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CASE REPORT

Oral Bullous Pemphigoid Induced by Gabapentin: A Case Report

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ABSTRACT

Drug eruptions typically present with maculapapular rashes and blisters over the body and trunk. Gabapentin was rarely associated with bullous pemphigoid however, the link is still possible, involving localized oral lesions in which oral inspection is indeed essential. We reported a rare case of gabapentin induced oral bullous pemphigoid in an elderly patient who presented with localized lips and gums swelling. The association with gabapentin was almost missed due to the atypical presentation. We ceased the drug immediately. His condition improved by co-management with a dermatologist and application of high dose topical steroid. This case highlighted the importance of adequate history taking, thorough physical examination and immediate management of acute dermatological cases which can save the patient's life.

KEYWORDS: Gabapentin, oral, bullous pemphigoid

INTRODUCTION

Adverse drug reactions are defined by the World Health Organization (WHO) as a response to a medication that is noxious and unintended in the person to treat [1]. The event could be a consequence of a preventable medication and technical error, known side effect because of the medication administration, or an unforeseen effect such as an allergic reaction, which is unexpected [2]. The drug eruptions are common, affecting up to 3 percent of hospitalized patients and among the commonest reason for outpatient visits [1,2]. One of the diagnosis under drug eruptions include bullous pemphigoid with worldwide prevalence of 0.012% [3]. Bullous pemphigoid is one of the chronic autoimmune skin diseases that is associated with generalized bullous lesion. However, it is rarely diagnosed. It often leads to production of pruritic and large blisters with erosions, typically on skin and mucous membrane [3,4]. Physical agents, viral infections and drugs are among the common inducing factors. Gabapentin is among the associated drugs [3,4]. Despite its primary usage for seizure control, gabapentin is also prescribed by primary care doctors to reduce neuropathic pain [5]. It has a good safety profile and can be tolerated by patients. It has a low incidence of adverse reactions such as gastrointestinal symptoms, instability, and headache. Even though rarely reported, gabapentin has been linked with bullous pemphigoid incidence affecting the trunk and limbs but sparing the

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oral cavity [3-5]. Thus, isolated oral lesion is indeed a rare manifestation of bullous pemphigoid induced by gabapentin in which the conclusion towards the diagnosis could be delayed.

CASE PRESENTATION

A 66-year-old man came to our clinic complaining of sudden onset of swollen upper and lower lips for two days. It was associated with itchiness and tenderness. He also noticed a localized erythematous rash over his left cheek since the onset of his oral lesion. On further questioning, he had a prior history of taking tablet gabapentin 300 mg three times a day for one week before the onset of the lesions. His medical practitioner had prescribed the drug to reduce the neuropathic pain of his foot secondary to his diabetic peripheral neuropathy. He had no history of insect bite or trauma. He had no previous history of allergy to foods or drugs. He is a non-smoker. He had no other comorbidities except his underlying diabetes mellitus.

On clinical assessment, he was afebrile with stable vital signs. Face inspection revealed several tense bullous lesions over his swollen upper lips with desquamative lesions over his gums as shown in Figure 1. Figure 2 is a closer view of the patient's lip with desquamative lesions. Other system examinations were unremarkable. His blood sugar was noted to be within normal range. We immediately withheld the drug and referred him to the dermatology team for further evaluation and management. He has benefited from histopathological analysis of the edge of his blister lesion. No other investigation was done due to diagnosis being supported clinically with typical bullae presentation. His symptoms gradually improved after applying high potency topical corticosteroid for one week.

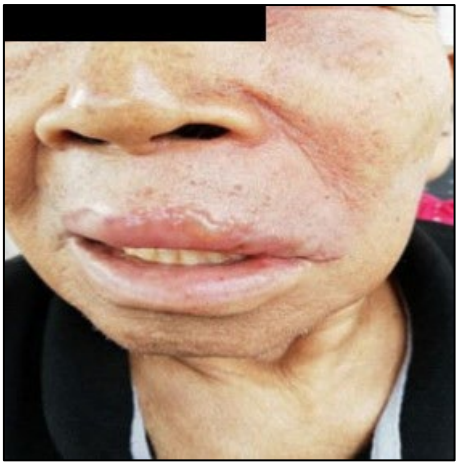

Figure 1 Several bullous lesions over the patient's swollen upper lips with desquamative lesions over the patient's gums

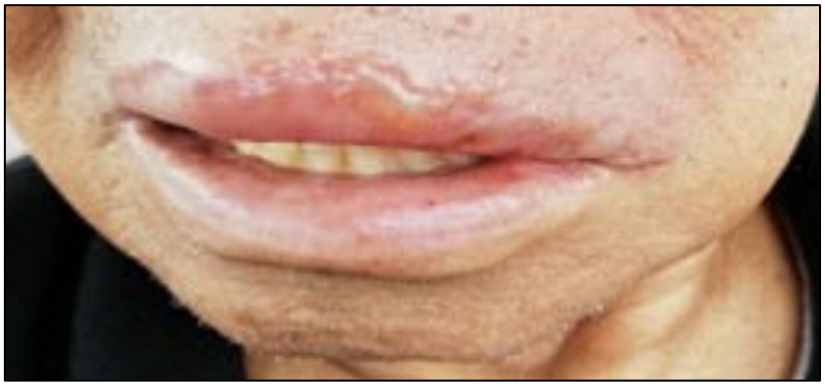

Figure 2 Closer view of the desquamative lesions

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DISCUSSION

Multiple drugs have been implicated in the pathogenesis of the bullous pemphigoid, including antibiotics, antihypertension, non-steroidal anti-inflammatory drugs, antidiabetics, and antiepileptics [3,4]. It typically appears as tense bullae on normally appearing skin, especially involving the scalp, abdomen, extremities, axilla, and groin. It may be accompanied by erythema multiforme or target lesions on palms and soles [3-5]. Nevertheless, oral involvement can be seen in 10%–20% of cases. The oral lesions are smaller, appear more slowly, and are less painful than those seen in pemphigus vulgaris. This might lead to the delay complaints by patients and therefore late diagnosis and management by the health care providers [3,4,6]. Gingival lesions also had been reported to consist of generalized oedema, inflammation, and desquamation with localized areas of discrete vesicle formation. These also might be misdiagnosed as infective gingivitis especially if the timeline association with drug intake has not been asked properly [3,4,6].

Drug-induced pemphigus can develop within days, weeks, or months following consumption of the offending agent. It can occur due to either oral or topical administration of the drugs. Therefore, timeline relation between onset of the rashes or lesions with the exact day the patient was prescribed with the drugs is indeed essential. Thus, rather than wait for the patient to complain, each health care provider should be cautious enough to do adequate history taking and appropriate physical examination to avoid medical errors. In a high-risk group of patients especially in elderly or on polypharmacy or having underlying comorbidities, it is practical to give early follow up to identify potential drug induced reactions in the first few weeks whenever a new drug has been prescribed [6].

Approaches of managing oral lesions in primary care need to be performed in the systematic manner to identify the subsequent management pertaining to the probable diagnosis. First, adequate history taking, and physical examination should be done in order to identify either the patients present with alarming clinical features or stratified as a high-risk group. This includes the possibility of malignancy, autoimmune disease, infections, or drug eruptions. Second, is to identify concomitant systemic symptoms such as fever, joint pain, or cutaneous stigmata of specific diseases. Presence of systemic symptoms signify underlying serious disorder rather than localized causes alone. Third, is to stratify the patient either safely to be followed up at home or need to be admitted. This includes identification of patient age, comorbid, inability to take orally and psychosocial factors together with a support system at home. Nevertheless, in whatever steps that had been taken, the moment the physician felt indecision in the definitive diagnosis of the patient, further opinion from the tertiary centre needs to be sought immediately [7].

Few differential diagnoses can be made based on the oral blister and bullae lesions such as impetigo, urticaria, toxic epidermal necrolysis (TEN), eczema, bullous lupus erythematosus, erythema multiforme and pemphigus foliaceous. About the case, our patient had no other systemic symptoms and no prior history of skin lesions which make the diagnosis of lupus erythematosus, erythema multiforme, urticaria or eczema to be unlikely. There is also no association of purulent discharges with crusted lesions on skin inspection, which made the diagnosis towards skin infection to be unlikely. The lesions are also localized without other severe skin peeling characteristics, and these made the diagnosis of TEN to be excluded from clinical suspicion. Other than that, Nikolsky sign is also absent in this case, which indirectly makes the diagnosis to be not related with pemphigus foliaceous [3-5].

Gabapentin is an antiepileptic medication, commonly used for the treatment of neuropathic pain and postherpetic neuralgia. Nevertheless, each medication has its own side effects. The commonest side effect includes neurological symptoms such as ataxia, dizziness, drowsiness, and fatigue. Therefore, prior to its administration especially in geriatric patients, risk of fall should always be emphasized. Nevertheless, the other important side effect that needs to be informed especially in high-risk groups such as in elderly patients is the alarming skin eruptions such as Stevens-Johnson syndrome, even though it may occur in less than 1%. However, the other skin eruptions that may occur in elderly but not commonly reported is bullous pemphigoid. Gabapentin-induced bullous pemphigoid may occur even in those patients without

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prior history of allergy, atopy or adverse reaction to any drugs as in this case [3]. The symptoms typically occur within three weeks of initiation but may occur within days and one week as reported in our case [3]. In previous literature, there have been two cases of gabapentin induced bullous pemphigoid which also occurs in elderly and with underlying diabetes mellitus [3,8]. In comparison to our case, the symptoms reported in previous articles however were only presented with maculapapular rashes without involving the oral area [3,8].

Bullous pemphigoid is an autoimmune blistering disease that initially presented with pruritic eczematous and papular skin lesions which later followed by development of subepithelial blister formation that typically occurs on the upper extremities and spread to the trunk and lower extremities.[3-5] However, in our case, there is absence of prodromal lesions and the presentation only confined on the oral and lips area. This rare presentation might cause diagnostic challenges to the treating practitioner. Other similar diagnoses that might be presented with oral blisters includes primary herpetic gingivostomatitis, herpes zoster infection, herpangina, hand-foot-and-mouth disease, necrotizing ulcerative gingivitis and erythema multiforme. Malignancy such as ulcerative squamous cell carcinoma and chronic infection such as tuberculous ulcer may also mimic the oral blister presentation. Nevertheless, the underlying timeline association with drug initiation would narrow down the diagnosis towards drug induced oral eruptions. Onset at the age of more than 60 years old, with prominent features of vesicles together with presence of desquamative gingivitis would further support the diagnosis of oral bullous pemphigoid [3-5].

Nevertheless, idiopathic bullous pemphigoid is more common in elderly compared to drug induced bullous pemphigoid which is more frequently encountered in younger age groups. Therefore, the association of drugs as the precipitating factor could be missed in elderly unless high clinical suspicion and complete drug review have been made. The clinical presentation of both conditions would be similar, in which failure to recognize the aetiology especially drug in elderly would delay the successful management of the patient [3-5]. Diagnosis of bullous pemphigoid can be made clinically especially at primary care level to expedite the referral and specific management. However, the role of skin biopsy is essential for confirmation of the skin lesion. In a condition whereby the histopathological findings of the lesion is not supportive towards bullous pemphigoid, subsequent serum testing to detect circulating anti-basement membrane zone antibodies should be done in order to rule in the lesion in which clinically relevant towards bullous pemphigoid [3-8].

The most important management for bullous pemphigoid is the abrupt discontinuation of the drug or initiating agent [3-5]. Although high-potency topical corticosteroid therapy is highly effective for bullous pemphigoid, however considering the location of the lesion in our case is confined to the oral area which is not feasible for our patient to utilize, oral prednisolone would be the good alternative. The response would be rapid as in our case which usually resolved within one month on systemic corticosteroid. Nevertheless, the prognosis of bullous pemphigoid is variable. Long-term remission may occur after months to years [3-5].

CONCLUSION

This case highlights the importance of adequate drug history in a case associated with any dermatological complaints. Detailed oral examination should be routinely done whenever drug eruptions are suspected as the pathognomonic features might not only be confined to the body and trunk. At primary care level, essential knowledge on the adverse effects of the offending medication that can induce skin emergencies is indeed crucial. Prompt action to withhold the drug is necessary in primary care to save the patient's life.

Conflict of Interest

Authors declare none.

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Authors' contribution

Literature search and manuscript was prepared by all authors. The manuscript was edited by Shaiful Ehsan. All authors approved the final version of the manuscript submitted for publication.

Informed Consent

This case report is published with the consent of the patient.

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