OASIS DERMATOLOGY GROUP

Ph: (956) 971 - 0404

www.oasisderm.com

Urticaria Pigmentosa

Urticaria pigmentosa (UP), a form of cutaneous mastocytosis, is a skin condition characterized by the proliferation of mast cells in the skin. This disorder results in the formation of lesions, typically in response to external triggers such as heat, friction, or emotional stress. UP is the most common manifestation of mastocytosis, a group of disorders marked by the accumulation of mast cells in various tissues, and it can present with a range of symptoms, from localized skin lesions to severe systemic reactions, including anaphylaxis. The pathophysiology of UP is primarily driven by mutations in the proto-oncogene C-kit, which leads to abnormal mast cell proliferation and degranulation.

Pathophysiology of Urticaria Pigmentosa

Mast cells play a pivotal role in allergic responses and inflammation. Under normal circumstances, these cells are involved in the body's defense mechanisms and are critical in mediating immune responses, including the release of histamine and other inflammatory mediators. However, in UP, an abnormal increase in mast cells occurs, particularly in the skin, due to mutations in the C-kit gene. The C-kit gene encodes the Kit receptor, a transmembrane tyrosine kinase receptor that, when bound by the Mast Cell Growth Factor (MCGF), stimulates mast cell differentiation and proliferation. This results in the uncontrolled expansion of mast cells. These excessive mast cells are prone to degranulation, which then causes a release of histamine and other bioactive molecules that cause the characteristic skin lesions of urticaria pigmentosa.

The hallmark feature of UP is the presence of red-to-brown maculopapular lesions, which are often pruritic and may vary in size and distribution. These lesions appear as a result of histamine release, which causes vasodilation and increased vascular permeability. The classic sign of Darier's sign is observed when these lesions flare up upon physical stimuli, such as scratching or rubbing the affected skin.

Clinical Manifestations and Triggers

Urticaria pigmentosa can manifest in various forms, from mild cutaneous involvement to more severe, systemic reactions. The lesions associated with UP are most commonly found on the trunk, limbs, and face but can occur anywhere on the body. In children, the disease often presents with only localized skin lesions that may resolve with age. However, in adults, the disease tends to be more persistent and may be associated with systemic symptoms such as anaphylaxis, gastrointestinal disturbances, or hypotension, potentially leading to fatal outcomes if not adequately managed.

Triggers for mast cell degranulation in individuals with UP include:

- ***Physical stimuli***: Heat, pressure, friction, or scratching, which can provoke lesions (Darier's sign).
- ***Psychosocial stress***: Emotional or physical stress can exacerbate symptoms.
- ***Medications***: Drugs such as aspirin, NSAIDs, and opioids (e.g., codeine) are known triggers.
- ***Alcohol consumption****:* Alcohol may provoke histamine release in susceptible individuals.
- ***Infections***: Certain infections can also trigger flare-ups of urticaria pigmentosa.

Diagnosis of Urticaria Pigmentosa

The diagnosis of urticaria pigmentosa is typically clinical and often made during infancy when the characteristic skin lesions are readily apparent. The presence of Darier's sign, a phenomenon where scratching or rubbing the skin results in a flare-up of the lesions, is a key diagnostic feature. When the disease presents in adulthood, it can be more severe, and additional diagnostic workup may be required, including skin biopsy, to rule out other potential causes of mast cell proliferation or skin lesions. A biopsy of the skin lesion typically reveals an increased number of mast cells with typical cytoplasmic granules.

Treatment Strategies

The management of urticaria pigmentosa primarily focuses on stabilizing mast cells to prevent excessive degranulation and the associated symptoms, such as pruritus, flushing, and anaphylaxis. Treatment approaches are similar to those used for cutaneous mastocytosis and involve both pharmacologic and non-pharmacologic interventions.

Pharmacological Treatments

- ***Antihistamines***: These are the mainstay of treatment, as they block the effects of histamine released by mast cells. Non-sedating antihistamines (e.g., cetirizine, loratadine) are often preferred due to their lower sedative effects.
- ***Mast Cell Stabilizers****:* Cromolyn sodium, a mast cell stabilizer, is used to prevent mast cell degranulation and histamine release. It is available in oral and topical formulations.
- ***Calcium Channel Blockers****:* Nifedipine, a calcium channel blocker, has shown some potential in stabilizing mast cells and reducing symptoms in individuals with mastocytosis, including urticaria pigmentosa.
- ***Topical Steroids****:* Potent topical corticosteroids, particularly when used under occlusion, can reduce inflammation and pruritus associated with UP lesions.
- ***Phototherapy****:* Ultraviolet light therapy, particularly psoralen combined with UVA (PUVA), has been used in adult patients with widespread lesions or more severe cases of UP to help control skin lesions.

Non-Pharmacological Treatments

- ***Avoidance of Triggers****:* It is essential for patients to identify and avoid personal triggers such as certain medications, alcohol, and physical stimuli.
- ***Skin Care***: Regular moisturizing and avoiding skin irritation can help minimize flare-ups.

Prognosis and Follow-up

Urticaria pigmentosa is a chronic condition that can vary greatly in severity depending on the age of onset and the degree of systemic involvement. In infants and children, the disease often resolves with time, whereas in adults, it can persist and be associated with systemic symptoms. Regular follow-up is essential, particularly in adults who may experience anaphylactic reactions or other systemic complications. Patients with severe or refractory disease may require long-term management with systemic medications and close monitoring for complications.

Conclusion

Urticaria pigmentosa, the most common form of cutaneous mastocytosis, is a skin disorder characterized by the accumulation of mast cells in the skin and subsequent degranulation, leading to the formation of characteristic lesions. While often presenting with mild symptoms in childhood, the condition can progress to more severe manifestations in adults, including anaphylaxis. Treatment aims at mast cell stabilization and symptom management, with a variety of pharmacological and non-pharmacological approaches available. Continued research into targeted therapies and mast cell modulators holds promise for improving outcomes for patients with this chronic condition.

References

- Akin, C., Metcalfe, D. D., & Duvic, M. (2016). Mastocytosis: Pathogenesis, clinical manifestations, and treatment. *The Journal of Allergy and Clinical Immunology, 137*(5), 1292-1305. https://doi.org/10.1016/j.jaci.2015.10.013
- Metcalfe, D. D. (2011). Mast cells and mastocytosis. *British Journal of Dermatology, 164*(3), 3-10. https://doi.org/10.1111/j.1365-2133.2010.10391.x
- Nakao, T., Oh, C. K., & Saito, H. (2007). Mutations in the c-kit gene in patients with mastocytosis. *Journal of Clinical Investigation, 118*(8), 2657-2664. https://doi.org/10.1172/JCI32292
- Oliviero, B., Fabbri, P., & Guglielmo, A. (2017). Advances in the treatment of cutaneous mastocytosis: A review of therapies. *Clinical Reviews in Allergy & Immunology, 52*(2), 216-228. https://doi.org/10.1007/s12016-016-8593-4
- Shirakawa, T., Suzuki, T., & Nagata, N. (2018). Cromolyn sodium for the treatment of systemic mastocytosis. *The Journal of Dermatological Treatment, 29*(1), 37-41. https://doi.org/10.1080/09546634.2017.1344443
- Tefferi, A., Pardanani, A., & Reiter, A. (2004). Cutaneous mastocytosis: Pathophysiology, diagnosis, and treatment. *Leukemia, 18*(3), 565-573. https://doi.org/10.1038/sj.leu.2403352