

Darier's sign

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INTRODUCTION

Darier's sign refers to the urtication and erythematous halo that are produced in response to rubbing or scratching of lesions of cutaneous mastocytosis.

Darier's sign is named after the French dermatologist Ferdinand-Jean Darier who first described it. The first description of mastocytosis was made by Nettleship and Tay^[1] in 1869, and in 1878, Sangster coined the term urticaria pigmentosa.^[2]

METHOD OF ELICITATION

In classical Darier's sign, gentle rubbing or stroking of the lesions, is followed by local itching, erythema and weal formation within 2-5 min. This may persist from 30 min to several hours. In young children, there may be vesiculation in the stroked lesion. Although classically positive in lesional skin, this sign may even be demonstrated on clinically normal skin in patients of mastocytosis.

In pseudoxanthomatous mastocytosis, a variant of diffuse cutaneous mastocytosis, there will be only erythema without urtication on rubbing as against a classic Darier's sign.^[3]

PATHOPHYSIOLOGY

In cutaneous mastocytosis, there is an increased number of functionally normal mast cells in the dermis. When the skin is stroked, there is degranulation of the mast cells with the release of inflammatory granules that contain histamine, slow-releasing substance of anaphylaxis (SRSA), eosinophil chemotactic activating factor (ECAAF) and heparin [Figure 1].



Figure 1: Darier's sign

It is the histamine that is responsible for the response.

It is also suggested that besides exocytosis of single or multiple granules, there is another pattern of degranulation when mast cells rupture. This happens following physical stimuli such as stroking. A gentle action gives rise to exocytosis, while a strong action leads to rupture of the cells.^[4]

Exact pathophysiology of Darier's sign in lymphoma and leukemias, is not known. One hypothesis suggested that mast cell proliferation may be related to lymphokine release, thereby explaining their close relation with lymphocytes.^[5] Another hypothesis suggested that laminin increases mast cell attachment to the lymphocytes.^[6] In juvenile xanthogranuloma, the histiocytes of the lesions undergo macrophagic differentiation to dermal dendrocytes, and the distribution of mast cells in the skin coincides with that of dermal dendritic cells.^[7]

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CONDITIONS ASSOCIATED WITH DARIER'S SIGN

1. **Cutaneous mastocytosis:** In urticaria pigmentosa, the most frequent clinical form of cutaneous mastocytosis, Darier's sign was present in 94% of cases.^[8]
2. **Leukemia cutis:** Leukemia cutis occurs in 25–30% of infants with congenital leukemia and is frequently associated with acute myeloid leukemia than with acute lymphoblastic leukemia. Urticaria-pigmentosa-like lesions have been reported in acute lymphoblastic leukaemia.^[9,10]
3. **Juvenile xanthogranuloma:** It is the most common form of non-Langerhans cell histiocytosis. Nagayo *et al.* reported Darier's sign in this disorder.^[7]
4. **Histiocytosis X:** Foucar *et al.* described positive Darier's sign in a patient with 'mast cell rich variant' of histiocytosis X.^[11]
5. **Lymphoma:** On rare instances, Darier's sign has been reported in cutaneous large T-cell lymphoma and in non-Hodgkin's lymphoma.^[12,13]

DIFFERENTIAL DIAGNOSIS

1. **Pseudo-Darier's sign:** It is a transient piloerection and elevation or increased induration of a lesion induced by rubbing and is observed in congenital smooth muscle hamartomas. A positive pseudo-Darier's sign can be helpful in clinically distinguishing congenital smooth muscle hamartoma from congenital hairy nevus.^[14]
2. **Dermatographism ("skin writing"):** It is a form of physical urticaria that consists of local erythema due to capillary vasodilatation, followed by edema and a surrounding flare due to axon reflex induced dilation of arterioles, which is observed after the firm stroking of skin. The cause of this phenomenon is thought to be hypersensitivity of the mast cells rather than an increase in the mast cells, as observed in mastocytosis.^[15]

SIGNIFICANCE

Darier's sign is pathognomic of cutaneous mastocytosis although some patients may have little or no wealing or itching even when the skin reveals a dense population of mast cells, particularly in those with a long history of the disorder. However, Darier's sign is not 100% specific for mastocytosis since it has been described, albeit rarely, in juvenile xanthogranulomas and acute lymphoblastic leukemia.^[15]

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REFERENCES

1. Nettleship E, Tay W. Rare forms of urticaria. *BMJ* 1869;2:323-30.
2. Sangster A. An anomalous mottled rash, accompanied by pruritus, factitious urticaria and pigmentation, 'urticaria pigmentosa (?). *Trans Clin Soc London* 1878;11:161-3.
3. Beer WW, Emslie ES. Diffuse cutaneous mastocytosis. *Br J Dermatol* 1968;80:841-3.
4. Zhu KJ, Zhu TC, Shi YH, Ge ZH. A histopathological and electron microscopical observation of urticaria pigmentosa. *Indian J Dermatol Venereol Leprol* 1990;56:152-5.
5. Prokocimer M, Polliack A. Increased bone marrow mast cells in preleukemic syndromes, acute leukaemia and lymphoproliferative disorders. *Am J Clin Pathol* 1981;75:34-8.
6. Thompson HL, Burbelo PD, Segui-Real B, Yamada Y, Metcalfe DD. Laminin promotes mast cell attachment. *J Immunol* 1989;143:2323-7.
7. Nagayo K, Sakai M, Mizuno N. Juvenile xanthogranuloma with Darier's sign. *J Dermatol* 1983;10:283-5.
8. Kiszewski AE, Durán-Mckinster C, Orozco-Covarrubias L, Gutiérrez-Castrellón P, Ruiz-Maldonado R. Cutaneous mastocytosis in children: A clinical analysis of 71 cases. *J Eur Acad Dermatol Venereol* 2004;18:285-90.
9. Yen A, Sanchez R, Oblender M, Raimer S. Leukemia cutis: Darier's sign in a neonate with acute lymphoblastic leukemia. *J Am Acad Dermatol* 1996;34:375-8.
10. Raj S, Khopkar U, Wadhwa SL, Kapasi A. Urticaria-pigmentosa-like lesions in acute lymphoblastic leukaemia (2 cases). *Dermatology* 1993;186:226-8.
11. Foucar E, Piette WW, Tse DT, Goeken J, Olmstead AD. Urticating histiocytosis: A mast cell rich variant of histiocytosis X. *J Am Acad Dermatol* 1986;14:867-73.
12. Ollivaud L, Cosnes A, Wechsler J, Gaulard P, Bagot M, Haioun C, *et al.* Darier's sign in cutaneous large T-cell lymphoma. *J Am Acad Dermatol* 1996;34:506-7.
13. Lewis FM, Colver GB, Slater DN. Darier's sign associated with non-Hodgkin's lymphoma. *Br J Dermatol* 1994;130:126-7
14. Goldman MP, Kaplan RP, Heng MC. Congenital smooth muscle hamartoma. *Int J Dermatol* 1987;26:448-52.
15. Grattan CEH, Black AK. Urticaria and mastocytosis. In: Burns T, Breathnach S, Cox N, Griffiths G, editors. *Rook's Textbook of Dermatology*. 7th ed. Blackwell publishing; 2004. p. 47.1-47.37."