

Bullous Fixed Drug Eruption Secondary to Chlorthalidone



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A fixed drug eruption (FDE) is a delayed hypersensitivity reaction characterized by solitary or multiple hyperpigmented oval lesions¹ that may affect any part of the body.² These lesions have a predilection for the trunk, lips, hands, and genital mucosa, and may recur on the same sites upon introduction of the causative agent.³ The drugs most commonly associated with FDE are antibiotics, analgesics, and anticonvulsants.^{1,4} We present a case of chlorthalidone-induced bullous FDE.

A 60-year-old woman with a medical history of hypertension and seasonal allergic rhinitis presented with a 4-year history of a recurring annual rash. Her only medication was chlorthalidone, which the patient had been taking consistently for the past 15 years. On presentation, she exhibited violaceous, pruritic, painful, 4-cm, circular papules with central blistering (Figure 1, A) located in her eyelids (Figure 1, B), lips (Figure 1, C), trunk, and extremities. The lesions recurred on the same location each year and lasted for approximately 1 week with complete resolution in 1 month (Figure 1, D). Laboratory workup was within normal limits including complete blood cell count with differential, complete metabolic panel, erythrocyte sedimentation rate, C-reactive protein, C3, C4, antinuclear antibody, and urinalysis. Initial biopsy with hematoxylin and eosin stain and immunofluorescence was nonconclusive. She was initially treated with desloratadine 5 mg, hydroxyzine 25 mg, and betamethasone cream daily without improvement. A repeat biopsy from a late-phase lesion revealed nonspecific postinflammatory hyperpigmentation. The main differential diagnosis included necrotizing angitis, erythema multiforme, and Steven-Johnson syndrome. Chlorthalidone was held because of a suspected FDE. Following this intervention, the patient remained lesion free for the last 18 months with the exception of hyperpigmented cutaneous changes on previously affected areas (Figure 1, E). Patch testing

and challenge were declined. The patient was instructed to avoid all thiazide-type diuretics and use equally efficacious alternatives.

FDE is a delayed cutaneous allergic reaction to a specific drug.⁵ Usually there is only 1 causative drug, but multiple drugs have been involved.⁶ Intraepidermal CD8+ T cells are thought to be responsible for cutaneous manifestations in FDE, producing large amounts of IFN- γ . After drug reexposure, cutaneous lesions may occur because of prolonged expression of intercellular adhesion molecule-1 in basal keratinocytes by participation of CD8+ effector/memory T cells.^{7,8}

Chlorthalidone, a thiazide-type diuretic that inhibits distal convoluted tubule sodium and chloride resorption, is a commonly used oral antihypertensive. FDE has not been previously reported in association with chlorthalidone administration.⁹ FDE is a clinical diagnosis and histological findings are usually supportive.³ The initial treatment of FDE is discontinuation of the causative agent, after which lesions typically improve, leaving only hyperpigmented changes on previously affected areas.⁷ To our knowledge, this is the first case reported in the literature of FDE secondary to chlorthalidone use. This case demonstrates the importance of a thorough medical history of clinical presentation to elucidate a causal agent and that drug sensitization in FDE may range from weeks to years. Although not validated, patch testing, intradermal testing with delayed readings (usually at 24 hours),¹⁰ and challenge should be performed when possible because they are useful tools for diagnosis.

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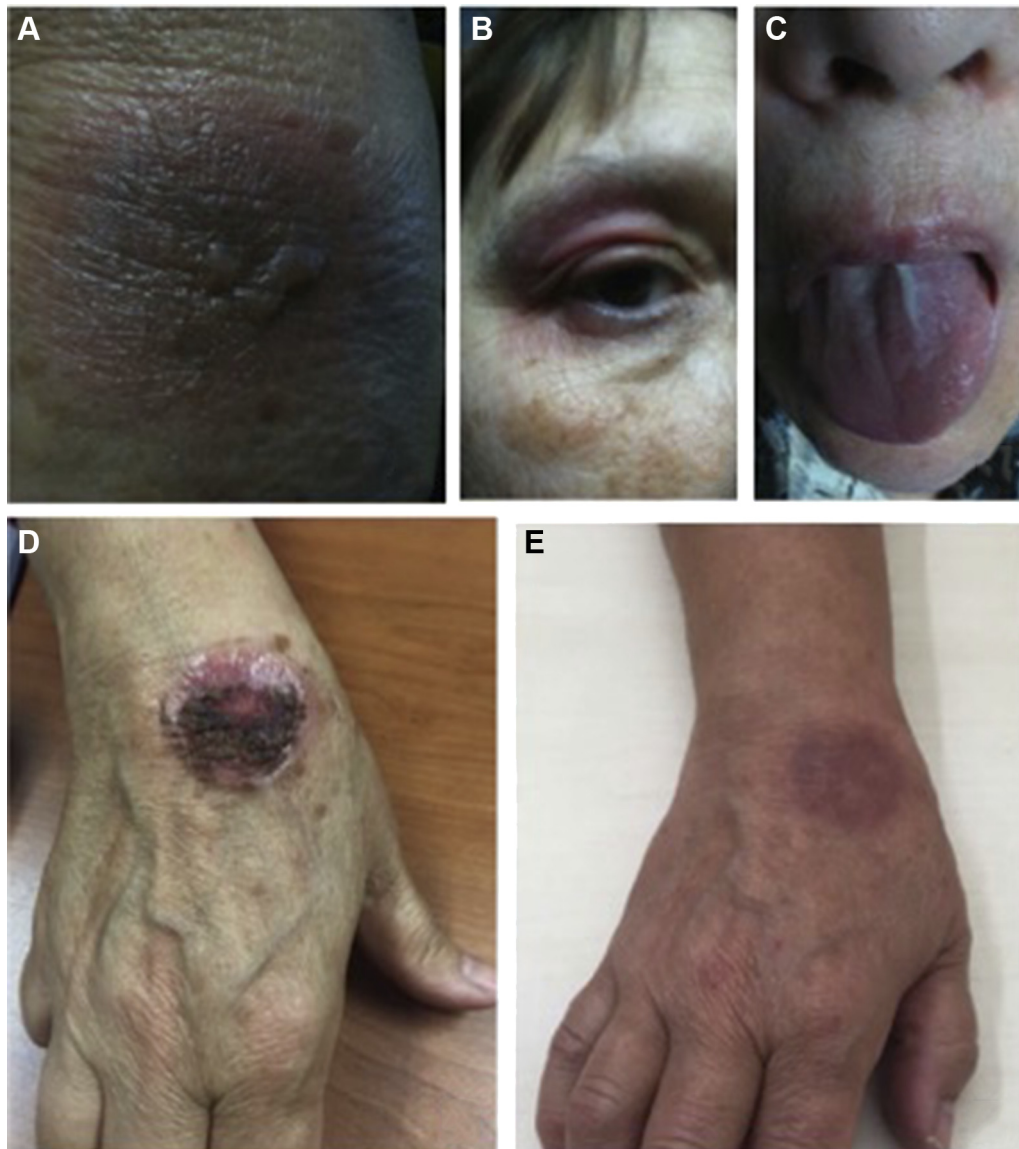


FIGURE 1. Circular violaceous papules on the patient's extremity (A), eyelid (B), and lip (C). D, Healing oval lesion. E, Lesion 18 months later with only hyperpigmented changes present.

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