Indian J Hematol Blood Transfus (July-Sept 2019) 35(3):567–569
https://doi.org/10.1007/s12288-019-01116-7

CORRESPONDENCE

Plasmablastic Lymphoma Versus EBV-Positive Myeloma

Divya Bansal[1] · Neha Singh[1] · Narendra Agrawal[2] · Anurag Mehta[1]

Received: 12 October 2018 / Accepted: 12 March 2019 / Published online: 15 March 2019

EBV-Positive Myeloma Versus Plasmablastic Lymphoma

Hematolymphoid neoplasms with plasmablastic lymphoma (PBL) and plamablastic/anaplastic myeloma (PBM) show significant morphological and/or immunophenotypic overlap which may make it very difficult for pathologists to make a definite and specific histopathological diagnosis [1]. Features such as renal dysfunction, significant paraprotein, osteolytic bony lesions, hypercalcemia and diffuse bone marrow involvement favor a diagnosis of PBM. In contrast, EBER expression in neoplastic cells, HIV coinfection and high proliferative index support a diagnosis of PBL. When myeloma-defining signs are incomplete or absent, the presence of oropharyngeal soft tissue lesion or lymphadenopathy favor a diagnosis of PBL, regardless of bone marrow disease. The distinction is very important as the treatment of these entities differ remarkably. PBL is an aggressive disease with relapsing clinical course and has higher rates of disease progression and fatality despite use of state of the art treatment modalities. Current guidelines recommend intensive regimens such as EPOCH (infusional etoposide, vincristine, doxorubicin with bolus cyclophosphamide and prednisolone) and Hyper-CVAD (hyperfractionated cyclophosphamide, vincristine, doxorubicin and dexamethasone alternating with methotrexate and cytarabine). On the other hand, myeloma is managed with Bortezomib-based regimens followed by autologous stem cell transplantation (ASCT). Despite extensive work-up, few cases remain to be classified into any of the two categories and thus are labelled as Indeterminate [2, 3]. We present one such case with overlapping features thereby making the diagnosis very intriguing.

A 62 year old male presented with sudden onset breathlessness for 15 days. On examination, he had pallor and splenomegaly. Hemogram showed Hb: 8 g/dl, TLC: 8100/cumm and Platelet count: 154,000/cumm. PS showed rouleaux formation with presence of 9% plasmacytoid cells. Viral markers for HIV, HCV, HBV were negative; serum calcium was within normal limits. Serum creatinine was raised (4.3 mg/dl). PET-Scan showed bone marrow infiltrative disease along with mild splenomegaly in the absence of any lymphadenopathy or soft tissue masses. Skeletal survey was unremarkable. Serum β2-microglobulin was raised (27.8 mg/L) and serum albumin was 3.6 g/dl. Serum electrophoresis revealed M band of 3.5 g/L in gamma region. Serum immunofixation showed a strong band in IgG/Kappa region. Bone marrow examination revealed near-total replacement of normal hematopoietic components by plasmablasts and large bizarre cells with anaplastic features admixed with scattered bi/multinucleated forms. Immunohistochemistry revealed diffuse and strong positivity for CD138 and CD38 with clonal restriction for Kappa light chain and negative expression of PAX-5, CD20, CD3, CD56, ALK-1 and lambda light chain with Ki-67 index of 5–10%. Cytogenetics revealed normal karyotype. Expression of EBER by in situ hybridization technique was strongly positive (Fig. 1). Diagnosis of PBM was favored over PBL on the basis of following features: (a) very low proliferative index (PBL have higher values in the range of 80–100%). (b) presence of two CRAB features i.e. anemia and renal failure (c) diffuse bone marrow

✉ Neha Singh
drnehasingh123@gmail.com

[1] Department of Pathology and Lab Services, Rajiv Gandhi Cancer Institute and Research Center, Rohini, Delhi, India

[2] Department of Hemato-Oncology, Rajiv Gandhi Cancer Institute and Research Center, Rohini, Delhi, India

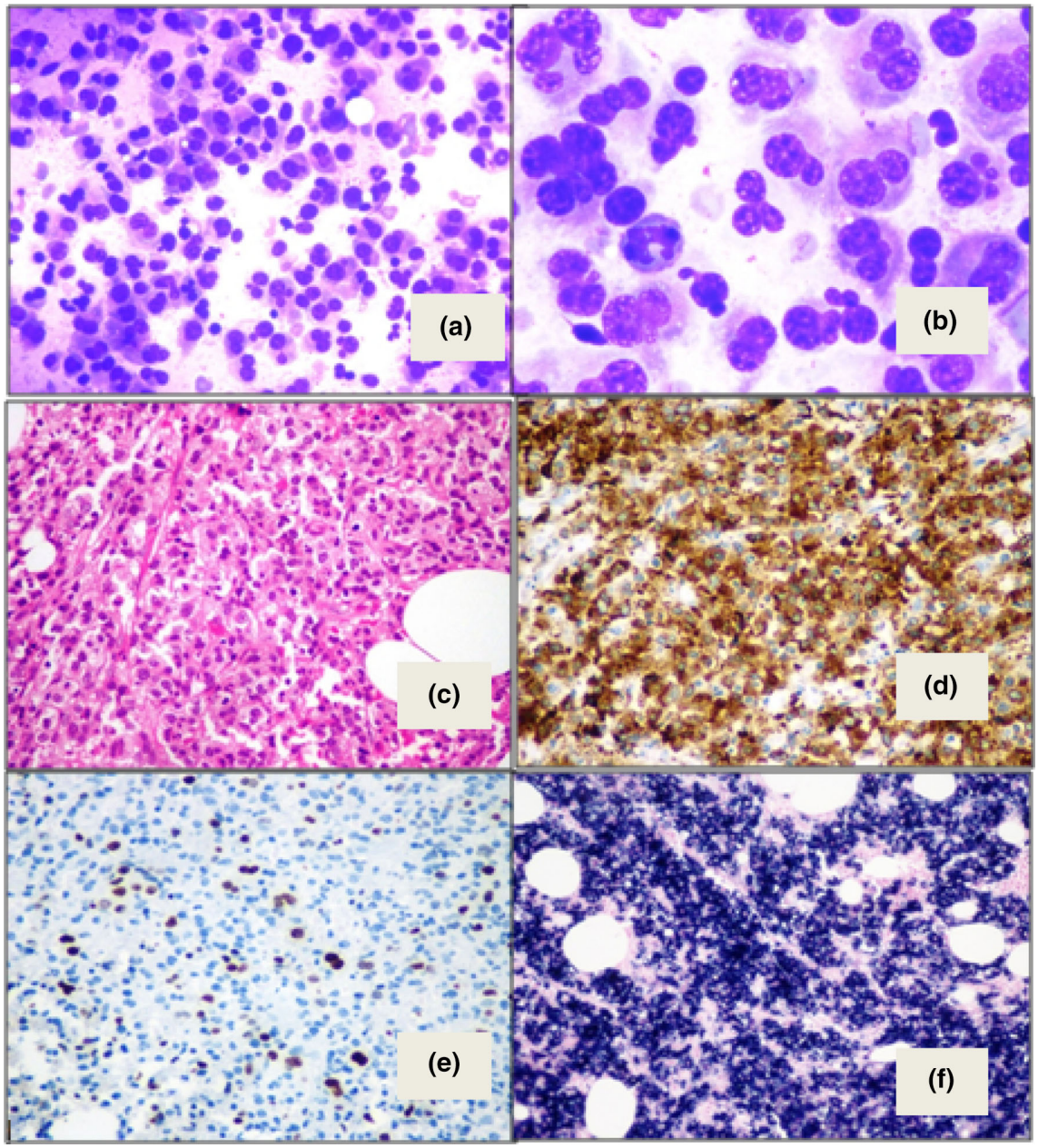

Fig. 1 **a**, **b** Bone marrow aspirate shows large bizarre cells with anaplastic/plasmablastic morphology (70%). **c** Bone marrow biopsy shows cells with similar morphology without any significant mitosis. **d** Clonal Kappa restriction by IHC. **e** Low Ki-67 index. **f** EBER-ISH positive. **a** Low power view of bone marrow aspirate smears showing large bizarre cells with plasmablastic/anaplastic morphology. **b** 100X view of bone marrow aspirate smears showing large bizarre cells with plasmablastic/anaplastic morphology. **c** Bone marrow biopsy shows cells with similar morphology without any significant mitosis. **d** Clonal Kappa restriction by IHC. **e** Low Ki-67 index. **f** EBER-ISH positive

involvement is consistent with myeloma (bone marrow is involved in only up to 25% of immunocompetent patients in PBL (d) absence of any oral cavity or gastrointestinal or soft tissue lesions. The patient was started on bortezomib(2 mg/m^2 on days 1,4, 8, 11 of every cycle), pomalidomide (4 mg OD for 14/21 days every cycle) and dexamethasone 20 mg weekly.

EBV—encoded RNA in situ hybridization study (EBER)-positivity was the most important feature in favor of PBL in this patient. However, it is absent in up to 40% of PBL cases. Moreover, myeloma may also be rarely associated with EBV infection. Few case reports have shown that EBER-positive myeloma in immunocompetent patients may be associated with significant plasmablastic cytomorphologic features, suggesting that tumors may

have been driven by EBV to gain proliferative advantage [4]. Apart from this, MYC alterations are found in approximately 50% of PBL cases and 15% of myeloma cases with as much as 50% frequency in its plasmablastic variant, thereby limiting its value in distinguishing PBL from PBM [2]. There is a need for identifying distinctive immunophenotypic or genetic signatures to improve differentiation of plasmablastic neoplasms in overlapping cases.

Compliance with Ethical Standards

Conflict of interest The authors state that there is no conflict of interest present.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

References

1. Harmon CM, Smith LB (2016) Plasmablastic lymphoma a review of clinicopathologic features and differential diagnosis. Arch Pathol Lab Med 140:1074–1078
2. Ahn JS, Okal R, Vos JA et al (2017) Plasmablastic lymphoma versus plasmablastic myeloma: an ongoing diagnostic dilemma. J Clin Pathol 70(9):775–780
3. Castillo JJ, Bibas M, Miranda RN (2015) The biology and treatment of plasmablastic lymphoma. Blood 125:2323–2330
4. Chang ST, Liao YL, Lu CL et al (2007) Plasmablastic cytomorphologic features in plasma cell neoplasms in immunocompetent patients are significantly associated with EBV. Am J Clin Pathol 128:339–344