Editorial

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VEXAS Syndrome: A Novel Autoinflammatory Disorder Linking Genetics and Hematology

Michael O'Connor*

Department of Rheumatology, Trinity College Dublin, Ireland

***Author for Correspondence:**
michael.oconnor@tcd.ie

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Introduction

VEXAS syndrome is a recently identified autoinflammatory condition that has reshaped understanding of adult-onset inflammatory diseases. First described in 2020, VEXAS stands for Vacuoles, E1 enzyme, X-linked, Autoinflammatory, Somatic syndrome. It is caused by acquired mutations in the UBA1 gene, which plays a critical role in protein ubiquitination. Unlike inherited disorders, VEXAS arises from somatic mutations, typically affecting older adults, particularly men.

Pathogenesis and Clinical Features

The underlying mutation in the UBA1 gene disrupts normal cellular protein degradation pathways, leading to systemic inflammation. Patients commonly present with recurrent fevers, skin lesions, pulmonary inflammation, and hematologic abnormalities such as anemia and thrombocytopenia. Bone marrow examination often reveals characteristic cytoplasmic vacuoles in myeloid and erythroid precursor cells.

VEXAS syndrome frequently overlaps with conditions such as relapsing polychondritis, vasculitis, and myelodysplastic syndromes, making diagnosis challenging. Genetic testing for UBA1 mutations is essential for confirmation.

Diagnosis and Management

Diagnosis relies on a combination of clinical suspicion, laboratory findings, and molecular testing. Elevated inflammatory markers, cytopenias, and bone marrow abnormalities often guide clinicians toward further evaluation.

Treatment remains challenging, as conventional immunosuppressive therapies often provide limited benefit. High-dose corticosteroids may offer temporary relief, while targeted therapies such as JAK inhibitors and hypomethylating agents are being explored. Hematopoietic stem cell transplantation is currently the only potentially curative option, though it carries significant risks.

Conclusion

VEXAS syndrome represents a groundbreaking discovery at the intersection of immunology and hematology. Its identification highlights the importance of somatic mutations in adult-onset inflammatory diseases. Although therapeutic options are still evolving, increased awareness and ongoing research are expected to improve diagnosis and management. Understanding VEXAS syndrome not only benefits affected patients but also provides broader insights into the mechanisms of autoinflammation and hematologic disease.