

Case Report

## An Unusual Course in Bullous Morphea

İlknur Kıvanç Altunay, MD, Hilal Kaya Erdoğan\*, MD, Nurhan Döner, MD, Damlanur Sakız,<sup>1</sup> MD.

Address: Dermatology and <sup>1</sup>Pathology Departments, Şişli Etfal Training and Research Hospital, Istanbul, 34377, Turkey.

\* Corresponding Author: Dr. Hilal Kaya Erdoğan, Şişli Etfal Training and Research Hospital, Istanbul, 34377, Turkey.

E-mail: hilalkayaaa@yahoo.com

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**Key Words:** bullous morphea, drug reaction

### Abstract

**Observations:** We report a 75-year-old woman with bullous morphea characterized by disseminated erythematous-pigmentous plaques and a few blisters on some morphea plaques at the beginning of first visit. While she was under narrow band UV therapy, she discontinued the treatment and refused to have any more after 13 sessions. One month later, she reapplied with extensive bullae and facial edema with severe itching. We learned that she had taken naproxen sodium one a day for two days ten days ago. Bullous drug reaction was diagnosed and systemic cortisone was started. She was in remission after fifteen days. The patient had very different clinical picture on her second visit with extensive, large and cadaverous bullae, facial erythema and edema. It seems to be a bullous drug reaction based on bullous morphea. However, it remains a mystery whether this clinical presentation is a peculiar drug reaction or is really a mere exacerbation of existed bullous morphea.

### Introduction

Bullae formation in lesions of morphea is an interesting condition and is rarely reported in the literature [1]. Etiopathogenesis is not clear and therapy is unsatisfactory [1, 2, 3, 4, 5]. Herein, we present a patient of bullous morphea (BM) with a confusing course and evaluate this clinical picture in detail.

### Case Report

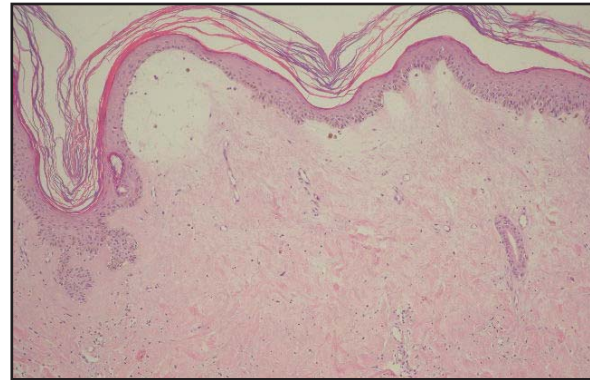
A 75 year old female patient was admitted to our clinic with disseminated erythematous-pigmentous plaques and scant blisters that occurred in a few plaques after a febrile disease. The patient complained of hardening of her skin. Her medical history revealed the presence of hypertension, diabetes mellitus, glaucoma and urinary incontinence. The medications used were niphedypin, gliclazide, lata-

noprost eye drop and tolterodine. These medications had been used for over a year. Her family history was unremarkable.

Dermatological examination revealed disseminated ivory-white, indurated plaques with pseudobullae impression located mostly on the abdomen and gluteal regions (Figure 1). Routine laboratory tests were within normal limits except hyperglycemia. Serological investigation including ANA, anti-SS-A, anti-SS-B, anti-Sm, anti-RNP, dsDNA, anti Scl-70, anti Jo-1 and *Borrelia* antibody tests were all negative. Skin biopsy revealed epidermal atrophy, decreased number of epithelial adnexial structures, thickened and homogenized collagen bundles with narrowed spaces between them, scant perivascular mononuclear infiltration and prominent papillary edema resulting in blister formation (Figure 2). Direct immunofluorescence examination of the skin was negative. A new blister



**Figure 1.** Ivory-white, indurated plaques with pseudo-bullae impression located on the gluteal region.



**Figure 2.** Thickened and homogenized collagen bundles with narrowed spaces between them, scant perivascular mononuclear infiltration and prominent papillary edema resulting in blister formation (H+E, x 40).

formed on the right lumbar region during her hospitalization. A second skin biopsy was performed from this new blister. Biopsy specimen of this blister demonstrated epidermal hyperkeratosis, thinning and severe subepidermal edema resulting in blister formation. There were many erythrocytes in blister fluid. Perivascular lymphocyte infiltration, thick and sclerotic collagen bundles were observed in dermis.

A diagnosis of bullous morphea was made and narrow-band UVB therapy was initiated (3 days/week). However, she stopped phototherapy by herself after 13 sessions (total cumulative dose: 18,6/cm<sup>2</sup>) and her follow-up visits failed. After one month, she was readmitted with a different clinical picture consisting of severe pruritus, facial erythema and mild edema of eyelids and widespread new bullae formations on different body areas (**Figure 3 a,b and c**). Nikolsky's sign was negative and there was no mucosal involvement. The patient revealed that she had used a nonsteroidal anti-

inflammatory drug 'naproxen sodium' for her myalgias. Punch biopsy obtained from a bullous lesion showed focal spongiosis, spongiotic vesiculation and lymphocytic exocytosis in the epidermis, perivascular inflammatory infiltration including lymphocytes and eosinophils in the papillary dermis and also sclerotic collagen in a focal area in the papillary dermis.

Direct immunofluorescence examination was negative. Laboratory examinations were unremarkable except hyperglycemia (153 mg/dl) and eosinophilia (18%). Considering a possible drug reaction, naproxen sodium was stopped and 40mg/day prednisolone therapy was started. Rapid healing was observed with desquamation. Prednisolone therapy was tapered gradually and stopped in one month. New blister formation was not observed in the follow-up period. After one month, we applied patch test with naproxen sodium on the back of the patient, and the test proved to be negative.



**Figure 3a, 3b and 3c.** Pemphigoid-like bullae and eroded areas on different regions of the body. Clinical photograph showing loss of eyebrow with multiple skin colored papules

## Discussion

Bullous morphea was first described by *Morrow* in 1896 [6]. Etiopathogenesis is still unknown. Various theories have been proposed [1, 2, 3, 4, 5]. *Templeton* suggested that bullae formation is attributed to lymphedema caused by dilated lymphatic vessels, which occurs as a result of lymphatic obstruction from the sclerodermatous process [7]. In addition, the observation of the lower extremities as the most common site of involvement suggests that the dilatation of lymphatic channels and the increase in venous pressure might play a role [4]. *Pautrier* suggested that vascular changes like arteritis and phleboscrosis play a role in bullae formation [8]. *O'Leary* found a correlation between local trauma and blister formation. *Kavala et al*, reported a case which had bullae on intertriginous areas and supported *O'Leary's* theory [2]. *Daoud et al*, found the eosinophil granule major basic protein (MBP) in the base of morphea blisters. They concluded that eosinophils and especially major basic protein are responsible for blister formation in some cases of morphea [1].

The fact that the patient attended to our clinic with more severe and different clinical picture and pemphigoid-like bullae made us think that the disease would be triggered by a noxious factor, possibly a drug. The presence of bullae on the intact skin areas besides morphea plaques, blood and tissue eosinophilia, rapid recovery with the cessation of suspected drug and rapid healing with desquamation after administration of corticosteroid therapy strongly supported that opinion. It was reported that naproxen sodium can cause bullous drug reactions as fixed drug eruption (FDE) or pseudoporphyria [9, 10]. However, the reaction in our patient was consistent with neither bullous FDE nor pseudoporphyria clinically and histopathologically, because there was neither sharply demarcated erythematous plaques healing with pigmentation clinically nor dyskeratotic cells and hydropic degeneration of basal cells histopathologically regarding FDE. Additionally, negative patch test excluded FDE.

Focused on pseudoporphyria, clinical signs such as scars, adherent crusts, erosions, milia and its histopathological findings including cell poor infiltrate, festooning of dermal papillae and thickened vessel walls were absent in our case. Thus, clinical and histopat-

ological findings which our patient showed was not in accordance with those generally seen in pseudoporphyria.

When considering other patterns of bullous drug eruptions such as drug induced pemphigus or pemphigoid, toxic epidermal necrolysis etc, we observed that both histopathological and immunofluorescence findings in our case failed to show any of these. Therefore, the burst of bullae after intake of naproxen sodium while the patient was in a stable period connotes that this is either a different bullous reaction accompanying BM, possibly drug eruption, or merely an exacerbation of BM. It is problematic which pathogenetic mechanism here plays a role. However, we can speculate that an immunologic pathway consisting of eosinophils and MBP might be a possible trigger for bulla formation, which supports *Daoud* and *et al's* report explaining bullae in BM. Thus, this issue still remains to be investigated.

## References

1. Daoud MS, Su WP, Leiferman KM, Perniciaro C. Bullous morphea: clinical, pathologic, and immunopathologic evaluation of thirteen cases. *J Am Acad Dermatol* 1994; 30: 937-943. PMID: 8188883.
2. Kavala M, Zindanci I, Demirkesen C, Beyhan EK, Turkoglu Z. Intertriginous bullous morphea: A clue for the pathogenesis? *Indian J Dermatol Veneerol Leprol* 2007; 73: 262-264. PMID: 17675738.
3. Gallagher TC. Bullous morphea. *Dermatol Online J* 2002; 8: 11. PMID: 12546766
4. Jia H, Chen XH, Shi JH, Zhao CX, Cao YH, Zeng XS, Chen XS. A case of bullous morphea reported in mainland China. *Int J Dermatol* 2002; 41: 949-950. PMID: 12493000
5. Su WP, Greene SL. Bullous morphea profunda. *Am J Dermatopathol* 1986; 8: 144-147. PMID: 3717524
6. Rowell MR, Goodfield MJD. The connective tissue diseases. In: *Textbook of Dermatology*. Eds. Champion RH, Burton JL, Burns DA, Breathnach SM. 6 th ed. Oxford: Blackwell Science, 1998: 2437-2575.
7. Templeton HJ. Localized scleroderma with bullae. *Arch Dermatol Syphilol* 1943; 43: 360-365.
8. Pautrier LM. Sclerodermie a evolution rapide, en plaques multiples. Importance des lesions vasculaires initiales et tardives dans l'etude de la sclerodermie. *Bull Soc Fr Dermatol* 1929; 36: 928-938.
9. Judd LE, Henderson DW, Hill DC. Naproxen-induced pseudoporphyria. A clinical and ultrastructural study. *Arch Dermatol* 1986; 122: 451-454. PMID: 3954412
10. Leivo T, Heikkilä H. Naproxen-induced generalized bullous fixed drug eruption. *Br J Dermatol* 2004; 151: 232. PMID: 15270899.