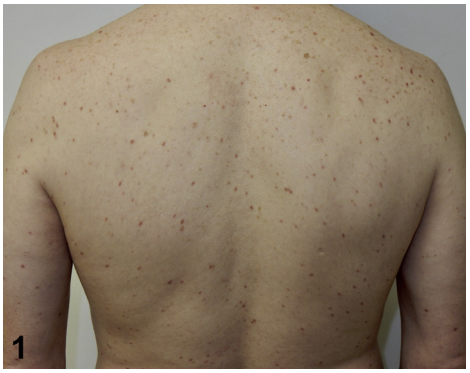
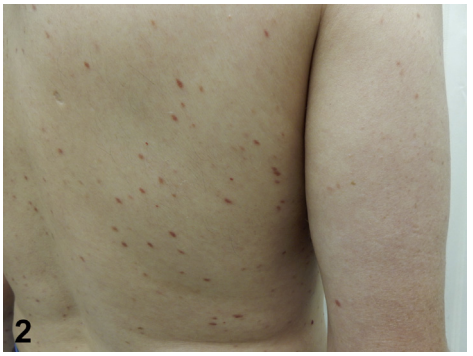
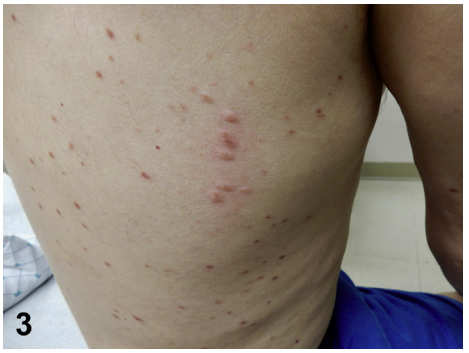
Pigmented pruritic papules in a middle-age man

Katherine T. Burke, MD, and Michael A. Cardis, MD
Washington, DC







A 46-year-old man presented with a 5-year history of brown papules that had been steadily increasing in size and number. They periodically became swollen and intensely pruritic, especially with physical exercise. He experienced 2 anaphylactic events in the past, 1 following a bee sting and the other idiopathic, both requiring advanced life support measures. Review of systems elicited a history of indigestion, abdominal pain, and diarrhea. Physical examination found innumerable reddish-brown macules and thin papules scattered over the trunk, arms, and upper thighs (Fig 1). Stroking of individual lesions elicited urtication within minutes (Figs 2 and 3).

Question 1: Which is the most likely diagnosis?

A. Mastocytosis

B. Darier disease

C. LEOPARD syndrome

D. Becker melanosis

E. Generalized eruptive histiocytoma

Answers:

A. Mastocytosis — Correct. Cutaneous mastocytosis, specifically urticaria pigmentosa type, is characterized by a progressive eruption of numerous red-brown, thin papules that urticate upon gentle friction (Darier sign). A thorough evaluation with a complete blood count with differential, liver function tests, and serum tryptase levels should be performed in adults

From the Medstar Washington Hospital Center/Georgetown University Hospital, Washington, DC.
Funding sources: None.
Conflicts of interest: None disclosed.
Correspondence to: Michael A. Cardis, MD, 5530 Wisconsin Ave, Suite 730, Chevy Chase, MD 20745. E-mail: michael.a.cardis@medstar.net.

JAAD Case Reports 2020;6:273-5.
2352-5126

https://doi.org/10.1016/j.jdcr.2020.01.027

presenting with cutaneous mastocytosis. Even in the absence of systemic symptoms, bone marrow biopsy and aspiration should be considered in adults, as the risk of systemic mastocytosis is high (73%-97%).[1-3]

B. Darier disease — Incorrect. Also known as *keratosis follicularis*, Darier disease is a heritable genodermatosis characterized by acantholytic dyskeratosis leading to an eruption of keratotic papules in a seborrheic distribution.

C. LEOPARD syndrome — Incorrect. LEOPARD syndrome is a RASopathy named after its common constellation of clinical features which include Lentigines, Electrocardiographic conduction defects, Ocular hypertelorism, Pulmonary stenosis, Abnormal genitalia, Retardation of growth, and sensorineural Deafness. Lentigines, and café noir spots, which morphologically present as macules and patches, respectively, are numerous in this condition and do not urticate upon manipulation.

D. Becker melanosis — Incorrect. Seen as part of Becker nevus, the clinical presentation is typically that of an isolated hyperpigmented patch with a unilateral distribution on the upper chest or back. They may exhibit pseudo-Darier sign—seen as transient induration of the area with gentle rubbing.

E. Generalized eruptive histiocytoma — Incorrect. Generalized eruptive histiocytoma is a form of non-Langerhans cell histiocytosis characterized by recurrent red-brown papules that are axially distributed. The lesions self-resolve leaving behind hyperpigmented macules and do not confer a Darier sign.

Question 2: Which gene plays a role in most cases of this patient's condition?

A. *BRAF*

B. *KIT*

C. *GNAQ*

D. *PTPN11*

E. *PRKAR1A*

Answers:

A. *BRAF* — Incorrect. Activating *BRAF* mutations play a role in the pathogenesis of benign melanocytic nevi and malignant melanoma.[4]

B. *KIT* — Correct. A somatic mutation involving codon 816 of the *KIT* gene is the most common genetic abnormality seen in patients with sporadic mastocytosis.[2]

C. *GNAQ* — Incorrect. *GNAQ* mutations are frequently associated with common and cellular blue nevi as well as some forms of malignant melanoma such as the uveal type.[4]

D. *PTPN11* — Incorrect. This is the gene implicated in LEOPARD syndrome, a familial lentiginosis syndrome. *PTPN11* encodes *SHP2* and is involved in the RAS-MAPK signaling pathway.[5]

E. *PRKAR1A* — Incorrect. Mutations in the *PRKAR1A* gene are implicated in most patients with Carney complex, a genodermatosis in which the cutaneous findings feature numerous lentigines and blue nevi. The gene plays a role in both endocrine tumor formation and proliferation of melanocytic lesions.[5]

Question 3: Which of the following may trigger a flare for this condition?

A. Oral antihistamines

B. Phototherapy

C. Bisphosphonates

D. Nonsteroidal anti-inflammatory drugs (NSAIDs)

E. Topical corticosteroids

Answers:

A. Oral antihistamines — Incorrect. Both H1 and H2-receptor blocking antihistamines are recommended for controlling symptoms associated with mastocytosis including pruritus, flushing, indigestion, and tachycardia.[3]

B. Phototherapy — Incorrect. Psoralen plus ultraviolet A or narrowband ultraviolet B therapy can be used to control pruritus and cutaneous whealing in patients with mastocytosis.[3]

C. Bisphosphonates — Incorrect. Most systemic mastocytosis in adult patients have involved skeletal pathology (osteosclerosis, osteopenia, osteoporosis, or osteolysis). Bisphosphonates block the bone-resorbing effect of osteoclasts and modulate the survival and function of osteoblasts and are the first-line treatment for osteoporosis related to mastocytosis.[3]

D. NSAIDs — Correct. Alcohol, NSAIDs, polymyxin, dye contrast, narcotics, and some systemic anesthetics are known to precipitate mast cell degranulation and should be avoided or used with caution in patients with mastocytosis.[3,6]

E. Topical corticosteroids – Incorrect. Steroids applied to the skin under occlusive dressings can decrease dermal mast cell volume and ultimately lead to fading of cutaneous lesions.[3]

Abbreviation used:

NSAID: nonsteroidal anti-inflammatory drug

REFERENCES

1. Berezowska S, Flaig M, Ruëff F, et al. Adult-onset mastocytosis in the skin is highly suggestive of systemic mastocytosis. *Mod Pathol*. 2014;27:19-29.
2. Valent P, Akin C, Metcalfe DD. Mastocytosis: 2016 updated WHO classification and novel emerging treatment concepts. *Blood*. 2016;129(11):1420-1427.
3. Valent P, Akin C, Escribano L, et al. Standards and standardization in mastocytosis: consensus statements on diagnostics, treatment recommendations and response criteria. *Eur J Clin Invest*. 2007;37:435-453.
4. Roh MR, Eliades P, Gupta S, Tsao H. Genetics of melanocytic nevi. *Pigment Cell Melanoma Res*. 2015;28(6):661-672.
5. Lodish MB, Stratakis CA. The differential diagnosis of familial lentiginosis syndromes. *Fam Cancer*. 2011;10(3):481-490.
6. Jennings S, Russell N, Jennings B, et al. The Mastocytosis Society survey on mast cell disorders: patient experiences and perceptions. *J Allergy Clin Immunol Pract*. 2014;2(1):70-76.