

## Intermittent plaque on the neck



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**Key words:** drug reaction; fixed drug eruption; loratadine; rash; scaly plaque.



A 33-year-old man presented with a rash on the right side of his neck that recurred several times in the same location over the last 3 months (Fig 1). It persisted for several days without itching, burning, or alleviating factors. He is an accountant without relevant occupational exposures. No changes of personal care products were noted. Medical history is significant for seasonal allergies. He initially denied using any medications but later recalled taking loratadine infrequently for his seasonal allergies. Physical examination found a large erythematous plaque with central violaceous hue and fine scale on the right side of his neck.

### Question 1: What is the most likely diagnosis?

- A. Erythema annulare centrifugum (EAC)
- B. Granuloma annulare (GA)
- C. Fixed drug eruption (FDE)
- D. Pseudolymphoma

- E. Erythema migrans (EM)

### Answers:

- A. EAC – Incorrect. EAC presents with erythematous papular lesions that advance peripherally to form arcuate or annular plaques with central clearing and only occasionally pigmentary changes.

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Funding sources: None.

Conflicts of interest: None disclosed.

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JAAD Case Reports 2018;4:1024-6.  
2352-5126

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<https://doi.org/10.1016/j.jidcr.2018.09.018>

These ring-like lesions may show a trailing scale behind the advancing edge.

**B.** GA — Incorrect. Plaque centers are often hypopigmented relative to the edges. The ring-shaped lesions do not scale. No surface change is a crucial finding in differentiating GA from other annular eruptions.

**C.** FDE — Correct. A recurrent rash in the same fixed location with intermittent use of loratadine is consistent with FDE. The reaction can occur hours to days after ingestion of an offending drug and then resolves within days to weeks. The residual hyperpigmentation may remain for weeks to months.<sup>1</sup> Common medications causing FDE include sulfonamides, nonsteroidal anti-inflammatory drugs, tetracyclines, barbiturates, aspirin, and oral contraceptives.<sup>2</sup> Identification and elimination of the offending agent is central to the treatment. Topical steroids and oral antihistamines are used for symptomatic relief.<sup>2</sup> In this case, loratadine was the inciting agent, which has been reported rarely in the literature.

**D.** Pseudolymphoma — Incorrect. Typical lesions of pseudolymphoma are pruritic smooth papules or plaques on the head or neck. Recurrence in the same location is not seen in pseudolymphoma.

**E.** EM — Incorrect. EM has a slow outward expansion over 3 to 6 weeks with a central clearing and targetoid appearance. FDEs do not typically expand.

**Question 2: What is the pathophysiology for this phenomenon?**

- A.** Immunologic reaction
- B.** Infection/inoculation
- C.** Trauma
- D.** Malignant degeneration
- E.** Phototoxic reaction

**Answers:**

**A.** Immunologic reaction — Correct. Although the pathophysiology is only partially known, it is thought to be caused by the offending drug acting as a hapten by binding to proteins in basal keratinocytes and melanocytes.<sup>3</sup> CD8<sup>+</sup> T cells then migrate into the epidermis and are activated by the drug hapten. The stimulated CD8<sup>+</sup> T cells attack the drug-altered epidermal cells and release of interferon- $\gamma$ . The recruitment of CD4<sup>+</sup> T cells and neutrophils occurs, which furthers the inflammatory reaction. Upon re-exposure to the same antigen, the CD8<sup>+</sup> T cells respond more rapidly and robustly.<sup>2,4</sup>

By acting phenotypically similar to effector memory T cells, these CD8<sup>+</sup> T cells contribute to the tissue injury and necrosis when re-exposed to inciting antigen.<sup>4</sup>

**B.** Infection/inoculation — Incorrect. This would be the pathophysiologic explanation for EM. Infection occurs after tick bite and inoculation of the spirochete *Borrelia burgdorferi*.

**C.** Trauma — Incorrect. There was no history of trauma to this site before the appearance of the lesion.

**D.** Malignant degeneration — Incorrect. Malignant lesions such as squamous or basal cell carcinoma do not heal and recur, but instead they persist and progress.

**E.** Phototoxic reaction — Incorrect. Phototoxic reactions are from the absorption of ultraviolet light by a systemic drug. The drug then releases reactive oxygen species and free radicals that damage the skin. An FDE is immunologic in nature and not phototoxic.

**Question 3: What is the histopathology?**

**A.** Focal spongiosis and parakeratosis with an underlying superficial perivascular infiltrate of lymphocytes, often with a coat-sleeve appearance.

**B.** Palisaded granuloma with epithelioid histiocytes surrounding an anuclear dermis with altered collagen and pallor from mucin deposition.

**C.** Superficial and deep perivascular infiltrate and lichenoid tissue reaction with dyskeratotic cells within epidermis; pigmentary incontinence from damaged melanocytes.

**D.** Lymphoid cells throughout the dermis in a nodular and diffuse pattern with germinal center formation and tingible body macrophages present.

**E.** Superficial and deep lymphoid infiltrates admixed with a few eosinophils and plasma cells.

**Answers:**

**A.** Incorrect — This would be the typical histopathology seen in EAC. Although a perivascular infiltrate is seen within both EAC and FDE, coat-sleeve appearance is more specific to EAC.

**B.** Incorrect — This would be the typical histopathology seen in GA. The presence of mucin is key to diagnosis of GA; mucin is not normally present histologically in FDE.

**C.** Correct — FDE will manifest as a lichenoid tissue reaction with dyskeratotic necrotic cells

within the epidermis along with vacuolar changes at the dermoepidermal junction and edema at the papillary dermis. Superficial and deep interstitial and perivascular infiltrate composed of lymphocytes, eosinophils, and occasionally neutrophils is commonly found within the papillary and mid-dermis.<sup>2,5</sup> Damage to the melanocytes within the basal layer leads to pigmentary incontinence and leakage of melanin into the papillary dermis that is engulfed by macrophages.

**D.** Incorrect – This would be the typical histopathology seen in pseudolymphoma. The presence of germinal centers and tingible bodies are present in pseudolymphoma and not seen in FDE.

**E.** Incorrect – This would be the typical histopathology seen in EM. The histology of EM is not always very specific. However, polymerase chain reaction analysis can confirm the presence of *Borrelia spirochetes* within a tissue sample.

#### Abbreviations used:

EAC: erythema annulare centrifugum  
EM: erythema migrans  
FDE: fixed drug eruption  
GA: granuloma annulare

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