

Don't let the diagnosis VEX(as) you!

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History of Present Illness

- A 66-year-old male patient presents with a history of a rash since 2019. He was previously diagnosed with tumid lupus which was well-controlled with topical steroid until recently.
- A few months ago, his rash began flaring more frequently and intensely. The lesions are slightly itchy but otherwise asymptomatic. The rash appears in different locations when it flares. He also has associated swelling of the hands, tongue and intermittent mouth ulcers.
- The patient is up to date on colonoscopy and prostate cancer screening.

Medical History/Surgical History: Benign prostatic hyperplasia, pulmonary embolism, deep venous thrombosis

Medications: Tamsulosin, apixaban, aspirin

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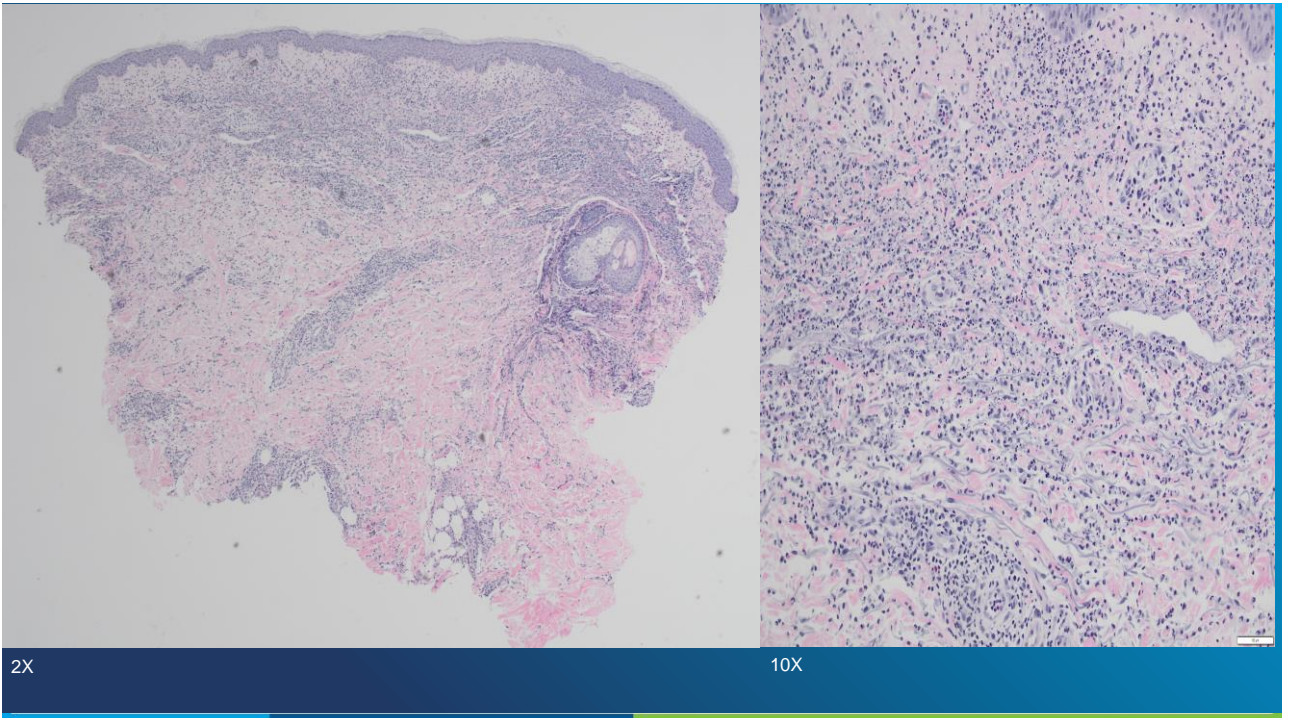
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Laboratory Data

Abnormal:

- 8/2/2022
 - Bone marrow biopsy demonstrated mild erythroid dysmorphism with occasional precursors with cytoplasmic vacuoles. UBA 1 tier 1 Variant c. 121 A.C, Allele Frequency 65.9% which is consistent and confirmatory of VEXAS Syndrome.
- 9/22/2022
 - CBC with Hgb of 13.3 units with macrocytosis
 - Urinalysis with 1 WBC, 1 RBC, moderate oxalate crystals, moderate mucous threads, and trace protein

Normal:

- 5/20/2022
 - Stool ova and parasites, stool CEA and CRP, iron panel, UPEP, B12, ESR, C3,C4, CMP, ANA
 - CT Chest unremarkable

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Clinical Course

- Favored diagnosis: VEXAS Syndrome
- Previous treatments: Fluocinonide, triamcinolone, prednisone
- Current treatments: Ruxolitinib (Jakafi) 5mg, augmented betamethasone dipropionate 0.05% cream, Prednisone 5mg
- Clinical course: Started on ruxolitinib 5mg twice daily and has noted improvement in the cutaneous findings with no significant side effects.

Key Points

- This rare and newly discovered disease has only been reported in males.
- It is caused by a mutation in the *UBA1* gene located on the X chromosome. *UBA1* encodes the E1-enzyme, which initiates ubiquitination in the protein degradation process.
- Diagnosis relies on high clinical index of suspicion. Final diagnosis relies on bone marrow aspiration and genetic testing.

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So what is VEXAS Syndrome?

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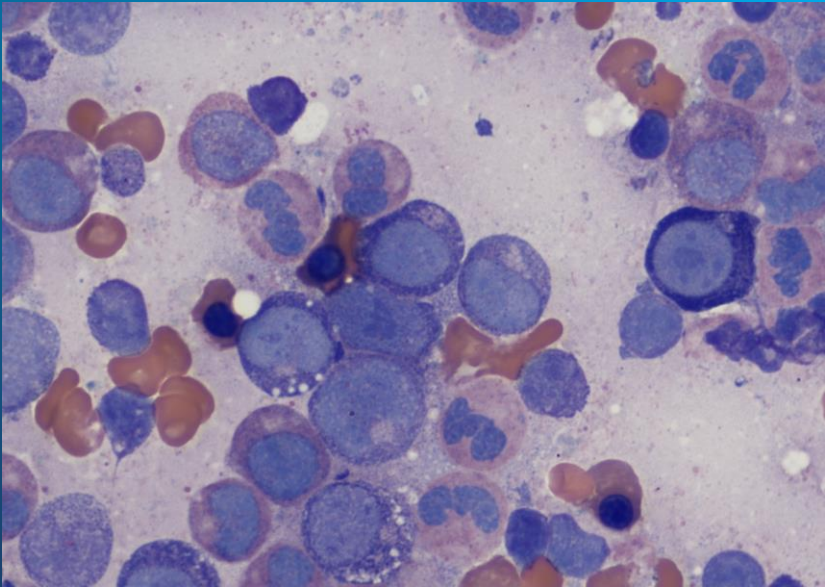
Background

- **V**acuoles, **E**1 enzyme, **X**-linked, **A**utoinflammatory, **S**omatic
- First described in 2020
- Fevers + myeloid autoinflammation
- Acquired, somatic mutation in the X-linked UBA1 gene
 - E1 enzyme
- Males > 50 years old
- Prevalence and incidence unknown

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**Give me a
V!
Vacuoles**



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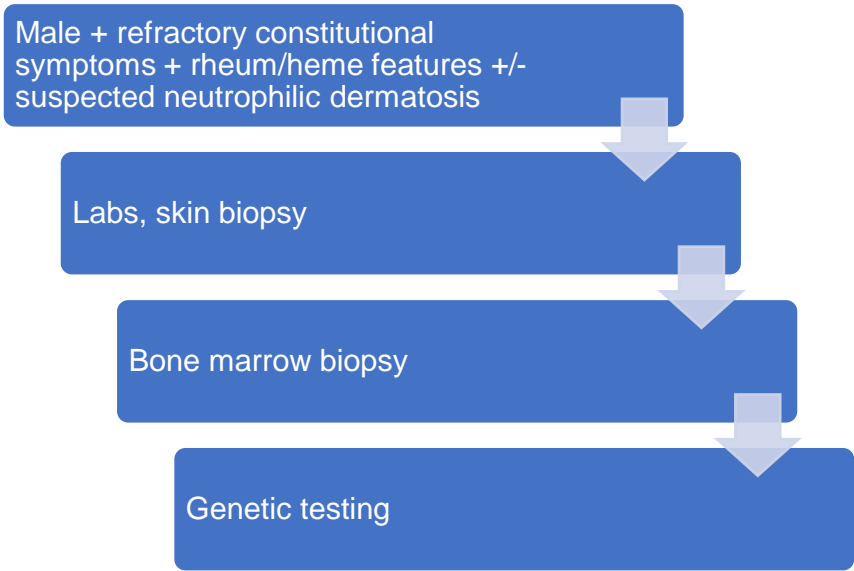
Cutaneous features



Argobi Y et al. *Dermatol Reports*. 2021.

Zakine et al. *JAMA Dermatol*. 2021.

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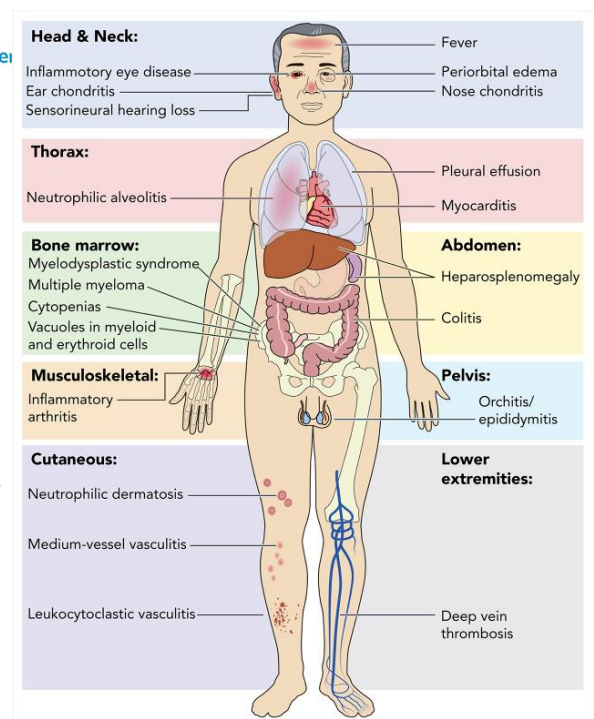
Complications

- High morbidity and mortality (up to 40%)
 - Progressive anemia
 - Respiratory failure
 - Complications from therapy
- Thrombotic events
- Multi-organ failure

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Clinical features

- Progressive hematologic and rheumatologic findings
- Involves the skin, lungs, bone marrow, blood vessels
 - Fevers
 - Neutrophilic cutaneous and pulmonary inflammation
 - Vasculitis
 - Cytopenias
 - Bone marrow failure



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Treatment

- High dose systemic steroids with steroid sparing agent
 - TNF-inhibitors, methotrexate, anti-IL-6 agents, cyclosporine, JAK inhibitors
- Azacytidine
- Bone marrow transplant

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Conclusion

- VEXAS = Vacuoles, E1 enzyme, X-linked, Autoinflammatory, Somatic
- **UBA1** gene mutation on the X-chromosome
- Affects **males** in the 5th decade of life or later
- **Fever** of unknown origin + progressive **rheumatologic and hematologic** features +/- **cutaneous** findings
- Refractory to treatment
 - **Steroids** are first line
 - Azacytidine

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