Primary Plasma Cell Leukemia

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Primary plasma cell leukemia (pPCL) is defined as the presence of 5% or more circulating plasma cells on manual white blood cell differential count in newly diagnosed patients who meet the diagnostic criteria of multiple myeloma (MM) as defined by the consensus of the International Myeloma Working Group (IMWG).1,2 It is important to note that the new cutoff point (>=5% circulating plasma cells) was based on a recent change of the previous definition which was based on a higher cutoff (>=20% circulating plasma cells).1 Plasma cell leukemia is considered under the category of high-risk MM and more appropriately, under the category of ultra-high-risk MM.3 Secondary plasma cell leukemia can be diagnosed using the same cut-off, but in patients with previous diagnosis of MM at time of relapse or refractory disease. Reviewing peripheral blood smear in all patients with newly diagnosed MM is important to diagnose pPCL or consider obtaining peripheral blood flow cytometry to better quantify the percentage of circulating plasma cells. Plasma cells can be identified by their eccentric nucleus, perinuclear halo, and basophilic cytoplasm. (Figure.1) Malignant plasma cells are clonal which means that their cytoplasm contains either kappa or lambda light chains, but not both.

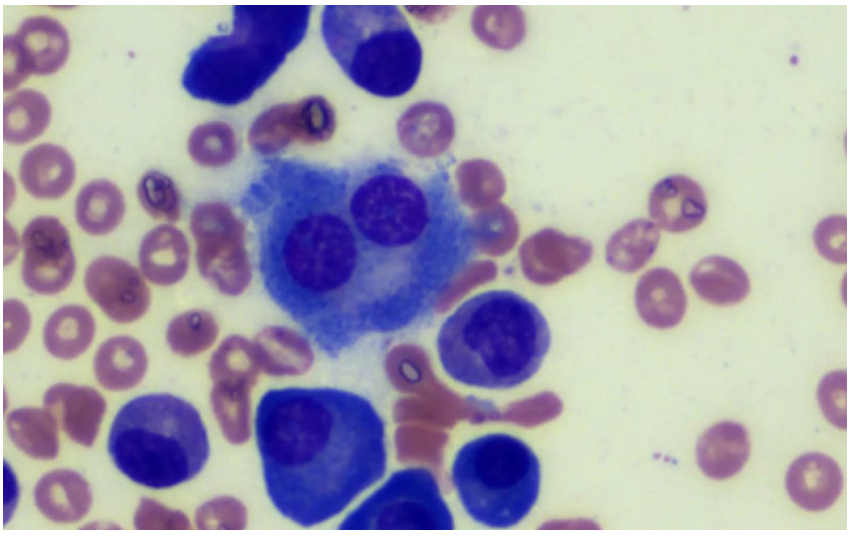

Figure.1. Plasma cells with one bi-nucleated plasma cell.

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The prognosis of primary PCL is poor, with modest improvement in more recent years. Median survival is usually less than one year.4 The poor prognosis is likely related to the high burden of proliferative disease, higher association with high-risk cytogenetics such as del17p and the presence of extramedullary disease.5 When identified, prompt initiation of treatment is needed.

Treatment of primary PCL is largely based on retrospective data and limited prospective data given that most clinical trials of MM excluded patients with PCL. It is important to consider the risk of tumor lysis syndrome and initiate prophylaxis with close monitoring of serum creatinine, uric acid calcium, and phosphorus levels.

In our experience at the University of Arkansas for Medical Sciences, we prefer the initiation of multi-agent chemotherapy with Daratumumab, Kyprolis (Carfilzomib), Thalidomide, Dexamethasone, Platinum (Cisplatin), Adriamycin (Doxorubicin), Cyclophosphamide, and Etoposide (DARA-KTD-PACE) in patients who are deemed appropriate for autologous stem cell transplantation (ASCT). The efficacy of this regimen is based on Total Therapy 7 (NCT03004287) phase II clinical trials which exclusively enrolled high-risk MM patients including patients with pPCL.6 We intend to treat patients with tandem ASCT after induction chemotherapy with subsequent extended treatment with triplet or quadruplet-based regimens. In patients with poor functional status who are deemed inappropriate for intensive chemotherapy, we prefer quadruplet-based regimens with Daratumumab, Kyprolis (Carfilzomib), Revlimid (Lenalidomide), Dexamethasone (DARA-KRD) or Daratumumab, Velcade (Bortezomib), Revlimid (Lenalidomide), and Dexamethasone (DARA-VRD). Personalization of treatments according to the patient's age, functional status, comorbidities, and availability of MM treatments are vital. In many cases, ineligibility for intensive chemotherapy may change since pPCL is associated with a high tumor burden and after initial treatment, improvement in patients' performance status may happen. After induction therapy and ASCT, extended therapy with a triplet regimen that includes a proteasome inhibitor is preferred.

In patients with t(11;14), the use of Venetoclax can be considered given its activity in this subgroup of patients.7 It is important to initiate and enroll patients in clinical trials focused on high-risk MM, especially the ultra-high risk MM including pPCL. The use of chimeric antigen receptor-T cells and bispecific antibodies is promising though there is lack of enrollment of patients with pPCL in most clinical trials results reported to date. Future efforts should focus to include various immune based therapies in the treatment of pPCL in an effort to improve the clinical outcomes.

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