

CASE REPORT

Probable multifocal bullous fixed drug eruption

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ABSTRACT

Background: Fixed drug eruptions (FDEs) are a form of delayed-type hypersensitivity mediated by CD8+ T cells triggered by offending agents resulting in recurrent lesions. Multifocal bullous subtypes are rarer but do exist and can mimic other blistering diseases posing a diagnostic challenge in the emergency department setting.

Case Presentation: A 54-year-old Malay lady presented to the emergency department with a painful blistering rash over bilateral extensor forearm and elbow. They appeared as dusky, well-demarcated round plaques with central tense bullae. She had six to seven similar episodes over the past two years, recurring every three to four months with self-resolution each time. Skin biopsy demonstrated superficial perivascular dermatitis with pigmentary incontinence. Direct immunofluorescence and autoimmune serology with blistering disease BP 180 and BP 230 were negative. These findings support a diagnosis of probable multifocal bullous fixed drug eruption. The culprit agent was not identified, and the patient was advised for cessation of potential triggers.

Conclusion: Early dermatology review with skin biopsy in patients presenting with blistering diseases is important for accurate diagnosis and to exclude other life-threatening blistering diseases. FDE may occur without clearly identifiable drug triggers and thorough history taking is essential.

Keywords: Fixed drug eruption, bullous dermatoses, adverse drug reaction, emergency medicine.

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Background

Fixed drug eruptions (FDEs) are a form of classic delayed-type hypersensitivity (DTH) mediated by CD8+ T cells, characterized by recurrent lesions that occur at the same sites upon exposure to the offending agent. While FDEs typically present as solitary pruritic macules, some can present as widespread bullous lesions with systemic symptoms. [1] Common triggers include drugs such as acetaminophen, non-steroidal anti-inflammatory drugs (NSAIDs) and antibiotics. [1,2] Recurrent FDE without a significant preceding history of drug intake has also been reported, possibly related to non-specific exogenous factors such as food / UV exposure. [1] The multifocal bullous variant demonstrated in this case is a rarer subtype that poses a diagnostic challenge, especially in the emergency setting.

Case Presentation

A 54-year-old Malay lady presented to the emergency department with a painful blistering rash over bilateral

arms. The lesions began as pruritic patches that turned erythematous, before evolving into painful blisters over 2–3 days.

She reported that she has had six to seven similar episodes in the past 2 years, occurring once every three to four months with recurring lesions over bilateral arms that self-resolved within a few days; none had previously blistered. She has no past medical history, no known drug allergies, and is not on any chronic medications. She denied recent use of over-the-counter medications, analgesics, traditional medications, or supplements prior to her rash. She had seen a general practitioner three days after onset and was given throat lozenges and promethazine, both started after the rash appeared. She works as a cleaner and has been doing so for the past 10 years with no recent changes in chemicals she is exposed to.

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61 Examination revealed multiple dusky well-demarcated
62 round plaques with central tense bullae on bilateral
63 extensor forearm and elbow as seen in Figure 1 covering
64 an area of 3%–4% body surface area with intervening
65 normal skin. She had no oral ulceration, genital lesions,
66 or conjunctival injection.

67 Initial investigations including a full blood count and
68 renal function were normal with no eosinophilia.

69 She was reviewed by the dermatologist in the emergency
70 department the same day. She declined admission and was
71 discharged with next-day dermatology review, at which
72 a skin biopsy for histology was performed. The biopsy
73 demonstrated superficial perivascular dermatitis with
74 pigmentary incontinence. Direct immunofluorescence,
75 indirect immunofluorescence, and autoimmune serology
76 with blistering disease BP 180 and BP 230 were negative.
77 Grocott-Gomori Methenamine Silver (GMS) stain was
78 negative for fungal organisms. Taken together with the
79 clinical history, these findings support a diagnosis of
80 probable multifocal bullous fixed drug eruption.

81 The culprit agent could not be reliably identified. At the
82 dermatology visit, the patient brought all the products
83 she used and disclosed two medicated nasal inhalers
84 bought in Thailand (one liquid and one solid stick; brand
85 and ingredients not documented), which she had used
86 intermittently since early 2025, and a camphor, menthol,
87 and methyl salicylate medicated oil (Axe Brand), which
88 she had inhaled occasionally at work since shortly before
89 this episode. Neither product was in use before her
90 first episode in 2023, the frequency of use before each

episode could not be recalled, and no re-exposure was 91
documented. The patient was advised to stop using all 92
nasal inhalers and the oil and was referred to an allergist 93
for patch testing. 94

Clobetasol propionate 0.05% cream twice daily was 95
started after the biopsy and continued for 15 days; no 96
systemic treatment was required. At review on day 16, 97
all lesions had healed, leaving round hyperpigmented 98
patches at the same sites, with no new lesions. She was 99
scheduled for dermatology review at six months. Patch 100
testing was not subsequently performed, and no further 101
attendance or recurrence has been recorded in our 102
institution to date; formal follow-up beyond day 16 is not 103
documented. 104

Discussion 105

FDE without an obvious drug history 106

While FDEs are classically associated with a positive 107
preceding drug history, there was an absence of a clearly 108
identifiable culprit drug in this case despite thorough 109
history taking. While FDEs are commonly incited by 110
agents such as NSAIDs and certain classes of antibiotics, 111
they can also be triggered by non-prescription agents. 112
These include herbal / traditional remedies such as 113
ginkgo biloba [3], certain foods such as nuts and seafood 114
[4], and topical decongestants in a case series by Shelley 115
et al. [5] The latter being a potential trigger in this case. 116
Patients may not regard these products as medications, so 117
clinicians should specifically enquire about all over the 118
counter products, traditional medications, topical agents, 119



Figure 1. Clinical photographs demonstrating multiple well-demarcated round violaceous plaques with central bullae on bilateral extensor forearm and elbow.

and even foods when evaluating for suspected FDE, especially in the absence of an obvious conventional drug trigger. In cases where the culprit agent cannot be identified from history alone, formal patch testing is recommended to identify the agent and to prevent recurrence. [6] In this case, neither product can be linked temporally to her earlier episodes, so the diagnosis is best described as probable FDE; the unidentified culprit is the main limitation of this report.

Histopathological findings

Histopathological findings in FDE include vacuolar interface dermatitis with superficial perivascular infiltration of eosinophils and lymphocytes. Other features include the presence of scattered apoptotic keratinocytes, pigment incontinence, and dermal melanophages. [4,7] In the present case, the skin biopsy demonstrated superficial perivascular dermatitis with pigmentary incontinence, consistent with FDE in a resolving or post-inflammatory phase. These findings are supportive rather than specific, as the biopsy was taken around day ten when the lesions were already resolving. Negative direct and indirect immunofluorescence and negative bullous pemphigoid (BP180/BP230) antibodies make bullous pemphigoid unlikely but do not confirm FDE and were interpreted in the clinical context.

Differentiating from other blistering pathologies

The multifocal bullous variant of FDE can closely mimic other blistering diseases and careful clinical and pathological correlation is essential. In this case, the strongest arguments for FDE were the recurrent lesions at identical sites and the absence of mucosal or systemic involvement.

Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are a continuum of severe adverse drug reactions. It typically involves widespread skin lesions consisting of blisters arising on erythematous or purpuric macules with mucosal involvement. It is also associated with systemic features such as fever and raised inflammatory markers and carries significant morbidity and mortality risk. [8] In contrast, our patient had no mucosal involvement, normal biochemistry results, and a clear history of recurrent morphologically similar lesions at the same bilateral extensor sites. However, generalized bullous FDE (GBFDE) can also present similarly to SJS/TEN and involve mucosal surfaces with systemic features, [1,4] making clinical diagnosis challenging, and in such cases, granulysin expression in skin lesions can be useful in establishing the diagnosis.[7]

Bullous pemphigoid (BP) is the most common form of autoimmune blistering disease, driven by circulating immunoglobulin G (IgG) autoantibodies against the hemidesmosomal antigens BP180 and BP230. [9] The gold standard for diagnosis of BP is detection of immune deposits of IgG and / or complement component 3 along the basement membrane zone (BMZ) using direct immunofluorescence. In the present case, both serological and direct immunofluorescence testing were negative, making BP unlikely.

Erythema multiforme (EM) is an acute, self-limiting disease typically associated with hypersensitivity reactions to viruses such as herpes simplex virus. While drugs are also a potential etiology for EM, it is implicated in less than 10% of cases. [10] EM is characterized by classical targetoid erythematous lesions with a predominantly acral distribution, and mucosal involvement is estimated to be up to 60%. [10] While FDE shares many clinical and pathologic features of EM, it can be distinguished histopathologically from EM by the presence of fewer neutrophils and more prominent melanin incontinence. [4,7] In the current case, absence of classic targetoid morphology, combined with a recurrent fixed pattern favoured FDE over EM.

Role of early dermatology review

This case highlights the importance of early dermatologist involvement in patients presenting to the emergency department with blistering diseases. Early skin biopsy with histopathology and immunofluorescence studies allows for a definitive diagnosis to be established and excludes life-threatening conditions such as SJS/TEN. Without histopathological confirmation, FDE risks being misclassified as SJS/TEN or EM, exposing patients to unnecessary systemic immunosuppression and potentially prolonged hospitalization. Allergy assessment with patch testing is equally important, as without it recurrence cannot be prevented.

The rash in this case resolved within two weeks with topical corticosteroid therapy, before the suspected products were stopped, consistent with the self-limiting course of FDE.

Conclusion

Multifocal bullous fixed drug eruption is a rare but clinically important differential diagnosis for patients presenting to the emergency department with multiple blistering lesions. Its resemblance to more serious conditions such as SJS/TEN and autoimmune bullous diseases demand early recognition. This case highlights the importance of early dermatology review and skin biopsy, which can establish an accurate diagnosis and safe management of blistering diseases in the emergency setting. It also highlights that FDE may arise without a clearly identifiable classical drug trigger, and a thorough history inclusive of non-prescription products, traditional medications, and topical preparations is essential.

List of Abbreviations

BMZ	Basement membrane zone	
BP	Bullous pemphigoid	
DTH	Delayed-type hypersensitivity	
EM	Erythema multiforme	
FDE	Fixed drug eruption	
GBFDE	Generalized bullous fixed drug eruption	
GMS	Grocott-Gomori Methenamine Silver	
IgG	Immunoglobulin G	
NSAIDs	Non-steroidal anti-inflammatory drugs	
SJS	Stevens-Johnson syndrome	
TEN	Toxic epidermal necrolysis	

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252	References	
253	1. Shiohara T. Fixed drug eruption: pathogenesis and diagnostic	264
254	tests. <i>Curr Opin Allergy Clin Immunol</i> . 2009;9(4):316–21.	265
255	https://doi.org/10.1097/ACI.0b013e32832cda4c	266
256	2. Lee CH, Chen YC, Cho YT, Chang CY, Chu CY. Fixed-	267
257	drug eruption: a retrospective study in a single referral	268
258	center in northern Taiwan. <i>Zhonghua Pifuke Yixue Zazhi</i> .	269
259	2012;30(1):11–5. https://doi.org/10.1016/j.dsi.2012.02.002	270
260	3. Cohen PR. Fixed drug eruption to supplement containing	271
261	ginkgo biloba and vinpocetine: a case report and review	272
262	of related cutaneous side effects. <i>J Clin Aesthet Dermatol</i> .	273
263	2017;10(10):44–7.	274
	4. Anderson HJ, Lee JB. A review of fixed drug eruption	275
	with a special focus on generalized bullous fixed drug	276
	eruption. <i>Medicina (Kaunas)</i> . 2021;57(9):925. https://doi.org/10.3390/medicina57090925	277
	5. Shelley WB, Shelley ED. Nonpigmenting fixed drug	278
	eruption as a distinctive reaction pattern: examples caused	279
	by sensitivity to pseudoephedrine hydrochloride and	280
	tetrahydrozoline. <i>J Am Acad Dermatol</i> . 1987;17(3):403–7.	281
	https://doi.org/10.1016/S0190-9622(87)70220-5	282
	6. Traineau H, Milpied B, Soria A, Assier H, Tetart F, Bernier	283
	C, et al. In situ patch test and repeated open application	284
	test for fixed drug eruption: a multicenter study. <i>J Allergy</i>	285
	<i>Clin Immunol Pract</i> . 2024;12(2):460–8. https://doi.org/10.1016/j.jaip.2023.10.021	286
	7. Cho YT, Lin JW, Chen YC, Chang CY, Hsiao CH, Chung WH, et	287
	al. Generalized bullous fixed drug eruption is distinct from	288
	Stevens-Johnson syndrome/toxic epidermal necrolysis	289
	by immunohistopathological features. <i>J Am Acad</i>	290
	<i>Dermatol</i> . 2014;70(3):539–48. https://doi.org/10.1016/j.jaad.2013.11.015	291
	8. Paulmann M, Reinkemeier F, Lehnhardt M, Mockenhaupt	292
	M. Case report: generalized bullous fixed drug	293
	eruption mimicking epidermal necrolysis. <i>Front Med</i>	294
	(Lausanne). 2023;10:1125754. https://doi.org/10.3389/fmed.2023.1125754	295
	9. Daniel BS, Murrell DF. Review of autoimmune blistering	296
	diseases: the Pemphigoid diseases. <i>J Eur Acad Dermatol</i>	
	<i>Venereol</i> . 2019 Sep;33(9):1685–94. https://doi.org/10.1111/jdv.15679	
	10. Sokumbi O, Wetter DA. Clinical features, diagnosis, and	
	treatment of erythema multiforme: a review for the	
	practicing dermatologist. <i>Int J Dermatol</i> . 2012;51(8):889–	
	902. https://doi.org/10.1111/j.1365-4632.2011.05348.x	