

Multiple myeloma diagnosed by flow cytometry plotting of CD19-positive and negative plasma cells

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Dear Editor,

An 85-year-old man was diagnosed with idiopathic pulmonary fibrosis seven years ago and was being treated with prednisolone (PSL) at an average dose of 16 mg/day for six months. He was admitted to our hospital due to back pain. Laboratory findings were as follows: white blood cell count, 11,010/ μ L (neutrophils, 87.8%; eosinophils, 0.1%; monocytes, 5.9%; and lymphocytes, 6.2%); hemoglobin, 9.8 g/dL; platelet count, 21.1 \times 10⁴/ μ L; lactate dehydrogenase, 355 U/L (normal range, 124-229 U/L); Ca, 8.0 mg/dL; blood urea nitrogen, 29.8 mg/dL; Cr, 0.66 mg/dL; total protein, 5.7 g/dL; albumin, 2.8g/dL; C-reactive protein, 1.48 mg/dL; immunoglobulin (Ig) G, 1,533 mg/dL (normal range, 870-1,700 mg/dL); IgM, 61 mg/dL (normal range, 35-220 mg/dL); and IgA, 49 mg/dL (normal range, 110-410 mg/dL). Serum concentrations of λ free light chain (FLC) were 77.7 mg/L (normal range, 5.7-26.3 mg/dL), with a κ/λ FLC ratio of 0.26 (normal range, 0.26-1.65). Moreover, M-protein of IgG- λ type was detected using immunoelectrophoresis in serum and urine. β 2 microglobulin level was 2.7 mg/L (normal range, 0.9-2.0 mg/L). The serum carcinoembryonic antigen and prostatic-specific antigen were 4.9 ng/mL (normal value, <5.0 ng/mL) and 3.180 ng/mL (normal value, <4.000 ng/mL), respectively. Urinalysis revealed neither proteinuria nor hematuria. Magnetic resonance imaging showed bone fractures in thoracic vertebrae. Multiple punched-out osteolytic lesions of a skull were not radiographically detected. No tumor in the lung, liver, gall bladder, and

pancreas were observed in computed tomography findings. Furthermore, no gastric or colonic wall thickness or stenosis suggestive of tumors was noted. However, a diverticulum of the ascending colon was observed. A bone marrow aspiration smear revealed a nucleated cell count of 235,000/ μ L comprising 3% plasma cells composed of small-sized plasma cells with dense basophilic cytoplasm and perinuclear clear zone and medium-sized cells with abundant cytoplasm (**Figure 1** and **Figure 2**). The ratio of small-sized to medium-sized plasma cells was about 1 to 4. Cytogenetic analysis in bone aspiration specimens revealed 46, XY and 47, XY, +8. Multiparameter flow cytometry (FCM) (BML, Inc., Tokyo, Japan) collected plasma cells possessing CD38 and plotted CD19-positive and CD19-negative cells; the number of CD19-negative cells was significantly larger than that of CD19-positive cells (**Figure 3**). The ratio of CD19-positive to CD19-negative cells was about 1 to 5. Therefore, medium-sized plasma cells were thought to coincide with CD19-negative cells.

Generally, malignant plasma cells (myeloma cells) isolated from the multiple myeloma (MM) patients lack the CD19 expression, while non-malignant plasma cells isolated from the healthy donors express the CD19 antigens. Monoclonal gammopathy of undetermined significance (MGUS) is composed of phenotypically non-malignant (CD19+) and malignant (CD19-) plasma cells [1]. Considered together, the patient's diagnosis was thought to be MM rather than MGUS with probable

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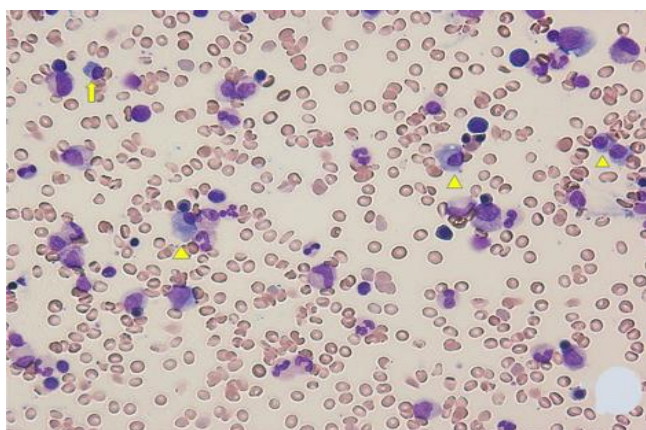


Figure 1. A bone marrow aspiration smear reveals plasma cell population composed of small-sized plasma cells with dense basophilic cytoplasm and perinuclear clear zone (arrow) and medium-sized cells with abundant cytoplasm (arrowhead) (May-Giemsa, $\times 400$)

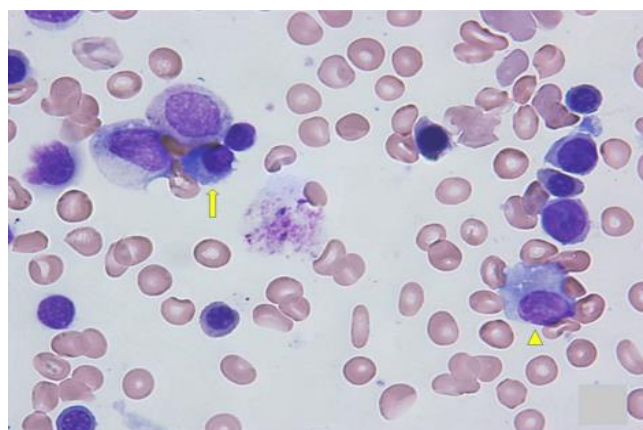


Figure 2. A bone marrow aspiration smear reveals plasma cell population composed of small-sized plasma cells with dense basophilic cytoplasm and perinuclear clear zone (arrow) and medium-sized cells with abundant cytoplasm (arrowhead) (May-Giemsa, $\times 1,000$)

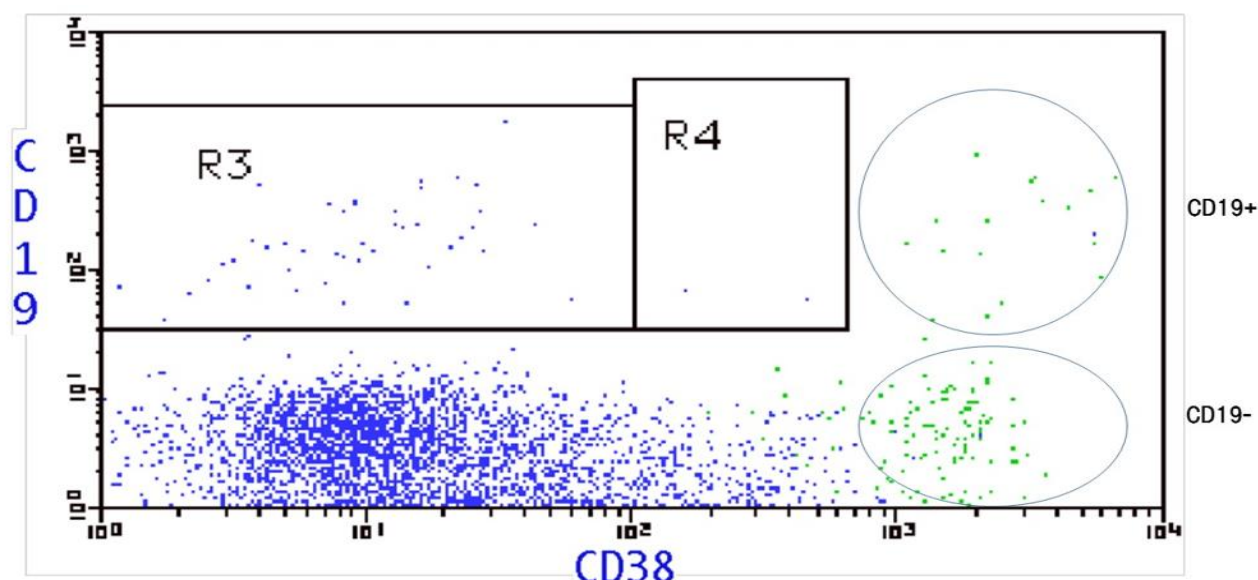


Figure 3. Flow cytometry revealed the plotting of plasma cells expressing the CD38 antigen, and classified them into CD19-positive and CD19-negative cells. The ratio of CD19-positive to CD-19 negative cells was approximately 1:5

steroid-induced osteoporosis, resulting in bone fractures in thoracic vertebrae.

In this case, the M-protein level was low, and the percentage of malignant plasma cells in the bone marrow was below 10%, which may be due to the PSL prescription.

In summary, multiparameter FCM may help with the diagnose of plasma cell disorders, such as MM or MGUS, in case of low percentage of plasma cell numbers and two kinds of plasma cells with morphological features in bone marrow aspiration.

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