

CORRESPONDENCE

Smoldering Multiple Myeloma Presenting as Immune Thrombocytopenia

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Received: 15 January 2019 / Accepted: 5 February 2019 / Published online: 13 February 2019
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Dear Editor,

Cytopenias associated with plasma cell dyscrasia are usually either disease-related (replacement of marrow hematopoiesis by clonal plasma cells) or therapy-related. Autoimmune cytopenias in association with plasma cell neoplasms are uncommon [1].

A 57-year-old lady presented to our hospital with a one-week history of generalized bluish spots over the body. History was negative for fever, oral ulcers, drug intake or autoimmune symptoms. No such previous episodes were elicited on history. Examination was unremarkable, except for the presence of multiple ecchymotic patches over arms and legs. Blood investigations were: hemoglobin-11 g/dl, white cell counts- $7.33 \times 10^9/L$, and platelets- $2 \times 10^9/L$. Peripheral smear showed normocytic normochromic red cells, marked thrombocytopenia and occasional large platelets. Blood chemistries were: serum calcium-9.2 mg/dl (8.5–10.1 mg/dl), protein-7.0 g/dl (6.4–8.2 g/dl), albumin-4.3 g/l (3.4–5.0 g/dl), creatinine-0.8 mg/dl (0.6–1.1 mg/

dl), vitamin B12 level-220 pg/ml (211–911 pg/ml), folate level-14.9 ng/ml (normal > 5.3 ng/ml), and lactate dehydrogenase-231U/L (100–190U/L). Viral markers (Australia antigen, anti-HCV antibody, and anti-HIV antibody) and anti-nuclear antibody were negative. Abdominal ultrasound revealed a normal spleen size (12 cm). Bone marrow aspiration smears showed prominent megakaryocytes, and increased number of plasma cells, constituting 20% of total marrow nucleated cells (Fig. 1a). Bone marrow biopsy was hypercellular for age, showing increased megakaryocytes, and an interstitial increase of plasma cells (Fig. 1b). These plasma cells were positive for CD38, and demonstrated lambda-restriction on immunohistochemistry (IHC), confirming their clonal nature. Cytogenetic and FISH analysis of the marrow aspirate was unrevealing. Serum and urine protein electrophoresis was negative, however, serum immunofixation revealed a faint 'M' band (IgA λ). Serum free light chain ratio (κ : λ) was 0.07 (κ -13.80 mg/l, λ -209 mg/l). Serum immunoglobulin and β 2-microglobulin levels were normal. PET-CT scan did not reveal any FDG-avid osteolytic bone lesion. Based on the presence of isolated thrombocytopenia, increased megakaryocytes on bone marrow examination, and exclusion of secondary causes of thrombocytopenia, a diagnosis of acute immune thrombocytopenia (ITP) was made. Marrow clonal plasmacytosis (20%), and absence of myeloma-defining events (MDE) led to a diagnosis of co-existing smoldering multiple myeloma (SMM). She was treated with pulse methylprednisolone (1gm/day \times 3 days) followed by oral prednisolone (1 mg/kg/day), which resulted in a rapid increase in the platelet count within 3-weeks. Thereafter, prednisolone was gradually tapered over the next 4-weeks and she continues to be in complete treatment free remission. She is on 3-monthly follow-up to monitor for progression to symptomatic myeloma. Association of ITP with

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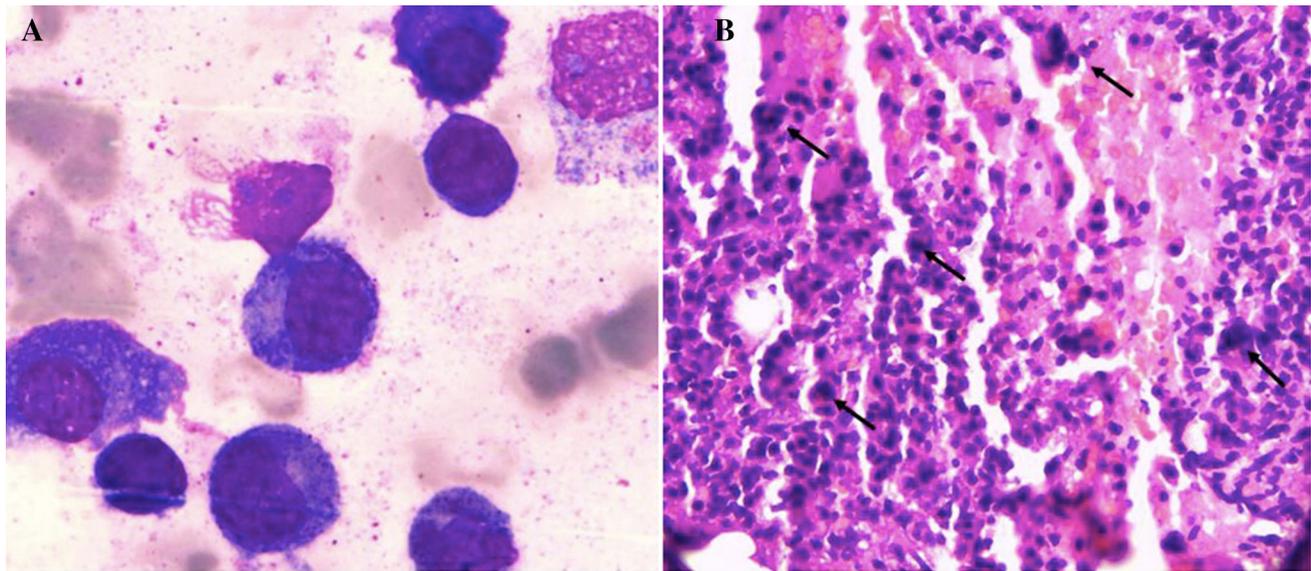


Fig. 1 **a** Photomicrograph of bone marrow aspirate smear, Leishman stained, showing increased plasma cells (100x). **b** Photomicrograph of bone marrow biopsy section, H&E stained, showing plasma cells & increased megakaryocytes (20x)

MM has been rarely reported [1]. Faller et al. [2] summarized 10 such reported cases from the literature. However, no case of SMM co-existing with ITP has been described so far. ITP in this case could possibly be a manifestation of immune dysregulation associated with SMM. Current case highlights certain crucial points. Firstly, since marrow plasmacytosis seen in autoimmune cytopenias could be reactive, a high-index of suspicion must be maintained to diagnose SMM/MM. This would require demonstration of the clonality of plasma cells by IHC, and a careful search for MDE. Secondly, in a case of SMM/MM, hematopoietic reserve of bone marrow must be diligently sought to ascertain the exact etiology of an underlying cytopenia. Normal/increased hematopoiesis favors the consideration of immune-mediated cytopenia over disease-related cytopenia. Since immune cytopenias are typically steroid-sensitive, such a distinction could potentially spare the patient from short and long-term toxicity of the anti-myeloma therapy.

Compliance with Ethical Standards

Conflict of interests The authors declare that there are no conflicts of interests.

Consent for Publication The authors state that an informed and written consent was obtained from the patient prior to the publication.

Ethical Approval The authors declare that the article follows the Helsinki declaration guidelines and the manuscript has not been submitted to any other journal.

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