

## Introduction

- Chronic urticaria is associated with a variety of underlying conditions including autoimmune disorders, thyroid disease, medications, infections, or exposure to allergens.
- Exact percentage of population with chronic urticaria with a known underlying condition has not been established and varies by study (Zuberbier et al., 2018).
- Mainstay treatment includes second generation H1-antihistamines

## Case description

- 22-year-old female with eight years of hive-like rash and angioedema
- Hives located on face, trunk, and limbs with variable duration between days to weeks
- Hives were initially exacerbated during illness, mechanical pressure, or stress, but have more recently worsened with no trigger.
- History of ecchymosis after resolution of hives
- Associated symptoms: Fever and polyarthralgias, swelling of lips and eyes sometimes painful



Patient presentation of hives

## Laboratory studies

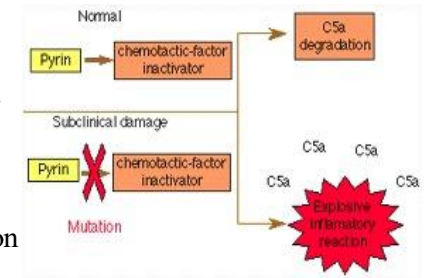
Laboratory Test	Results
CBC with Differential	WBC: K/uL, Hgb: g/dL, plt K/uL, ANC per microliter
Inflammatory markers	mildly elevated IL-10 elevated TNF alpha
Immunoglobulin Levels	IgA 256, IgD 223 (high), IgE 293 (high), IgM 117, IgA, IgG 1277  IgG subclass I 924 IgG subclass II 144 (low) IgG subclass III 51 IgG subclass IV 14.8
Lymphocyte Subsets	CD3 99% (47-76%), 1772 (1990- 5900) CD4 74% (31-56%), 1313 (1400-4300) CD8 25% (12-24%), 443 (500-1700) CD19 <1% (14-37%), <5 (61-260) CD16/56 1% (3-15%), 11 (160-950)
Periodic Fever 6 Gene NGS panel (DDC company)	Heterozygous variant for <i>MFEV</i> gene coding for familial Mediterranean fever (FMF)
Invitae Primary Immunodeficiency Panel (Invitae genetic testing)	Genetic testing of MEFV gene variant: Variants of Uncertain Significance for AP3D1 and TONSL
Biopsy of skin lesion	Mild edema within dermis; very sparse mixed inflammatory cell infiltrate that includes neutrophils and scattered eosinophils, consistent with vasculitis

## Treatment and Outcomes

- Patient initially started on Cetirizine BID, and Famotidine with some improvement but no alleviation of urticaria
- After diagnosis of atypical FMF, initiated colchicine with no significant improvement in symptoms, then trial of hydroxychloroquine, with limited course of improvement.
- Outcome and follow up: some improvement of urticaria but no alleviation of symptoms after prior treatments, follow up discussions are to trial Omalizumab or IL-1 blockade as escalation of therapy.

## Discussion and Conclusion

- There are established associations between several autoimmune disorders and chronic urticaria (Confino-Cohen et al., 2012).
- This case demonstrates the importance of recognizing underlying autoinflammatory disease in the setting of chronic urticaria and the utility of genetic testing in correlation of chronic urticaria to autoinflammatory disease.
- Gene mutation MEVF has been associated with chronic urticaria and FMF which ultimately helped better symptomatically treat with medications not used for chronic urticaria (Alonso, 2002)
- This case emphasizes consideration of autoinflammatory disease as a differential to hives prior to diagnosis of chronic urticaria



National Center for Biotechnology Information, 1998.

## References

- Alonso R, Cisteró-Bahima A, Enrique E, San Miguel-Moncín MM. Recurrent urticaria as a rare manifestation of familial Mediterranean fever. J Invest Allergol Clin Immunol. 2002;12(1):60-1.
- Confino-Cohen R, Chodick G, Shalev V, Leshno M, Kimhi O, Goldberg A. Chronic urticaria and autoimmunity: associations found in a large population study. J Allergy Clin Immunol. 2012 May;129(5):1307-13. doi: 10.1016/j.jaci.2012.01.043. Epub 2012 Feb 14. P
- Zuberbier T, et al. . The international EAACI/GA<sup>2</sup>LEN/EuroGuiDerm/APAAACI guideline for the definition, classification, diagnosis, and management of urticaria. Allergy. 2022 Mar;77(3):734-766. doi: 10.1111/all.15090. Epub 2021 Oct 20. PMID: 34536239.
- National Center for Biotechnology Information (US). Familial Mediterranean fever. Genes and Disease. Bethesda (MD): National Center for Biotechnology Information (US); 1998-.