Indian J Hematol Blood Transfus (Oct-Dec 2017) 33(4):630–632
DOI 10.1007/s12288-017-0780-5

CORRESPONDENCE

# CD138 Negative Plasma Cells in Relapsed CNS Multiple Myeloma

**Neha Singh[1] · Jatin S. Gandhi[1] · Narendra Agrawal[2] · Ajit Panaych[1] · Narender Tejwani[1] · Anurag Mehta[1]**

Received: 23 November 2016 / Accepted: 17 January 2017 / Published online: 7 February 2017


Dear Editor

CD138 (Syndecan-1) is a heparin sulphate proteoglycan responsible for growth factor binding, cell adhesion, apoptosis and control of myeloma growth [1]. CD138 negative plasma cells are a sub-population of malignant plasma cells (PCs) which may be more primitive and have a higher proliferative potential than CD138 positive plasma cells [1]. Certain studies have also suggested that CD138 negative cells play a key role in myeloma cells-mediated biomechanical changes of bone marrow stem cells in multiple myeloma (MM) patients [2]. We present a case of relapsed myeloma with CD138 negative plasma cells and CNS dissemination.

A 46 year old male presented with a swelling in the skull since three months without any constitutional symptoms. Physical examination was unremarkable except for a mass in the skull in the right parietal region. Complete hemogram showed Hb = 11.6 g/dl, TLC = 10,300/cmm, Plt = 306,000/cmm and a DLC of N62/L28/M6/E4. LFT and RFT were within normal limits. Viral serology was negative. Skeletal survey revealed lytic lesions in right parietal bone. Serum protein electrophoresis showed "M" spike of 3.33 g/dl in the gamma region. β2-microglobulin was markedly raised (2500 ng/ml). Patient underwent craniotomy, following which the biopsy of the extradural tumor mass showed features suggestive of plasmacytoma. Bone marrow evaluation revealed infiltration with 50% plasma cells including a few atypical forms. A final diagnosis of multiple myeloma was made on the basis of clinico-radiological, biochemical, tissue biopsy and bone marrow aspirate findings. Patient was started on Lenalidomide/Dexamethasone based regimen for 3 cycles followed by 2 cycles of VTD- based regimen Vincristine/Thalidomide/Dexamethasone) and underwent autologous stem cell transplantation (ASCT) with Melphalan conditioning in first complete remission (CR). He was thereafter kept on close follow-up on Thalidomide maintenance. However, his M band continued to rise while on therapy and he had to be shifted to CTD regimen followed by DT-PACE regimen but still showed poor response. 3 years post-ASCT, he was admitted with altered sensorium, visual hallucinations and right-sided hemiplegia. Positron Emission Tomography (PET-CT) showed metabolically active bony, hepatic, stomach, kidney and adrenal lesions with bilateral lung nodules, soft tissue, mesenteric and muscle deposits. However, no mass lesions were noted in the brain parenchyma (confirmed by MRI). Bone marrow was uninvolved at relapse. Serum Protein Electrophoresis showed a small monoclonal spike in gamma globulin region (0.42 g/dl). SFLC (kappa/lambda) ratio was 0.03. CSF cytology, with cell count of 10 WBCs/cumm showed numerous cells with plasmablastic morphology having moderate N/C ratio, round nucleus, prominent nucleoli and moderate amount of cytoplasm (Fig. 1a). Flowcytometry of CSF fluid was done which showed CD45+(dim)/CD38+(bright)/CD56+/CD138−/CD19−/CD20−/CD3− immunophenotype, with no clonal restriction for kappa or lambda light chains (Fig. 1b–i). Patient was started on Bortezomib based regimen, with Wide-Base Radiotherapy. However, his condition failed to improve and he left against medical advice.

*Disclaimers*: The identity of the patient is not disclosed here in this case. The authors state that there is no conflict of interest present.

✉ Neha Singh
drnehasingh123@gmail.com

[1] Department of Laboratory Medicine, 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

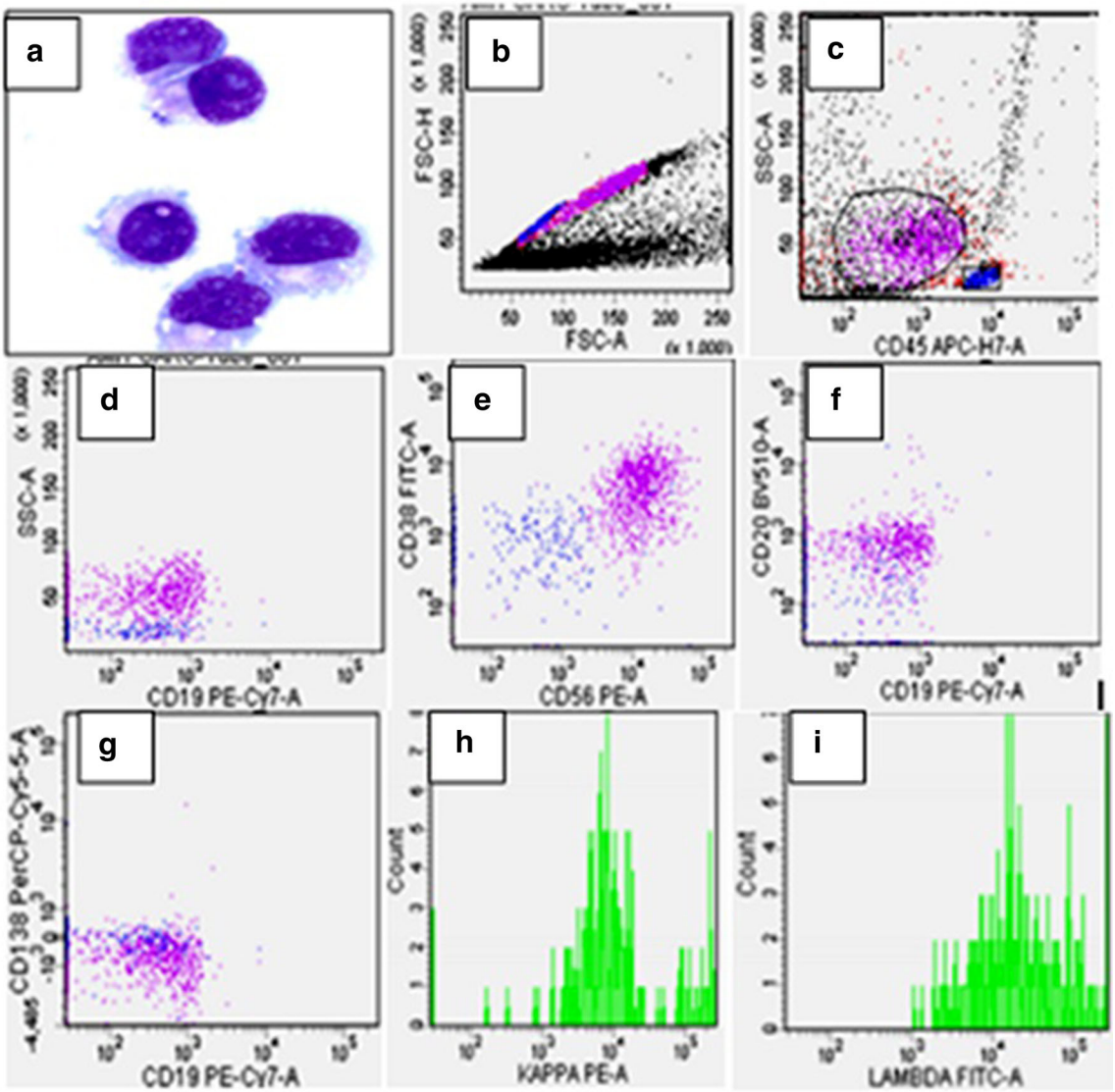


**Fig. 1** **a** Plasmablastic morphology in CSF. **b–i** Flowcytometry of CSF fluid using a panel of markers CD38, CD138, CD19, CD20, CD3, CD56, kappa and lambda light chains

Extension of multiple myeloma into the CNS is uncommon, estimated at 01% of patients associated with advanced disease and elevated β2-microglobulin levels [3]. CNS myeloma may present with solitary or multiple intra-parenchymal lesions and/or leptomeningeal disease with the presence of monoclonal plasma cells in the CSF and have an overall dismal survival (1–6 months). However, some studies have also documented CNS involvement in as many as 24% of cases at diagnosis and 76% in relapsed or refractory disease [3]. Presence of CD138 negative plasma cell clone in myeloma with CNS relapse is a rare event that impacts prognosis and overall survival of the patient. Patients with low levels of CD138 have a worse overall survival compared with high levels of CD138 in newly diagnosed as well as patients receiving high-dose chemotherapy followed by autologous SCT and respond poorly to lenalidomide [4].

Many studies have reported the existence of highly clonogenic MM cells lacking CD138 expression, and suggested that these cells may represent MM 'stem cells' [4]. Differential phenotypic expression of PCs include plasmablast (the most immature of all, characterized as CD138-/CD45++), early plasma cells (characterized as CD138+/CD45+) and mature PCs (CD138++/CD45-ve or weak). CD38++ and clonal Ig light chain expression is present at all stages [1]. In some settings such as in this case, proof of light chain restriction can be difficult; for instance, when very few abnormal plasma cells are present, when the abnormal plasma cells contain very low levels of cytoplasmic light chains, or when the disorder is bi-clonal

expressing both kappa and lambda light chains [5]. Expression of CD138 on myeloma cells has varied from 2 to 5% of CD138 negative plasma cells (Matsui et al.) to 75% (Witzig et al.) [1]. Reid et al. also found a statistically significant positive correlation between CD138 negative and CD45 expression on CD38+cells. Moreover, CD138-ve clonogenic cells are plasma cells rather than B cells and both CD138+/CD138- plasma cells have the potential to propagate myeloma clones in vivo even in the absence of CD19+B cells [6]. In the present case, flowcytometry done on the plasmablastic cells in the CSF fluid showed dim CD45+/CD38+(bright)/CD138-/CD19-/CD20-/CD56 +/ CD3- immunophenotype. The patient was then started on Bortezomib based regimen but his condition failed to improve, highlighting the poor prognosis associated with presence of CD138 negative plasma cells.

**Compliance with Ethical Standards**

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

**Ethical Approval** This case report does not contain any studies with human participants or animals performed by any of the authors.

## References

1. Reid S, Yang S, Brown R et al (2010) Characterization and relevance of CD138 negative plasma cells in plasma cell myeloma. Int J Lab Hematol 32:190–196
2. Wu D, Guo X, Su J et al. (2015) CD138-negative myeloma cells regulate mechanical properties of bone marrow stromal cells through SDF-1/CXCR4/AKT signaling pathway. Biochimica et Biophysica Acta 1853(2):338–347
3. Chen C, Masih-Khan E, Jiang H et al (2013) Central nervous system involvement with multiple myeloma: long term survival can be achieved with radiation, intrathecal chemotherapy, and immunomodulatory agents. Br J Haematol 162(4):483–488
4. Kawano Y, Fujiwara S, Wada N et al (2012) Multiple myeloma cells expressing low levels of CD138 have an immature phenotype and reduced sensitivity to lenalidomide. Int J Oncol 41:876–884
5. Kumar S, Kimlinger T, Morice W (2010) Immunophenotyping in multiple myeloma and related plasma cell disorders. Best Pract Res Clin Haematol 23(3):433–451
6. Hosen N, Matsuoka Y, Kishida S et al (2012) CD138-negative clonogenic cells are plasma cells but not B cells in some multiple myeloma patients. Leukemia 26(9):2135–2141