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Perspective

Prognosis Therapeutic Relapse Transplantation in patients with Plasma Cell Leukemia

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DESCRIPTION

Plasma Cell Leukemia (PCL) is a rare and aggressive subtype of Multiple Myeloma (MM), a malignant disorder of plasma cells in the bone marrow. In PCL, the malignant plasma cells proliferate rapidly and infiltrate the peripheral blood, leading to high levels of monoclonal plasma cells in circulation. PCL accounts for less than 5% of all cases of MM and is associated with a poor prognosis, with a median survival of only a few months. PCL can be classified into two subtypes based on the morphology of the malignant plasma cells: primary PCL (pPCL) and secondary PCL (sPCL). pPCL is a de novo form of leukemia and is diagnosed when the percentage of plasma cells in peripheral blood exceeds 20% or when the absolute number of circulating plasma cells is higher than 2 × 109/L. sPCL is a secondary form of leukemia that arises from pre-existing MM and is characterized by the transformation of a plasma cell clone to a leukemic phase.

The clinical features of PCL are similar to those of MM, including bone pain, anemia, hypercalcemia, renal impairment, and recurrent infections. However, PCL is more aggressive than MM and often presents with more severe symptoms, such as leukocytosis, splenomegaly, hepatomegaly, and lymphadenopathy. The diagnosis of PCL requires a thorough evaluation of the clinical and laboratory findings, including the detection of monoclonal plasma cells in peripheral blood and bone marrow aspirates, the presence of monoclonal protein in serum and urine, and the demonstration of end-organ damage. The treatment of PCL is challenging due to its aggressive nature and poor prognosis. Current treatment options for PCL are based on the same principles as those for MM, including induction therapy, high-dose chemotherapy; stem cell transplantation, and maintenance therapy. However, the optimal treatment strategy for PCL is still unclear due to the lack of randomized clinical trials specifically targeting this disease. In general, the treatment of PCL should be individualized based on the patient's age, comorbidities, performance status, and disease-related factors, such as cytogenetic abnormalities and response to therapy.

Induction therapy for PCL typically consists of a combination of chemotherapy agents, such as bortezomib, dexamethasone, and cyclophosphamide, with or without autologous stem cell transplantation (ASCT). ASCT is an effective treatment option for younger patients with PCL who have no significant comorbidities and achieve a good response to induction therapy. In contrast, older patients with PCL or those with significant comorbidities may not be eligible for ASCT and may benefit from less aggressive treatment regimens, such as lenalidomide-based therapy or palliative care. High-dose chemotherapy followed by ASCT is a standard treatment option for MM but has limited efficacy in PCL. The high tumor burden and rapid proliferation of malignant plasma cells in PCL may lead to a higher risk of treatment-related mortality and relapse after ASCT. Therefore, ASCT should be reserved for carefully selected patients with PCL who achieve a good response to induction therapy and have no significant comorbidities.

Maintenance therapy with immunomodulatory agents, such as thalidomide or lenalidomide, has been shown to prolong progression-free survival in MM but has not been extensively studied in PCL. The use of maintenance therapy in PCL should be based on the patient's response to induction therapy and the presence of residual disease. Patients with Relapsed/Refractory Multiple Myeloma (RRMM) can benefit from successful salvage therapy with Chimeric Antigen Receptor (CAR)-T cells. End-stage RRMM with PCL transformation is extremely aggressive and refractory to standard treatment. New treatments are desperately needed, and CAR-T therapy could be one of them. We describe a successful instance of PCL secondary to RRMM treated with CAR-T cell therapy that specifically targets B-Cell Maturation Antigen (BCMA). Four years after receiving her MM diagnosis, a woman underwent secondary PCL (sPCL) after completing five different therapy modalities, including proteasome inhibitors, immunomodulatory agents, cytotoxic drugs, and an anti-CD38 monoclonal antibody. She experienced a strict complete response following BCMA CAR-T therapy, which continued for 9 months.

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