Skin lesions, arthritis, chondritis, and cytopenias

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The pathogenesis of MDS (myelodysplastic syndrome) is intimately tied to excessive inflammatory activity in the bone marrow microenvironment, which can either directly or indirectly cause systemic inflammatory and autoimmune illnesses. Alternately, autoimmune/autoinflammatory diseases might promote clonal evolution and unbalanced bone marrow growth, both of which would promote the development of myeloid malignancy. These relationships raise the following query: are there any connections between myelodysplastic syndromes and autoimmune/systemic inflammatory disorders "hemato-inflammatory syndromes"? There are still many questions, including ones regarding its therapeutic strategy [1]. We have read with interest the perspective of the authors of the reference [2]. We believe that Figure 2 is an excellent approximation to the hypothetical pathophysiology of VEXAS-MDS. We have a patient who exemplifies this interesting relationship. However, regarding Figure 3 [2], we disagree; incorporating the UBA1 mutation in the systematic molecular evaluation of all MDS currently does not contribute to defining a targeted treatment.

A 61-year-old-man attended our department for evaluation of cytopenias. Four years earlier he presented with a leg-deep venous thrombosis with pulmonary embolism and persistent positive lupic anticoagulant; he was diagnosed of antiphospholipid syndrome. Several months later, after his initial presentation, he developed inflammatory arthralgias with persistent elevation of C-reactive protein 40 mg/dL (normal < 0.5), and negative rheumatoid factor, cyclic *citrullinated peptide,* and antinuclear antibodies. He received prednisone, methotrexate, and leflunomide with a lack of response. Six months later, he presented to the emergency room for painful erythematosus, and pustular skin rash on the dorse of the hands (Figure. A, B) with punch biopsy that showed neutrophilic dermatosis without vasculitis. Three months later, he developed chondritis of the nose and helix of the ear and was treated with a high dose of oral prednisone with a good response. Since his initial presentation, he has mild oscillate cytopenia:

white blood cells was around 6 × 10^9 per L (normal 4–11), neutrophils 4.2 × 10^9 per L (normal 2–8), lymphocytes 0.2 × 10^9 to 1 per L (normal 1.2–3.5), hemoglobin concentration 10 to 12 g/dL (normal 13.5–17), mean corpuscular volume 110 fL (80–100), and platelets 86 × 10^9 per L (normal 150–450) without remarkable findings in peripheral blood smears. A bone marrow aspirate showed normal cellularity with morphological dysplasia (megakaryocytic and granulocytic) including vacuolation of myeloid precursors (Figure. C, D).

Sanger sequencing of DNA extracted from bone marrow samples showed a somatic mutation affecting methionine-41 of the UBA1 gene (Figure. E, F). Next generation sequencing showed SRSF2 mutation with a variant allelic frequency of 3%. He started treatment with tocilizumab.

Figure: (A) Neutrophilic dermatosis lesions on the back of hands. (B, C) Bone marrow aspirates with normal cellularity, megakaryocytic and granulocytic dysplasia, including vacuolation of myeloid precursors (Wright stain; 40 and 100X objective, original magnification X400 and 1000 respectively); (E) Chromatograms show the wild-type sequence and (F) patient sequence with the *UBA1* p.Met41Thr, ATG ACG (denoted by an asterisk).

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