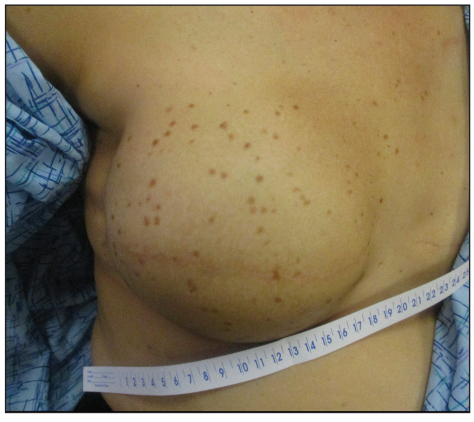
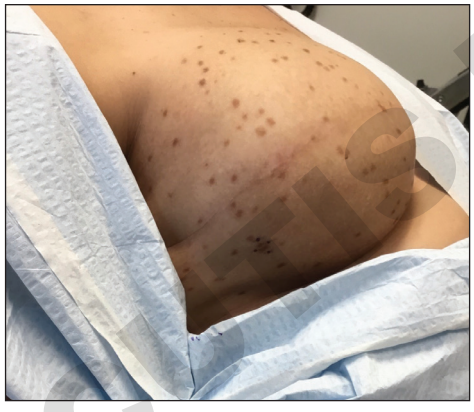
Diffusely Scattered Macules Following Radiation Therapy

Lauren E. Openshaw, BS; Ghada Al Sanna, MBBS; Tanya Nino, MD





A 41-year-old woman was referred to dermatology by her radiation oncologist for evaluation of a rash on the right breast at the site of prior radiation therapy of 4 to 6 weeks' duration. Approximately 2 years prior, the patient was diagnosed with triple-negative invasive ductal carcinoma of the right breast. She was treated with neoadjuvant chemotherapy, bilateral simple mastectomies, and 28 doses of adjuvant radiation therapy. Thirteen months after completing radiation therapy, the patient noted the onset of asymptomatic freckles on the right breast that had appeared over weeks and seemed to be multiplying. Physical examination at the time of dermatology consultation revealed multiple diffusely scattered, brownish-red, 3- to 5-mm macules concentrated on the right breast but also involving the right supraclavicular and right axillary areas, abdomen, and thighs.

WHAT'S THE **DIAGNOSIS?**

a. cutaneous mastocytosis
b. eruptive seborrheic keratoses
c. fixed drug eruption
d. lichen planus pigmentosus
e. solar lentiginosis

PLEASE TURN TO PAGE E37 FOR THE DIAGNOSIS

Lauren E. Openshaw is from the George Washington University School of Medicine, Washington, DC. Dr. Al Sanna is from the Department of Dermatology, Desert Pathology Medical Group, Los Angeles, California. Dr. Nino is from the Department of Dermatology, St. Joseph Heritage Medical Group, Orange, California.
The authors report no conflict of interest.
Correspondence: Lauren Openshaw, BS (laurenopenshaw13@gmail.com).
doi:10.12788/cutis.0953

THE **DIAGNOSIS:** Cutaneous Mastocytosis

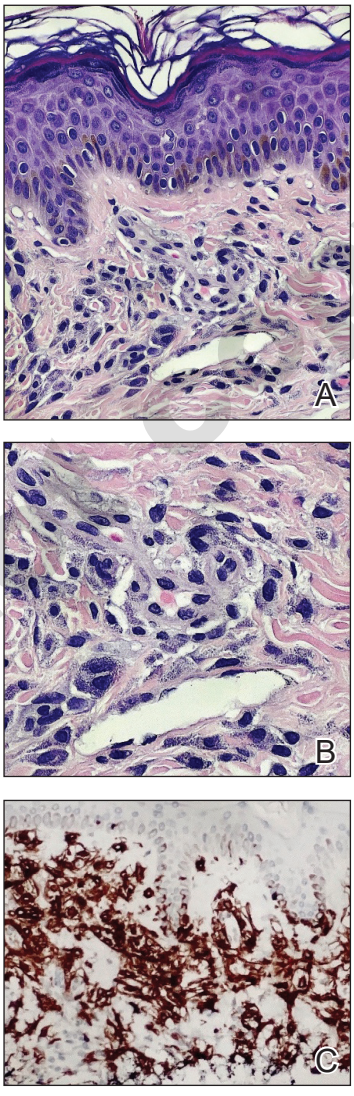
A shave skin biopsy from the right lateral breast and a punch skin biopsy from the right thigh showed similar histopathology. There were dermal predominantly perivascular aggregates of cells demonstrating basophilic granular cytoplasm and round to oval nuclei (Figure, A and B). These cells were highlighted by CD117 immunohistochemical stain (Figure, C), consistent with mastocytes. Additionally, occasional lymphocytes and rare eosinophils were noted. These histopathologic findings confirmed the diagnosis of cutaneous mastocytosis (CM). The patient's complete blood cell count was within reference range, but serum tryptase was elevated at 15.7 µg/L (reference range, <11.0 µg/L), which prompted a bone marrow biopsy to rule out systemic mastocytosis (SM). The result showed normocellular bone marrow with no evidence of dysplasia or increased blasts, granuloma, lymphoproliferative disorder, or malignancy. Fluorescence in situ hybridization for *PDGFRA* (platelet-derived growth factor receptor alpha) and *KIT* mutation was negative. Because CM developed predominantly on the right breast where the patient previously had received radiation therapy, we concluded that this reaction was triggered by exposure to ionizing radiation.

Mastocytosis can be divided into 2 groups: CM and SM.[1] The histologic differential diagnosis of CM includes solitary mastocytoma, urticaria pigmentosa, telangiectasia macularis eruptiva perstans, and diffuse mastocytosis.[2] Clinicopathologic correlation is of crucial importance to render the final diagnosis in these disorders. Immunohistochemically, mast cells express CD177, CD5, CD68, tryptase, and chymase. Unlike normal mast cells, neoplastic cells express CD2 and/or CD25; CD25 is commonly expressed in cutaneous involvement by SM.[2]

Macdonald and Feiwel[3] reported the first case of CM following ionizing radiation. Cutaneous mastocytosis is most common in female patients and presents with red-brown macules originating at the site of radiation therapy. Prior literature suggests that radiation-associated CM has a predilection for White patients[4]; however, our patient was Hispanic. It also is important to note that the presentation of this rash may differ in individuals with skin of color. In one case it spread beyond the radiation site.[2] Systemic mast call–mediated symptoms can occur in both CM and SM. The macules manifest as blanching with pressure.[5] Typically these macules also are asymptomatic, though a positive Darier sign has been reported.[6,7] The interval between radiotherapy and CM has ranged from 3 to 24 months.[2]

Patients with CM should have a serum tryptase evaluation along with a complete blood cell count, serum biochemistry, and liver function tests. Elevated serum tryptase has a high positive predictive value for SM and should prompt a bone marrow biopsy. Our patient's bone marrow biopsy results failed to establish SM; however, her serum tryptase levels will be carefully monitored going forward. At the time of publication, the skin macules were still persistent but not worsening or symptomatic.

Treatment is focused on symptomatic relief of cutaneous symptoms, if present; avoiding triggers of mast cell degranulation; and implementing the use of oral antihistamines and leukotriene antagonists as needed. Because



A, Histopathology revealed dermal perivascular aggregates of mast cells (H&E, original magnification ×200). B, Higher magnification demonstrated the typical basophilic granular cytoplasm and the bland round-oval dark basophilic nuclei of mast cells (H&E, original magnification ×200). C, Dermal mast cells were highlighted by CD117 immunohistochemical stain (original magnification ×200).

our patient was completely asymptomatic, we did not recommend any topical or oral treatment. However, we do counsel patients on avoiding triggers of mast cell degranulation including nonsteroidal anti-inflammatory drugs, morphine and codeine derivatives, alcohol, certain anesthetics, and anticholinergic medications.[8]

Additional diagnoses were ruled out for the following reasons: Although lichen planus pigmentosus presents with ill-defined, oval, gray-brown macules, histopathology shows a bandlike lymphocytic infiltrate at the dermoepidermal junction. Solar lentiginosis is characterized by grouped tan macules in a sun-exposed distribution. A fixed drug eruption is a delayed hypersensitivity reaction, usually to an ingested medication, characterized by violaceous or hyperpigmented patches, with histopathology showing interface dermatitis with a lymphoeosinophilic infiltrate. Eruptive seborrheic keratoses can result from sunburn or dermatitis but does not show mastocytes on histopathology.[8]

In conclusion, dermatologists should be reminded of the rare possibility of CM when evaluating an atypical eruption in a prior radiation field.

REFERENCES

1. Landy RE, Stross WC, May JM, et al. Idiopathic mast cell activation syndrome and radiation therapy: a case study, literature review, and discussion of mast cell disorders and radiotherapy [published online December 9, 2019]. *Radiat Oncol*. 2019;14:222. doi:10.1186/s13014-019-1434-6
2. Easwaralingam N, Wu Y, Cheung D, et al. Radiotherapy for breast cancer associated with a cutaneous presentation of systemic mastocytosis—a case report and literature review. *J Surg Case Rep*. 2018;2018:1-3. doi:10.1093/jscr/rjy317
3. Macdonald A, Feiwel M. Cutaneous mastocytosis: an unusual radiation dermatitis. *Proc R Soc Med*. 1971;64:29-30.
4. Kirshenbaum AS, Abuhay H, Bolan H, et al. Maculopapular cutaneous mastocytosis in a diverse population. *J Allergy Clin Immunol Pract*. 2019;7:2845-2847. doi:10.1016/j.jaip.2019.04.003
5. Soilleux EJ, Brown VL, Bowling J. Cutaneous mastocytosis localized to a radiotherapy field. *Clin Exp Dermatol*. 2008;34:111-112. doi:10.1111/j.1365-2230.2008.02931.x
6. Comte C, Bessis D, Dereure O, et al. Urticaria pigmentosa localized on radiation field. *Eur J Dermatol*. 2003;13:408-409.
7. Davidson SJ, Coates D. Cutaneous mastocytosis extending beyond a radiotherapy site: a form of radiodermatitis or a neoplastic phenomenon? *Australas J Dermatol*. 2012;54:E85-E87. doi:10.1111/j.1440-0960.2012.00961.x
8. Bolognia J, Schaffer JV, Duncan KO, et al, eds. *Dermatology Essentials*. 2nd ed. Elsevier; 2022.