or idiopathic thrombocytopenic purpura require prompt initiation of CLL-specific therapy. Finally, treatment is recommended in the presence of progressive and / or symptomatic lymphadeno- pathy (> 10 cm) and/or hepatosplenomegaly.

It is important to emphasize that the lack of data to support early intervention derives from the chemo-immunotherapeutic era; There are several ongoing trials aimed at clarifying this dogma, particularly in relation to high-risk patients, using new less toxic agents, such as ibrutinib. The advent of new biological agents capable of achieving durable responses in high-risk patients is changing the treatment paradigm of CLL, considerably reducing the number of patients evalua- ted for stem cell transplant. However, in the absence of prolonged follow-up data, allogeneic stem cell therapy should cinue to be considered for patients with relapsed or refractory CLL, with 17p deletion / TP53 mutation, once the treatment achieved remission. In fact, with the use of reduced intensity conditioning regimens, early mortality decreased, but survival at 5 years did not exceed 60%, mostly due to mortality unrelated to the disease, due to graft disease against the disease acute or chronic host.

Complications

Autoimmune Disorders

Among the non-hematological complications are acquired angioedema, glomerulonephritis and paraneoplastic pemphigus.

Conclusion

The prognosis of patients with CLL has improved markedly in recent years, with the advent of new biological agents, such as ibrutinib, idelalisib and venetoclax. Although long-term follow-up data are still lacking, ibrutinib has slowly surpassed chemoimmunotherapy as a standard first-line treatment for patients with unfavorable prognosis and for frail patients. Venetoclax and the combination of idelalisib and rituximab are currently among the most popular optimal treatment options for patients with relapse after treatment with ibrutinib. Among the new challenges are the management of agent-specific toxicity (eg, atrial fibrillation, colitis, tumor lysis) and the emergence of resistance. Finally, despite the advent of immunotherapy, the treatment of patients with Richter