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Hematologic Manifestations of the Newly Defined VEXAS Syndrome

A study of 16 patients provides a greater understanding of this new syndrome.

VEXAS (vacuoles, E1 enzyme, X-linked, autoinflammatory, somatic) syndrome is a newly recognized disease characterized by severe autoinflammatory symptoms, thrombosis, and progressive cytopenias. Researchers provide a retrospective update on hematological manifestations in 16 patients evaluated at the National Institutes of Health.

Among the findings:

- All patients were men; median age was 57 (range, 45–77) at disease onset.
- All patients had *UBA1* mutations.
- Systemic inflammatory symptoms included fatigue in all patients, recurrent fever (88%), lung infiltrates (87%), skin lesions (88%), ear chondritis (73%), and vasculitis (67%).
- Hematological findings included macrocytic anemia in all patients and thrombocytopenia (50%).
- Six patients (38%) were diagnosed with myelodysplastic syndrome (MDS); all were refractory to therapy.
- Two patients (13%) were diagnosed with multiple myeloma; one had some response to therapy but had relapse after autologous transplant.
- The most prominent abnormality on morphology review was cytoplasmic vacuoles in neutrophils and monocytes as well as myeloid and erythroid marrow precursors.
- No patient had progression to MDS with excess blasts or acute myeloid leukemia.
- Nine patients (56%) died from disease-related causes.
- Ten patients had thrombotic events; of 9 patients with venous thrombosis, 8 events were unprovoked, and the most common lab abnormality was a positive lupus anticoagulant test.

COMMENT

This novel syndrome, while rare, has striking and defining features that may facilitate diagnosis. These appear to be male predominance, *UBA1* mutations, vacuolization on smear and marrow review, recurrent thrombosis, and cytopenias. This syndrome is associated with a considerably increased risk for MDS, and although MDS did not progress to higher risk disease, no improvements were noted with treatment. Risk for thrombosis is also high, and some patients had recurrence while on anti-coagulation. Hopefully, greater understanding of VEXAS will lead to effective medical therapy.

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Obiorah IE et al. Benign and malignant hematologic manifestations in patients with VEXAS syndrome due to somatic mutations in UBA1. **Blood Adv** *2021 Aug 24; 5:3203. (https://doi.org/10.1182/bloodadvances.2021004976)*