Case Report

Successful Oral Corticosteroid with Doxycycline as Adjuvant Therapy in a Case of Refractory Bullous Pemphigoid

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Abstract

Bullous pemphigoid (PB) is a bullous autoimmune disease that often occurs in elderly people. It can be triggered by age, drug use, trauma, ultraviolet exposure, radiation, genetic roles and stress. Treatment of PB with topical and oral corticosteroid drugs remains the main option.[1] However, recent control trial studies have shown the efficacy and safety of using doxycycline to reduce accumulated treatment dose and mortality. A 68-year-old male presented with widespread, itchy bullae that ruptured, releasing clear fluid and forming dark crusts. Physical examination revealed multiple tense bullae and erosions on the neck, trunk, and upper extremities. He was treated with oral and topical corticosteroids, wound care, topical moisturizers, and anti-inflammatory antibiotics. Clinical improvement was noted within 7 days, with continued follow-up over 2–3 months. Combined with oral and topical corticosteroids, doxycycline offers potential as a steroid-sparing agent to attenuate inflammation and prevent recurrence of PB.

Keywords: Bullous pemphigoid; therapy; corticosteroids; doxycycline.

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Introduction

Bullous pemphigoid is the most common bullous autoimmune disease in the adult population. The disease usually presents with itchy, tense blisters often appearing as urticarial plaques. PB occurs most commonly in the elderly. The pathogenesis of PB is related to the immune system, namely humoral and cellular responses to BP 180 and BP 230 antigens.[3] Risk factors for BP include old age, neurological diseases, certain medications, and stress.[5]

Oral prednisolone has been the standard treatment for bullous pemphigoid for more than 50 years, but it also comes with significant clinical side effects in geriatric patients and an uncertain optimal dose.[6] However, recent control trial studies have demonstrated the efficacy and safety of using doxycycline, dapsone, and immunosuppression to reduce accumulated treatment dose and mortality.[2] Doxycycline is an effective short-term therapy, can be a sparing agent for corticosteroid therapy, a safe long-term therapy and does not cause eosinophilia.[7] Another study showed that treatment for PB with doxycycline 200 mg daily resulted in acceptable short-term efficacy and had a significant safety advantage at 1 year compared to starting treatment with prednisolone 0-5 mg/kg per day.[8]

Case Report

The patient, a 68-year-old male, came to the outpatient clinic of RSUD Dr. Soetomo Surabaya with a complaint of a blisters. The blisters contain fluid and appeared since 3 months ago. Initially its app-

eared on the left hand near the wrist, then spread to the head, armpits, face then back and both hands. Initially, they were small like prickly heat and then turned into grimaces, widening and filled with clear, transparent yellow liquid. Blisters are also accompanied by itching. In addition, the patient also felt pain and stinging when the bulae burst. The patient had been treated at the nearest health facility, received methylprednisolone 40mg (16mg-16mg-8mg) tablets orally, cetirizine once a day and fusidic acid cream twice a day, but there was no improvement. A previous history of this kind of disease was denied. Family history similar to the patient was denied. History of oil rubbing was denied. Previous history of food and drug allergy was denied. History of diabetes mellitus and hypertension was denied.

The dermatologic status of the coli, fascia, capitis, and superior extremity regions revealed multiple, partially confluent, discrete tense-walled ulcers measuring 0.5 cm in diameter, with some ulcers showing rupture, erosion, and brownish crusts. Nikolski sign was negative. Laboratory investigations were within normal limits. The patient was then subjected to punch biopsy for histopathologic examination with the results showing subepidermal nodules with parakeratosis, spongiotic, inflammatory infiltrates of histiocytes and lymphocytes and eosinophil cells among collagenous tissue, which supported the picture of bullous pemphigoid. The immunoflorescence examination showed positive results where band-like IgG deposits were found in the basement membrane-zone (BMZ).

The diagnosis of bullous pemphigoid was based on anamnesis, physical examination, histopathologic examination and immunoflorescence record. Then the patient received methylprednisolone injection therapy 0.5 ml (62.5 mg) once a day, cetirizine tablets 10 mg orally once a day, doxycycline 100 mg twice a day orally, desoxymethasone cream 0.25% on red rashes on the body and extremities, mometasone cream 1% on rashes on the face and body folds, fusidic acid cream 2% on wounds, and Vaseline album moisturizer applied to the whole body. On the 7th day of treatment, there were no new blisters, therefore the patient was discharged with methylprednisolone therapy which had been reduced to 48 mg per day, cetirizine tablets 10 mg once daily orally, and 2% fusidic acid cream for wounds. At the control visit at the outpatient clinic, no new blisters were found, so the treatment was continued by lowering the corticosteroid dose . The dose of methyl-prednisolone was decreased by 4 mg per week at each follow-up, approximately two to three months until the drug was not given.

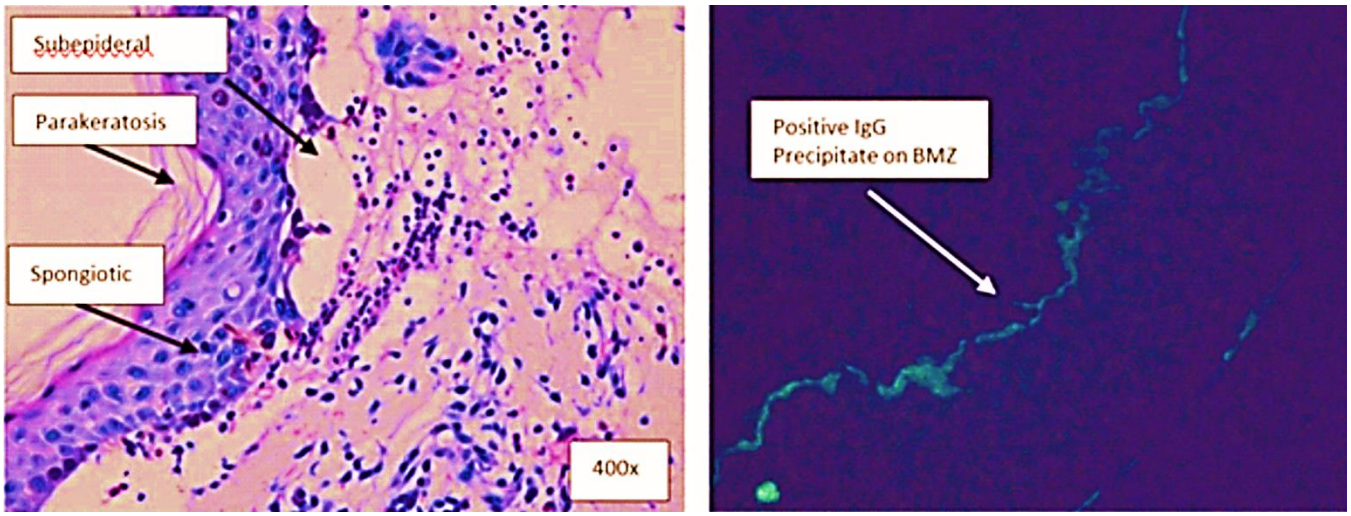

Figure 1: Subepidermal blister with eosinophils.

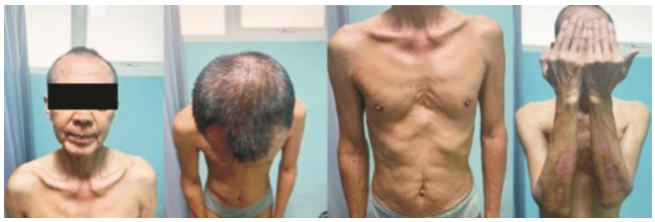

Figure 2: At the outpatient clinic (11 days after first admission). There were no blisters, the scar appeared pale in color.

Discussion

Bullous pemphigoid is the most common bullous autoimmune skin disease, and its incidence is increasing, partly due to its association with older age. To date the treatment of bullous pemphigoid is a challenge for clinicians. First-line treatment regimens, either oral corticosteroids or potent topical steroid applications can cause substantial morbidity and mortality in the elderly. In other literature, PB can be triggered by trauma, ultraviolet (UV) light, radiation therapy and there is a genetic role of certain human leukocyte antigens (HLA) that can increase the risk of developing the disease. There is also literature that mentions that psychiatric disorders can also be one of the comorbidities of PB, namely stress.[5,9] The patient's anamnesis denied any fever or trauma as well as previous drug consumption. The patient's work history was that of a college lecturer. It is suspected that exposure to high levels of stressors is one of the triggers in this case.

The standard treatment for PB is systemic corticosteroids, but treatment of PB ultimately depends on comorbidities and extent of disease. For localized disease, less than 20% body surface area in elderly patients, super-potent topical corticosteroids such as clobetasol can be used. Topical corticosteroids can be combined with nicotinamide plus tetracycline, minocycline, or doxycycline has shown success in some cases.[10]

For extensive disease, systemic prednisone at a dose of 0.5 to 1.0 mg/kg per day is recommended. This dose of systemic corticosteroid controls the disease in about two weeks and can be slowly tapered over six to nine months or more. This treatment regimen is limited by the patient's age, comorbidities and side effects.[3]

In this case, the patient was given intravenous methylprednisolone 62.5 mg (0.5 mL) per day and after seven days was then given orally at a dose of 48 mg in divided doses. Because there was clinical improvement with no new blisters, methylprednisolone therapy was reduced to a dose of 4 mg per week. Follow up the patient for approximately 2-3 months with additional therapy in the form of desoxymethasone cream 0.25% twice a day on red rashes, mometasone cream 1% twice a day for the administration of body folds and red rashes on the face neck, cetirizine 10 mg orally to treat pruritus, and also fusidic acid cream 2% twice a day applied to wounds or blisters that burst to prevent secondary infection. Doxycycline twice 100 mg orally was given for anti-inflammation. In addition, Vaseline album moisturizer was added to maintain skin moisture.

In this case, we show that the strategy of starting treatment for bullous pemphigoid with doxycycline 200 mg daily results in short-term efficacy compared to starting treatment with prednisolone 0-5 mg/kg per day. Doxycycline has been used as adjuvant therapy in PB due to its anti-inflammatory properties without immunosuppression. Inhibition of matrix metalloproteinases and neutrophilic activation caused by immune complex formation between IgG autoantibodies and PB anti-gens prevents disruption of the dermal-epidermal junction and can control PB recurrence. Williams et al, said that doxycycline played a role in disease control after 6 weeks of treatment compared to prednisolone 0.5 mg/kg/day, accompanied by a similar improvement in quality of life. Patients receiving doxycycline experienced significantly fewer side effects with a reduced risk of death.[6]

Tetracycline class antibiotics, such as doxycycline, are used to treat PB, as they have anti-inflammatory properties. In addition, some studies suggest that the addition of doxycycline is more effective in controlling new bullae and reducing the side effects of long-term steroids.[5,6] Another study provides new evidence that doxycycline has a positive effect in controlling PB when used for initial treatment rather than as a long-term treatment strategy. This study confirmed that oral corticosteroids

at a dose of 0-5 mg/kg per day are highly effective for mild to moderate disease compared to doxycycline. Doxycycline has a mechanism of action that can reduce the activation and proliferation of T cells, mast cells, and eosinophils, as well as inhibiting phospholipase A2 and proinflammatory cytokines. Side effects of doxycycline can be onycholysis and phototoxic.[6] In this case, there were no side effects of doxycycline administration.

Both drugs are relatively inexpensive and available worldwide. Where whole body applications of high potency topical corticosteroids over many months are ineffective. With the combination of oral doxycycline plus potent topical corticosteroid applications may be considered in preference to practices currently initiating treatment with oral prednisolone. This combination therapy can be a choice between short-term therapeutic effectiveness and long-term safety according to the severity of the PB patient's disease.[6]

In addition to the aforementioned drug treatment, patients are also given education on the prevention of disease recurrence, such as when doing outdoor activities, they should be protected by using sunscreen, closed clothes (long sleeves and pants), hats, and sunglasses. Other education relates to some of the side effects that may occur due to long-term use of topical corticosteroid therapy, and should not be used for more than two weeks. It is important to maintain control and medication adherence at outpatient clinic services to prevent relapse.

One study reported that 8 out of 30 adult patients with PB had remission after 15 months from active lesions.1 In well-treated patients, a 50% remission rate is achieved within three years of therapy. In this case, there was clinical improvement over a period of approximately 2-3 months of therapy. The prognosis of this patient is dubia ad bonam.

Conclusion

Treatment of Bullous Pemphigoid with systemic corticosteroid therapy combined with a steroid sparing agent, such as doxycycline, may show good results.

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Author's Contribution

DRM: Conceived, designed, edited the manuscript, given final approval of the version to be published, critical revisions

SW: Manuscript writing, final approval of the version to be published, agree to be accountable for all aspect of the work.

MAU: Manuscript writing, final approval of the version to be published, agree to be accountable for all aspect of the work

SA: Manuscript writing, final approval of the version to be published.

D: Conceived, designed, edited the manuscript, given final approval of the version to be published, critical revisions

CRSP: Manuscript writing, final approval of the version to be published, agree to be accountable for all aspect of the work.

References

1. Deotto ML, Spiller A, Sernicola A, Alaibac M. Bullous pemphigoid: An immune disorder related to aging. Exp Ther Med. 2022;23(1):50. Doi: 10.3892/etm.2021.10972.
2. Miyamoto D, Santi CG, Aoki V, Maruta CW. Bullous pemphigoid. A Bras Dermatol. 2019;94(2): 133-146. Doi 10.1590/abd1806-4841.20199007
3. Culton DA, Liu Zhi, Diaz LA. Bullous pemphigoid. In: Kang S, Amagai M, Bruck-ner AL, Enk AH, Margolis DJ, McMichael AJ, et al, editors. Fitzpatrick's Dermatology in General Medicine (9th ed). New York: Mc Graw Hill Inc; 2019.p.944-52.
4. Bernard P, Antonicelli F. Bullous Pemphigoid: A Review of its Diagnosis, Associations and Treatment. Am J Clin Dermatol. 2017;18(4):513-528. Doi: 10.1007/s40257-017-0264-2.
5. Rania M, Petersen LV, Benros ME, Liu Z, Diaz L, Bulik CM. Psychiatric comorbidity in individuals with bullous pemphigoid and all bullous disorders in the Danish national registers. BMC psychiatry. 2020;20(1): 411. Doi: 10.1186/s12888-020-02810-x.
6. Williams HC, Wojnarowska F, Kirtschig G, Mason J, Godec TR, Schmidt E, et al . Doxycycline versus prednisolone as an initial treatment strategy for bullous pemphigoid: a pragmatic, non-inferiority,

randomized controlled trial. Lancet. 2017;389 (10079):1630-1638.
Doi: 10.1016/S0140-6736(17)30560-3.

7. Kimura K, Kawai K. Doxycycline as an initial treatment of bullous pemphigoid in Japanese patients. Journal of Cutaneous Immunology and Allergy. 2020;3(4):80-5.
8. Singh S, Kirtschig G, Anchan VN, Chi C-C, Taghipour K, Boyle RJ, et al. Interventions for bullous pemphigoid Cochrane Database Syst Rev. 2023 Aug 11;8(8):CD002292.
Doi: 10.1002/14651858.CD002292.pub4.
9. Trisnowati DM, Budi HP, Gaspersz S, Durry M. Bullous Pemphigoid Treated with Corticosteroid: A Case Report. e-CliniC. 2022;10(2):400-5.
10. Mohammadi FK, Zoha S, Baleeqhuddin M, Ali SM, Faizan AM. A Case Report on Idiopathic Severe Bullous Pemphigoid. J. Drug Delivery Ther. 2020;10(4-s):223-5. Doi: 10.22270/jddt.v10i4-s.4311.