Case Study
VEXAS Syndrome

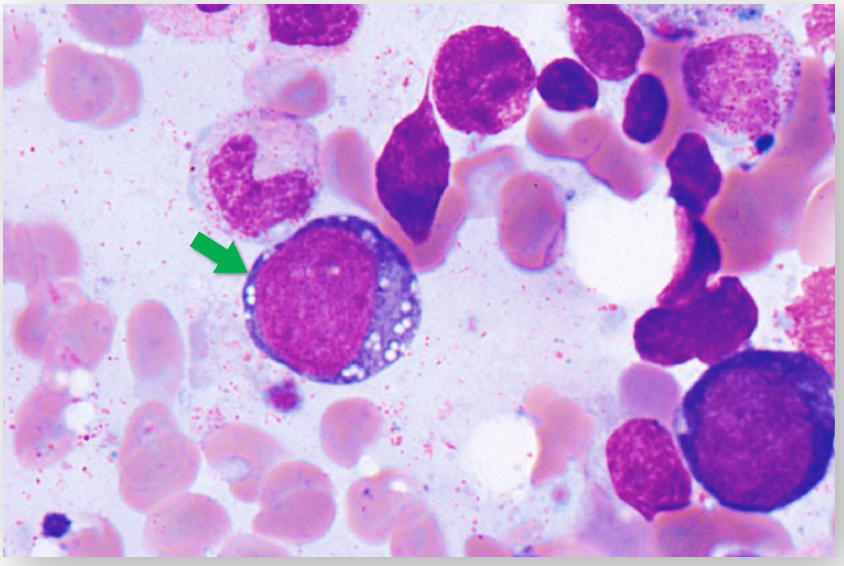
Detected by GTC's Hematology Profile and Liquid Biopsy

Recently described VEXAS (vacuoles, E1 enzyme, X-linked, autoinflammatory, somatic) is caused by mutations in the UBA1 gene.

GENOMIC® TESTING COOPERATIVE

Background

VEXAS syndrome is a disease with inflammatory and hematologic (blood) manifestations. The syndrome is caused by mutations in the UBA1 gene affecting the Met41 residue of the protein and resulting in decreased cellular ubiquitylation activity and hyperinflammation. This is an adults-onset fatal disease that may present as myelodysplastic syndrome, aplastic anemia or multiple myeloma, but characterized by fevers, low white cell count, vacuoles in bone marrow cells, dysplastic bone marrow, pulmonary inflammation, chondritis, and vasculitis. Detecting UAB1 gene mutations in the is the only way for confirming the diagnosis of this disease.



Clinical History

- 68-year-old male
- With low-grade myelodysplastic syndrome and inflammatory manifestations including arthritis, chondritis or other autoimmune disorders

Molecular Profiling Findings

- Mutations in genes:
  - UBA1
  - DNMT3A
  - TET2

V Vacuoles are often seen in cells identified in bone marrow biopsies

E **E1** ubiquitin activating enzyme, encoded by the UBA1 gene

X The UBA1 gene is located on the **X** chromosome

A Patients have **A**utoinflammation

S The mutations are **S**omatic, meaning they are acquired at some point in life and not inherited

Discussion

The presence of DNMT3A, and TET2 suggest early low-grade myelodysplastic syndrome (MDS). And the detection of UBA1 mutation along with the patient's symptoms confirmed the diagnosis of VEXAS. This patient was undiagnosed for long period of time and became transfusion dependent. By using any of our hematology DNA, DNA+RNA or cfDNA NGS panels; we are able to accurately diagnose VEXAS syndrome. This patient and most of the patients who are currently diagnosed with VEXAS have had numerous tests and tried multiple treatments. VEXAS should be considered in patients with systemic autoinflammatory disorders as well as patients with clinical presentation of myelodysplastic syndrome.

References

1. David B. Beck, M.D., et al. Somatic Mutations in UBA1 and Severe Adult-Onset Autoinflammatory Disease N Engl J Med 2020; 383:2628-2638, DOI: 10.1056/NEJMoa2026834

2. James A. Poulter, et al. Novel somatic mutations in UBA1 as a cause of VEXAS syndrome. Blood (2021) 137 (26): 3676–3681.

3. Marcela A. Ferrada, et al. Somatic Mutations in UBA1 Define a Distinct Subset of Relapsing Polychondritis Patients With VEXAS, Arithritis & Rheumatology, doi.org/10.1002/art.41743.

GENOMIC® TESTING COOPERATIVE

Genomic Testing Cooperative, LCA
175 Technology Dr, #100, Irvine, CA 92618
Tel: 1-949-540-9421 | Fax: 1-949-301-9719
Website: genomictestingcooperative.com
e-mail: gtc@genomictestingcooperative.com