Multiples aberrant phenotypes in multiple myeloma patient expressing $CD56^-$, $CD28^+$,$CD19^+$

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Recent immunophenotypic studies demonstrated that the expression of aberrant antigens in myeloma plasma cells (MPCs) is a common feature. The most frequent aberrant antigens in MPCs are: CD56 (75%) and CD117 (63%). Several reports suggest that multiple myeloma (MM) patients with CD56 negative MPCs present with aggressive disease and have a worse outcome.[1-3] Van Camp et al. were the first to demonstrate that in the context of high-dose chemotherapy and autologous stem cell transplantation, CD56 negative cases behaved similarly to CD56 positive cases.[4] These results are encouraging, but we would like to mention that other immunophenotypic and genetic characteristics have also demonstrated clinical impact. In particular, the rare phenotype, $CD19^+CD56^-$, which is generally found in normal plasma cells,[3] responds poorly to combination chemotherapy. Here, we describe a case in which plasma cells expressed the $CD19^+CD56^-$ phenotype as well as several other aberrant antigens ($CD20^+$, $CD22^+$, $CD28^+$, $CD33^+$, $CD117^+$, $HLA\text{-}DR^+$).

A 60-year-old man was admitted with back pain and weight loss over a 4-month period. Laboratory tests showed: red blood cell count: 2.8×10^{12}/L; hemoglobin: 7.5 g/dL; platelet count: 161×10^9/L; and leukocyte count 3.5×10^9/L. The creatinine level was normal, but serum ionic calcium was 1.30 mg/dL. The serum total protein concentration was 15.8g/dL and albumin 2.06 g/dL. Serum ß2-microglobulin was 7.2 mg/L, and monoclonal component was 7.69 in gamma globulin. IgG was 9160 mg/dL, IgA was 12 mg/dL and IgM < 4 mg/dL. Bence Jones kappa protein was

found in urine. A bone marrow (BM) biopsy revealed a hypercellular marrow with 95% of dysplastic plasma cells. There were extensive osteolytic bone lesions in the thoracic spine and bone fractures in L5. A diagnosis of multiple myeloma (IgG kappa, stage IIIA) was made.

Four-color flow cytometry of fresh BM cells revealed that the myeloma cells expressed CD38, CD138, CD19, CD20, CD22, CD33, CD28, CD117, HLA-DR but no CD56 or CD45 (Figure 1). The cells were positive for cytoplasmic immunoglobulin kappa light chain. Cytogenetic studies revealed a hyperdiploid karyotype and no rearrangement of the IgH gene or deletion of 13q14. The patient was treated with one cycle of the VAD (vincristine 0.4 mg/day, doxorrubicine 9 mg/day and dexamethasone 40 mg days 1-4, 9-12, and 17-21) regimen, and two cycles of the VMMD (vincristine 1.5 mg/day i.v, day 1; ranimustine 50 mg/day, day 1; dexamethasone 40 mg days 1-4, 9-12, and 17-21 and melphalan 8 mg p.o, days 1-6) and MP (melphalan 10 mg and prednisolone 50 mg p.o days 1-4) regimes, without any significant improvement. The patient died due to systemic infection.

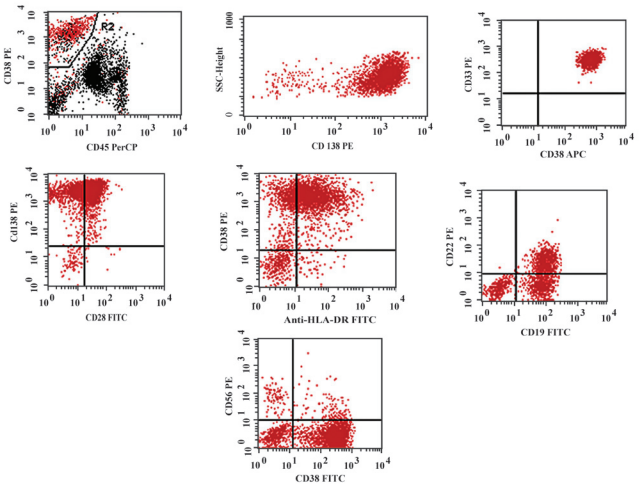

Figure 1– Four-color flow cytometry of fresh bone marrow cells showing myeloma cells expressing CD38, CD138, CD19, CD20, CD22, CD33, CD28, CD117, HLA-DR but no CD56 or CD45

Sahara et al. were the first to describe a MM case with the $CD19^{+}CD56^{-}$ phenotype that was refractory to combination chemotherapy. They also reported that the lack of CD56 was related to aggressive disease and significantly shorter survival than $CD56^{+}$ cases[5]. According to Lin et al., these CD56 negative cases should receive intensive treatment that can overcome the poor response[3]. However, it would be interesting to evaluate the cases reported by them in the context of other prognostic features: according to other aberrant antigens, such as $CD28^{+}$, and myeloid associated antigens. Interestingly, they did not find any association of CD56 negative cases with genetic risk groups, including deletion 13q, p53 gene mutation and IgH translocations.

Our case presents the rare $CD19^{+}CD56^{-}$ phenotype with several other aberrant antigens ($CD20^{+}$, $CD22^{+}$, $CD28^{+}$, $CD33^{+}$, $CD117^{+}$, $HLA\text{-}DR^{+}$). The CD28 antigen is not expressed on normal B cells or plasma cells and according to Shapiro et al., its presence is related to advanced disease. Conversely, this patient presented a hyperdiploid karyotype but no other genetic alteration with a defined prognosis group as reported by Kyle and would therefore be classified in a good prognosis group.[2,6] Mateo et al. reported that non-hyperdiploid MM cases are associated with positivity for CD28 and CD20 and negative for CD117, in contrast to the case presented here. These findings highlight the need of a more comprehensive evaluation that should include DNA ploidy status, IgH gene rearrangements, del 13q and del 17p.[7] However, the CD56 expression pattern could be used as a rapid prognostic risk factor to direct treatment and predict disease outcome.

References

1. Guikema JE, Hovenga S, Vellenga E, Bos NA. Heterogeneity in the multiple myeloma tumor clone. Leuk Lymphoma. 2004;45(5): 857-71.
2. Kyle RA, Rajkumar SV. Criteria for diagnosis, staging, risk stratification and response assessment of multiple myeloma. Leukemia. 2009;23(1):3-9.
3. Lin P, Owens R, Tricot G, Wilson CS. Flow cytometric immunophenotypic analysis of 306 cases of multiple myeloma. Am J Clin Pathol. 2004;121(4):482-8.
4. Van Camp B, Durie BG, Spier C, De Waele M, Van Riet I, Vela E, et al. Plasma cells in multiple myeloma express a natural killer cell-associated antigen: CD56 (NKH-1, Leu-19). Blood. 1990;76(2): 377-82.
5. Sahara N, Takeshita A. Prognostic significance of surface markers expressed in multiple myeloma: CD56 and other antigens. Leuk Lymphoma. 2004;45(1):61-5.
6. Shapiro VS, Mollenauer MN, Weiss A. Endogenous CD28 expressed on myeloma cells upregulates interleukin-8 production: implications for multiple myeloma progression. Blood. 2001; 98(1):187-93.
7. Mateo G, Castellanos M, Rasillo A, Gutiérrez NC, Montalbán MA, Martín ML, et al. Genetic abnormalities and patterns of antigenic expression in multiple myeloma. Clin Cancer Res. 2005;11 (10):3661-7.

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