Variant Morphology in Multiple Myeloma

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Abstract A 45-year-old man presented to the clinic with the chief complaints of low back pain, marked weight loss, and pallor of 2 months duration. He was found to have severe normocytic anemia with leukoerythroblastosis. Bone marrow aspirate resulted in a dry tap. Marrow trephine biopsy showed findings initially interpreted as poorly differentiated carcinoma involving marrow. Immunohistochemistry and protein studies established a diagnosis of IgG Kappa multiple myeloma. Correlation of marrow biopsy findings with clinical, radiological and immunological data remain an essential part of the diagnostic evaluation of multiple myeloma.

Keywords Myeloma · Carcinoma · Bone marrow morphology

Morphological analysis of bone marrow aspirate or trephine for the assessment of volume of plasma cell infiltrate remains a cornerstone in the diagnosis of multiple myeloma. In most cases the plasmacytic nature of the marrow infiltrate is readily apparent. However, rare cytological variants of myeloma cells including small cell, signet-ring cell, multilobated, clear cell, pleomorphic and monocytoid,

among others may present considerable diagnostic difficulty. Awareness of these variants may help facilitate timely diagnosis.

Case

A 45-year-old man was evaluated for low back pain, weight loss and pallor of 2 months duration. He denied cough, change in bowel habits, or overt blood loss. Physical examination showed mucosal pallor, tenderness over the lumbar spine and a spleen that was palpable 5 cm below the left costal margin.

His Hb was 4.8 g/dL, total leukocytes $4.3 \times 10^6/L$ and platelets $70 \times 10^6/L$. Examination of the blood smear showed normocytic normochromic red cells with rouleaux formation, occasional normoblasts and rare myelocytes. The serum creatinine was 1.3 mg/dL, serum calcium 7.8 mg/dL, total protein 14.1 g/dL, albumin 4.5 g/dL, and lactate dehydrogenase 351 U/L (11–190 U/L). Serum protein electrophoresis showed a monoclonal band in the gamma region. Serum immunofixation electrophoresis showed an IgGκ monoclonal band. The serum IgG level was 7.5 g/dL, IgA 23 mg/dL and IgM 20 mg/dL. Beta2 microglobulin was 7,253 ng/mL. Urine protein was 420-mg/24 h and showed no monoclonal band on electrophoresis. Skeletal survey showed multiple lytic lesions in the axial skeleton and proximal femora.

Bone marrow aspirate resulted in a dry-tap. Touch preparation of marrow biopsy showed scant cellular elements composed mostly of bare nuclei with no discernible nucleoli. Marrow core-biopsy showed replacement of marrow by sheets of atypical large cells, which had vesicular nuclei with small nucleoli, and abundant cytoplasm, which was vacuolated in areas. They were moderately pleomorphic

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Fig. 1 The *left panel* is a low power view of marrow diffusely infiltrated by the abnormal cells ($\times 100$). The *right panel* is the high power view of the pleomorphic cells with scattered bizarre forms ($\times 400$)

with scattered bizarre forms. Thin walled vascular sinusoids were seen between. The normal hemopoietic elements were depleted (Fig. 1). Trichrome stain showed no marrow fibrosis; a reticulin stain was not done. The cells were negative for CD45, pan-keratin, epithelial membrane antigen, and CD79a. There was focal strong cytoplasmic positivity for CD138 and strong diffuse cytoplasmic positivity for kappa light chain. The cells reacted negative for lambda light chain. A Ki-67 stain was not done.

Several architectural and cytomorphological variants of myelomatous infiltrate in bone marrow biopsies have been described [1]. Their incidence is unknown and they appear to be not widely recognized. In the differential diagnosis between atypical plasmacytic infiltrate and undifferentiated carcinoma, both may be positive for epithelial membrane antigen, vimentin, and cytokeratin and negative for CD45 [2, 3]. Likewise, absence of cytoplasmic CD79a has been noted in a third of the patients with myeloma [4]. Light chain restriction may not be obvious due to presence of extracellular light chains, prolonged fixation, the decalcification process, and plasma cell dysplasia that can result in false negative results [2, 5]. Fortunately the negative staining for cytokeratin and the unequivocal demonstration of light chain restriction in the marrow biopsy were diagnostic of a malignant plasma cell dyscrasia in our patient. The fortuitous

occurrence of unrecognized epithelial malignancy with lytic bone metastases, reactive marrow plasmacytosis and an incidental monoclonal paraproteinemia (pseudomyeloma) could lead to diagnostic difficulty. Correlation of marrow biopsy findings with clinical, radiological and immunologic data thus remains an essential part of the diagnostic evaluation of multiple myeloma.

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