Recurrent Pruritic Erythematous and Pigmented Plaques

consultant360.com/photo-quiz/recurrent-pruritic-erythematous-and-pigmented-plaques-fixed-drug-eruption

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A 37-year-old woman presented to a dermatology clinic for evaluation of recurrent, pruritic, inflamed plaques on her neck, thigh, back, and shoulder.

History. The lesions had flared at irregular sporadic intervals over the past year and resolved with hyperpigmentation (Figures 1 and 2). The patient's history was notable for atopic dermatitis, bilateral pulmonary embolism, and a 3-year history of recurrent candida infections, with the most recent infection occurring 2 months prior to presentation. The patient reported using triamcinolone 0.1% cream as needed for her atopic dermatitis and topical clotrimazole 2% cream for 3 nights when needed for vaginal candidiasis.

Empiric therapy with hydrocortisone cream 2.5% applied twice daily for 2 months was ineffective in resolving the hyperpigmentation. Her family history was remarkable for her mother, father, and sister all having sarcoidosis. She denied any allergies or exposure to any allergens. She did not associate the skin findings with any of her medications or over the counter substances. She was otherwise in good health.

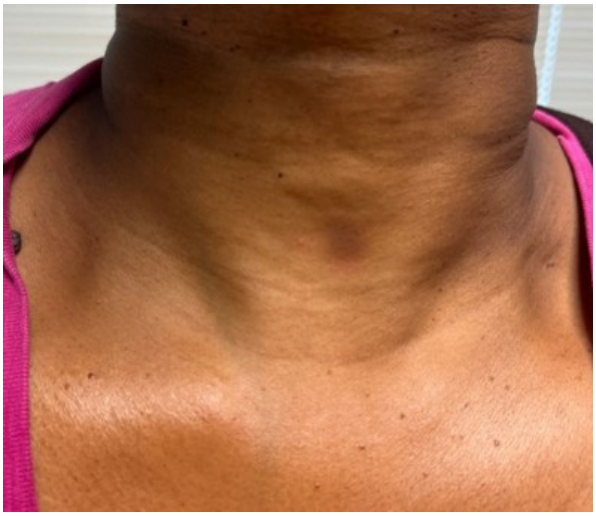

Figure 1. *Hyperpigmented area on the patient's anterior neck.*

Figure 2. *Hyperpigmented plaque on the patient's thigh.*

Diagnostic testing. Biopsies of the thigh for routine histology and direct immunofluorescence were performed at the time of the office visit. Necrotic keratinocytes, eosinophils, and melanophages were noted (Figures 3 & 4) in the biopsy results. The inflammation was distributed along the dermal-epidermal junction, but no blisters were encountered. No granulomas were identified and the biopsy for direct immunofluorescence failed to reveal deposition of immunoreactants along the dermal-epidermal junction or in any other location.

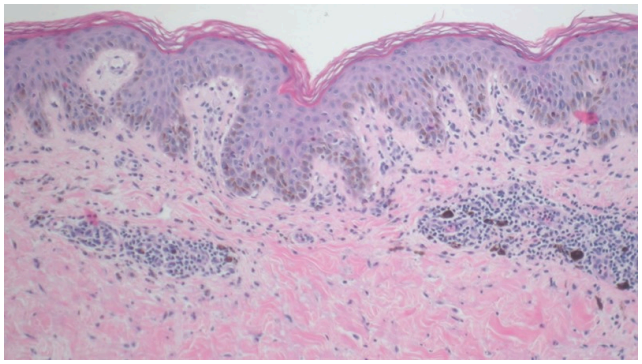

Figure 3.*Biopsy reveals necrotic keratinocytes and an inflammatory infiltrate with numerous melanophages (hematoxylin and eosin-stained sections, original magnification 100x).*

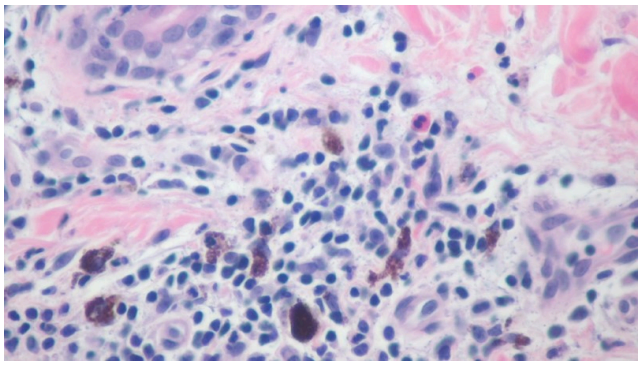

Figure 4. *Numerous eosinophils are evident within the inflammatory infiltrate and are found in proximity to melanophages (hematoxylin and eosin-stained sections, originalmagnification 200x).*

Answer and discussion on the next page.

Answer: B. Fixed Drug Eruption

Fixed drug eruptions typically present as erythematous edematous oval plaques. Medications, food, and even nutritional supplements can cause this reaction pattern. Medications are the most common cause and often include: [1-8]

Allopurinol	Lamotrigine
Amoxicillin	Melatonin
Anticonvulsants	Metronidazole
Atenolol	Minocycline
Barbiturates	Naprosyn
Carbamazepine	Omeprazole
Ceftriaxone	Ondansetron
Celecoxib	Paclitaxel
Chloral hydrate	Phenazone
Chlorhexidine	Phenolphthalein
Codeine	Prochlorperazine
Docetaxel	Pseudoephedrine
Fluoroquinolone	Sulfamethoxazole
Gabapentin	Tetracycline
Ibuprofen	Trimethoprim
Iodinated radiologic contrast media	

Sarcoidosis can present with a wide variety of lesions and, given the strong family history, was considered in the clinical differential diagnosis. A biopsy of sarcoidosis lesions typically reveals granulomas composed of multiple histiocytes, which were not identified in our patient.[9,10] Bullous pemphigoid may begin with nummular lesions, but a biopsy typically reveals early blister formation. The necrotic keratinocytes evident in our case

would not be characteristic of bullous pemphigoid. A biopsy for direct immunofluorescence reveals immunoglobulin G and C3 along the dermal epidermal junction.[9] Lesions of urticaria are typically transient and do not last for longer than 24 hours. A biopsy of lesions of urticaria reveals edema and a perivascular infiltrate but wouldn't have the epidermal changes noted on the biopsy results of our patient.[9]

Treatment and management. Initial lesions of fixed drug eruption often occur on the genitalia or the lips but can occur anywhere on the body surface. Lesions develop as late as 2 weeks after exposure to the inciting factor, so patients often fail to associate the eruption with a particular medication. Non-steroidal inflammatory medications, antibiotics, anticonvulsants, and allopurinol are common culprits.[9] Identification and discontinuation of the offending chemical are critical to resolution.

Outcome and follow-up. Once the biopsy results established a diagnosis of fixed drug eruption, the patient was asked for a more detailed medication history. She noted that she was given fluconazole 150 mg which she took intermittently over the previous 6 months for repeated cutaneous candida infections. This was then determined to be the culprit for the fixed drug eruption. An oral methylprednisone acetate 4 mg 6-day dosepak was administered for maintenance and the patient's eruptions resolved over 6 months following the discontinuation of fluconazole. A follow-up was not required.

Discussion. Fixed drug eruptions should be in the differential diagnosis whenever clinicians encounter an episodic eruption. Previous sites of involvement can become inflamed again, but new lesions may develop over time, so the eruption can be extensive at times.[9] A biopsy can help to better characterize the eruption and to exclude similar clinical presentations.

A careful medical history is crucial in identifying the offending agent. Identifying the source can be difficult because the offending agent is usually taken or received intermittently, may be an over-the-counter medication (and therefore not considered a drug by the patient), and because most drug reactions are widespread and symmetric.

Fixed drug eruptions are considered a type of type IV delayed hypersensitivity reactions.[9] Initial phase memory CD8+ cells release interferon after the offending agent damages the basal layer of the epidermis.[11] Patients can be reassured that lesions gradually fade after the inciting agent is stopped.

While a typical case of fixed drug eruption, this case highlights the need to often go back and take a more detailed patient history. Periodic exposure to medications, environmental

allergens, and other substances should be among the first question asked of patients presenting with a periodic eruption.

References

1. Blume JE, Ali L, Ehrlich M, Helm TN. Drug eruptions. Medscape. Updated July 7, 2022. Accessed July 3, 2023. https://emedicine.medscape.com/article/1049474-overview
2. Temiz SA, Ozer I, Ataseven A, Findik S. A case of entecavir-associated bullous fixed drug eruption and a review of literature. *Turk J Gastroenterol.* 2019;30(3):299-302. doi:10.5152/tjg.2018.17887
3. Flowers H, Brodell R, Brents M, Wyatt JP. Fixed drug eruptions: presentation, diagnosis, and management. *South Med J.* 2014;107(11):724-7. doi:10.14423/SMJ.0000000000000195
4. Fukushima S, Kidou M, Ihn H. Fixed food eruption caused by cashew nut. *Allergol Int.* 2008;57(3):285-287. doi:10.2332/allergolint.C-07-58.
5. Cho YT, Lin JW, Chen YC et al. Generalized bullous fixed drug eruption is distinct from Stevens-Johnson syndrome/toxic epidermal necrolysis by immunohistopathological features. *J Am Acad Dermatol.* 2014;70(3):539-48. doi:10.1016/j.jaad.2013.11.015
6. Shaker G, Mehendale T, De La Rosa C. Fixed drug eruption: an underrecognized cutaneous manifestation of a drug reaction in the primary care setting. *Cureus.* 2022;14(8):e28299. doi:10.7759/cureus.28299
7. Binns HM, Tasker F, Lewis FM. Drug eruptions and the vulva. *Clin Exp Dermatol.* Published online October 31, 2023. doi:10.1093/ced/llad369
8. Mysorekar VV, Sumathy TK, Shyam Prasad AL. Role of direct immunofluorescence in dermatological disorders. *Indian Dermatol Online J.* 2015 May-Jun;6(3):172-80. doi:10.4103/2229-5178.156386.
9. Helm KF, Foulke GT, Marks JG. *Differential diagnosis in dermatology.* 2nd Ed. JP Medical Publishers, 2018.
10. Clarke LE, Clarke JT, Helm KF. *Color atlas of differential diagnosis in dermatopathology*. Jaypee Brothers Medical Publishers, 2014.
11. Shiohara T, Mizukawa Y. Fixed drug eruption: the dark side of activation of intraepidermal CD8+ T cells uniquely specialized to mediate protective immunity. *Chem Immunol Allergy.* 2012;97:106-121. doi:10.1159/000335623.

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