22 - Plasma cell leukaemia

Summary:

- Plasma cell leukaemia is a rare leukaemic variant of multiple myeloma with a more aggressive clinical course.
- sFLC analysis and serum protein electrophoresis is an effective screen for plasma cell leukaemia.
- International Myeloma Working Group guidelines recommend the use of general multiple myeloma response criteria for monitoring plasma cell leukaemia, which includes sFLC analysis.

22.1. Introduction

Plasma cell leukaemia (PCL) is a rare and aggressive variant of multiple myeloma (MM), accounting for 2 - 4% of cases. It is defined by the presence of >20% plasma cells in the peripheral blood and/or an absolute plasma cell count >2 x 10^9/L. It can occur without evidence of MM (primary PCL; 60 - 70%), or may develop from leukaemic transformation of a pre-existing myeloma clone (secondary PCL; 30 - 40%) in 1 - 2% of advanced and refractory patients.

Both primary and secondary PCL have distinct clinical and biological features. The median age of primary PCL patients is approximately 10 years younger than both the general myeloma and secondary PCL populations. Primary PCL also has a more aggressive clinical presentation, with a higher tumour burden and an increased incidence of extramedullary and light-chain only disease (26 - 44%). Both forms of PCL have very poor outcomes, with the worst prognosis associated with secondary PCL. Overall survival for primary PCL patients is still inferior to that of patients with MM, but has significantly improved in recent years.

22.2. Diagnosis and monitoring of plasma cell leukaemia using sFLCs

Monoclonal proteins are present in the majority of PCL patients. In some cases, a monoclonal protein may be undetectable by serum protein electrophoresis, but clearly indicated by sFLC analysis. A combination of serum protein electrophoresis and sFLC analysis has been shown to be an effective screen for MM, including plasma cell leukaemia and sFLC analysis should form part of the initial diagnostic work-up of these patients (Chapter 23).

As there are no specific response criteria for assessing response to treatment in PCL, the International Myeloma Working Group recommend the application of the MM response criteria. These criteria incorporate sFLC analysis in the definitions of stringent complete response for all patients, and very good partial response and partial response for patients whose monoclonal protein is not measurable by serum or urine electrophoresis (Chapter 25.3.5).

A number of case reports highlight the utility of sFLC analysis for the diagnosis and monitoring of PCL. Successful treatment of primary plasma cell leukaemia expressing monoclonal light chains.

Clinical case history

Successful treatment of primary plasma cell leukaemia expressing monoclonal light chains.
A 40-year-old female presented with conjunctival haemorrhage. She also reported giddiness, fatigue, and weight loss. On examination she was afebrile, and had no organomegaly. Peripheral blood counts revealed she was anaemic (haemoglobin 10.6 g/dL) with a markedly raised total leukocyte count (39.6 x 10^9/L) and severe thrombocytopaenia (platelet count 1.0 x 10^9/L). A peripheral blood smear showed a prominence of plasma cells with occasional binucleate cells.

A bone marrow aspirate and biopsy revealed an almost complete replacement of normal marrow elements by sheets of plasma cells. By flow cytometry, these cells were CD38+, CD138+, CD117+ and expressed cytoplasmic λ light chain.

Serum total protein was low (46.0 g/L) and albumin, calcium and creatinine concentrations were normal. Serum β₂-microglobulin was elevated (12.95 mg/L). No monoclonal protein was detectable by serum protein electrophoresis and total immunoglobulins were all low (IgG 3.3 g/L; IgA 0.09 g/L and IgM 0.08 g/L). sFLC analysis showed markedly elevated λ sFLCs (3527 mg/L) with suppressed κ sFLCs (1.15 mg/L), resulting in a highly abnormal κ/λ sFLC ratio (0.00033).

Interphase fluorescence in situ hybridization analysis revealed IgH gene translocations and 13q deletions. Radiographs of the skull, dorsal spine, lumbar spine and femora did not reveal any lytic lesions.

After a diagnosis of primary PCL was made, treatment with RVd (lenalidomide, bortezomib and dexamethasone) was commenced. Following four cycles of therapy, the patient achieved a complete response with normalisation of κ sFLCs (8.1 mg/L), λ sFLCs (5.5 mg/L) and the κ/λ sFLC ratio (1.47).

She subsequently underwent high-dose chemotherapy with melphalan and autologous stem cell transplantation, and was reported to be in complete remission 9 months after her initial diagnosis.
These cells have abundant basophilic cytoplasm and an eccentrically placed nucleus with clumped chromatin (Leishman stain, x1000 magnification). (Reproduced with permission from Indian J Med Paediatr Oncol[5]).

References