Photo Quiz

What Are These Multiple Brown Macules and Papules in an 11-Month-Old Boy?

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CITATION:
Guerra N, Gallagher M. What are these multiple brown macules and papules in an 11-month-old boy? *Consultant.* Published online XX. doi:XX

Received November 8, 2022. Accepted March 17, 2023.

DISCLOSURES:
The authors report no relevant financial relationships.

ACKNOWLEDGEMENTS:
None.

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An 11-month-old boy was brought into the clinic by his mother for evaluation of multiple widespread tan-brown macules and papules located on the infant's back and chest (Figure 1).

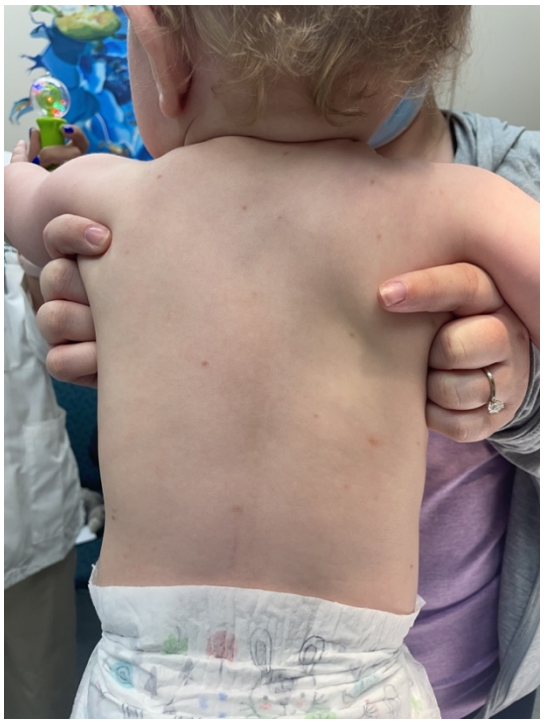

Figure 1. *Multiple tan macules and papules on the infant's back.*

History. The lesions had been present for approximately 7 months and had not been treated or evaluated previously. His mother reported that no at-home treatments, including topical ointments and creams, had improved or worsened the lesions and they were not triggered by any environmental stimuli. New lesions continued to appear, and all were asymptomatic without itch or pain. The patient had no significant past medical history or allergies. A physical examination showed numerous 1 to 3 mm light brown-tan macules and slightly raised papules on the back and chest.

Diagnostic testing. One of the lesions was lightly scratched with the wood-end of a cotton swab. After several minutes, the scratched lesion became itchy and erythematous, and wheal formation was observed. These findings were consistent with Darier sign (Figure 2).

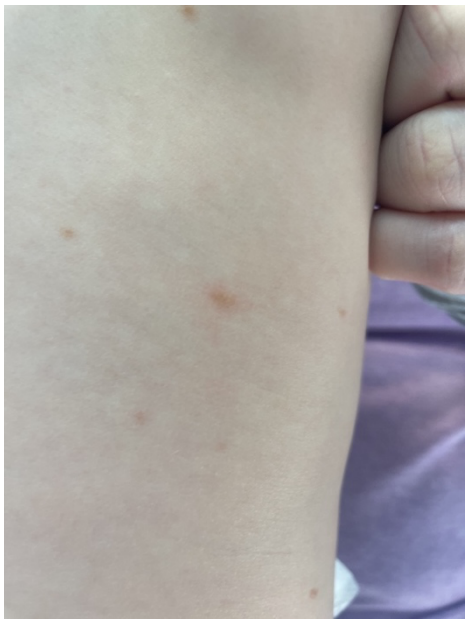

Figure 2*. Positive Darier sign.*

Based on these clinical findings, what is the most likely diagnosis?

A. Atopic dermatitis

B. Café-au-lait macules

C. Juvenile xanthogranuloma

D. Urticaria pigmentosa

Correct answer: D. Urticaria pigmentosa

The differential diagnosis for multiple brown macules and papules in children is broad and includes urticaria pigmentosa, atopic dermatitis, juvenile xanthogranuloma (JXG), and café-au-lait macules.

In contrast to our patient's presentation of persistent lesions on the chest and back, early atopic dermatitis typically presents with intermittent flares and remission of more widespread eczematous plaques. Lesions exhibit pruritis with physical examination findings of xerosis (dry skin), lichenification (skin thickening), and skin inflammation on the face, neck, and extremities.[1]

JXG typically presents during the first year of life. The classic clinical presentation of JXG consists of solitary or multiple yellow-orange-brown firm papules or nodules on the face, neck, or upper torso,[2] whereas the lesions of urticaria pigmentosa are flatter and have a predilection for the trunk, extremities, and flexural areas.[3] Contrary to the accumulation of mast cells in the dermis[4] as seen in urticaria pigmentosa, the histopathology of JXG shows collections of histiocytes in the superficial dermis.[2] The cutaneous lesions of JXG do not exhibit Darier sign, and children's lesions tend to resolve spontaneously with an unremarkable course.[2]

Café-au-lait macules are light- or dark-brown uniform melanin pigmentations with sharp demarcations, which may be associated with the autosomal-dominant condition neurofibromatosis type 1 (NF-1). They can range in size, from numerous freckle-like macules less than 2 mm to large brown macules greater than 20 cm. These macules do not exhibit Darier sign. With NF-1, café-au-lait macules are present at birth or within the first 3 years of life and may be associated nervous system, bone, and endocrine manifestations.[4]

Urticaria pigmentosa is characterized by disseminated tan macules to slightly raised brown papules with a widespread symmetric distribution and a positive Darier sign after rubbing.[4] The condition presents between birth and 2 years of age with a widespread symmetric distribution[2] classically on the trunk, extremities, and flexural areas.[3] Clinical diagnosis can be made using a Darier sign,[4] which avoids the need for a biopsy in young children. The condition typically resolves spontaneously with age, usually in puberty.[3,4]

Treatment and management. Treatment for urticaria pigmentosa is usually symptomatic and includes topical calcineurin inhibitors, topical corticosteroids, and more commonly used systemic medications, such as oral antihistamines. For more problematic cases, oral corticosteroids, omalizumab, and phototherapy can be used.[5] Management also includes avoidance of environmental triggers.[6]

Outcome and follow-up. The patient's mother was counseled on avoiding substances and environments that may provoke mast cell activation,[6] including NSAIDs and hot water. She was also informed that the lesions would likely resolve on their own by puberty, although there is a chance they may persist. A screening serum tryptase level, complete blood count, and comprehensive metabolic panel were ordered. The patient was lost to follow-up and results are unavailable.

Discussion. Urticaria pigmentosa is a classification of generalized cutaneous mastocytosis. Mastocytosis is a condition of abnormal accumulations of mast cells (mastocytomas) in the skin and internal organs, although most individuals present only with cutaneous manifestations (Table 1).[4] In the pediatric age group, 10% to 15% of cutaneous mastocytosis cases present as a solitary mastocytoma, which is clinically identifiable as a 1 to 5 cm erythematous, yellow or reddish-brown, round or oval macule, papule, plaque or nodule, with peau d'orange appearance and a rubbery consistency.[7] Mastocytomas contain physiologically active substances, including histamine, prostaglandin D2, heparin, and neutral protease/acid

hydrolases, which contribute to clinical findings of urticaria, gastrointestinal and cardiovascular symptoms, and flushing.[4]

Mast Cell Activators:

allergens, bacteria, cytokines, drugs, fungi, peptides, toxins and viruses		
System	**Mediators**	**Symptoms**
Cutaneous	CRH, chymase, histamine, interleukin-6, interleukin-8, interleukin-33, PAF, PGD2, YNF, tryptase	flushing, pruritis, urticaria, angioedema
Cardiovascular	CRH, chymase, interleukin-6, PAF, renin, TNF, tryptase	hypotension, syncope/near syncope, light-headedness, tachycardia
Digestive	CRH, chymase, histamine, interleukin-6, neurotensin, PAF, PGD2, serotonin, TNF, tryptase, VIP	abdominal cramps, diarrhea, esophageal reflux, nausea & vomitting
Systemic	CRH, chymase, histamine, interleukin-6, TNF	fatigue, generalized malaise, weight loss

Table 1. Effects of mast cells on different organ systems.[6]

Guidelines recommend all patients with any severity of suspected mastocytosis have a complete history and physical examination completed. Serum tryptase levels should also be checked to help guide further investigation.[6] If basal serum tryptase levels are 20 ng/mL or greater or symptomatic event-related levels are increased by 20% above baseline, bone marrow biopsy and genetic testing may be warranted to screen for systemic disease. However, if tryptase levels are elevated during a symptomatic event and no baseline levels are available, they should be rechecked 24 hours after the resolution of symptoms. If basal tryptase levels are normal or slightly elevated (11.5-20 ng/mL) and skin lesions are present, a skin biopsy is diagnostic.[6]

Conclusion. Urticaria pigmentosa is a form of cutaneous mastocytosis, a condition characterized by the accumulation of mast cells in different areas of the body. Most cases of mastocytosis are limited to the skin and resolve spontaneously during puberty. However, more severe cases may be systemic and require treatment. Urticaria pigmentosa can be diagnosed clinically, using the Darier Sign and a thorough history and physical examination. Further investigation may be indicated to rule out systemic disease.

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