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CASE REPORT

A Case of Generalized Seizure after Toxic Epidermal Necrolysis

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Toxic epidermal necrolysis (TEN) is a severe mucocutaneous adverse reaction characterized by extensive necrosis and epidermal detachment involving more than 30% of the body surface area (BSA). It is commonly triggered by antiepileptics, sulfonamide antibiotics, and non-steroidal anti-inflammatory drugs. A 22-year-old female without any underlying medical history presented with painful multiple erythematous bullae and plaques of varied sizes throughout the body for 1 day. On the second hospitalization day (HD), the bullae progressively coalesced, leading to epidermal detachment involving 60% of the BSA. On the fifth HD, the patient had a tonic–clonic seizure with eyeball deviation for 5 minutes. She was transferred to the intensive care unit (ICU) and administered lorazepam 4 mg and levetiracetam 1,500 mg. Brain computed tomography, magnetic resonance imaging, and cerebrospinal fluid examination showed no abnormalities. Although the patient had delirium and additional seizures while in the ICU, her condition improved without any complications after 5 weeks of inpatient treatment. Several complications of TEN such as dehydration, malnutrition, sepsis, and ophthalmic and pulmonary complications have been reported; however, seizures have not been reported yet. Herein, we report a case of seizure in a patient during treatment for TEN. **(Ann Dermatol 32(4) 334～336, 2020)**

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INTRODUCTION

Toxic epidermal necrolysis (TEN) is a severe mucocutaneous adverse reaction characterized by extensive necrosis and detachment of the epidermis involving more than 30% of the body surface area (BSA)[1]. It is most commonly caused by antiepileptic drugs such as lamotrigine, phenytoin, and carbamazepine[2]. There are many kinds of complications of TEN including sepsis, multiorgan failure, and pulmonary and ophthalmic complications[3]. To the best of our knowledge, cases of seizure after the onset of TEN have not yet been reported.

We received the patient's consent form about publishing all photographic materials.

CASE REPORT

A 22-year-old female presented with painful multiple erythematous bullae and plaques of various sizes on her entire body for 1 day (Fig. 1A, B). Five days ago, she had taken acetaminophen and nortriptyline for headache. Two days ago, she had taken ibuprofen and amoxicillin/clavulanate for fever and headache. We performed viral laboratory test and punch biopsy from the bullous lesion. Histopathologic examination revealed spongiosis and inflammatory infiltrates in the dermis and perivascular area. Immunofluorescence staining showed no specific findings. On the second hospital day (HD), the bullae progressively coalesced and detachment of the epidermis was observed. Nikolsky's sign was positive, and about 60% of the BSA was involved (Fig. 1C, D). The patient was administered methylprednisolone 2 mg/kg, and the areas of epidermal

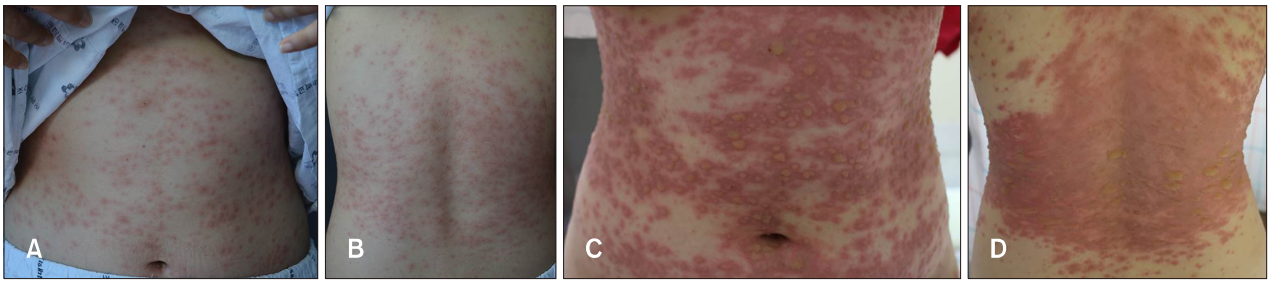

Fig. 1. (A, B) Multiple various sized erythematous bullae and plaques on whole body the 1st hospital day. (C, D) The bullae progressively coalesced and detachments of the epidermis were occurred on the 2nd hospital day.

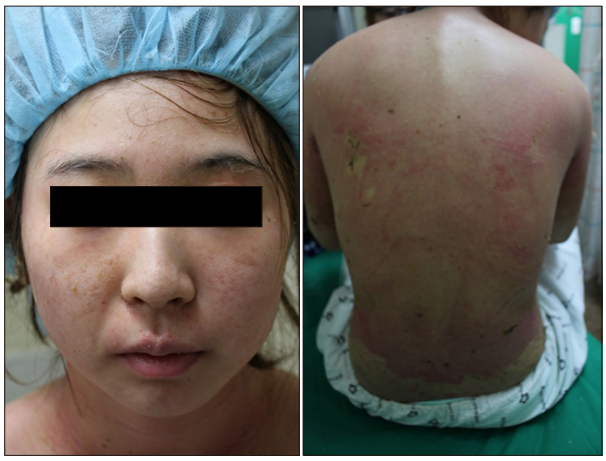

Fig. 2. The skin lesions were completely healed with only mild erythema.

detachment were treated with foam dressing. On the fourth HD, intravenous moxifloxacin 400 mg was administered because of dysuria and pyuria. On the fifth HD, the patient had a tonic-clonic seizure with eyeball deviation for 5 minutes. Subsequently, she was transferred to an intensive care unit (ICU) and administered lorazepam 4 mg and levetiracetam 1,500 mg. The findings of laboratory tests were as follows: alanine aminotransferase, 46.8 U/L (normal range, 5～40 U/L); aspartate aminotransferase, 38.1 U/L (normal range, 5～40 U/L); blood urea nitrogen, 14.5 mg/dl (normal range, 8～20 mg/dl); serum creatinine, 0.49 mg/dl (normal range, 0.5～1.3 mg/dl); serum sodium, 138 mEq/L (normal range, 136～146 mEq/L); serum potassium, 4.2 mEq/L (normal range, 3.5～5.0 mEq/L); and serum chloride, 106 mEq/L (normal range, 98～110 mEq/L). Brain computed tomography, magnetic resonance imaging, and cerebrospinal fluid examination revealed no abnormality. Although the patient experienced seizures two more times on the seventh and tenth HD, these were well controlled by lorazepam. On the 16th HD, the seizures completely stopped because of levetiracetam 1,000 mg alone, and the skin lesions completely healed (Fig. 2). The patient was transferred to the general ward; however, her Mini-Mental State Examination (MMSE) score was 20 points. Levetiracetam was discontinued on the 21st HD, and the MMSE of the patient slightly improved to 24 points; however, she developed retrograde amnesia and did not remember being treated in the ICU. She was discharged on the 25th HD, and no complications or sequelae were observed after 5 weeks of follow-up.

DISCUSSION

TEN is a life-threatening cutaneous condition affecting the skin and mucous membranes. Patients can be classified according to the BSA involved: Stevens-Johnson Syndrome (SJS), ＜10% BSA; SJS/TEN overlap, 11%～30% BSA; and TEN, ＞30% BSA1. Although the pathophysiology of TEN is unknown, medications are known to be the most important causative factors, especially antiepileptic drugs such as carbamazepine, lamotrigine, phenytoin, and phenobarbital[2]. The cutaneous lesions are characterized by irregularly shaped erythematous to dusky red maculopatches, blisters, and diffuse erythema. Mucous membranes are involved in more than 90% of patients who develop TEN[4]. Under the assumption that many immunological mechanisms affect the progression of the disease, many kinds of immunosuppressive and anti-inflammatory agents have been attempted to arrest its progression. A high dose of systemic steroids could lead to an increased risk of infection. Although intravenous immunoglobulin and cyclosporine A can also be used, their exact effects on disease progression are unclear[4,5].

During the acute phase, many complications of TEN such as dehydration, malnutrition, sepsis, and ophthalmic and pulmonary complications could occur[2,3]. Sepsis due to *Staphylococcus aureus* and *Pseudomonas aeruginosa* is the most common[2]. Extensive fluid loss due to epidermal detachment results in dehydration and electrolyte imbalance[2]. Approximately 20% to 75% of patients develop ophthalmic complications, whereas about 40% of patients

develop pulmonary complications including edema, atelectasis, and pneumonitis[3]. Epithelial defects and ulceration caused by ocular surface inflammation may cause visual impairment and eye discomfort[3]. However, neurologic complications of TEN including seizure have not yet been reported.

The causes of seizures are epilepsy, brain injury, infection, drugs, metabolic disorder, fever, and stress[6]. In the patient in the current case, the possible causes of seizure could have been metabolic disorder, stress, and medication. Dehydration, the main complication of TEN, can modify plasma osmolality and electrolyte balance, altering brain metabolism and function, leading to increased risk of seizure[2,7]. Exposure to stress results in secretion of hormones such as deoxycorticosterone, corticotropin-releasing hormone, and corticosterone, which impact neuronal excitability and seizure susceptibility[8]. The medications used to control symptoms including high-dose corticosteroids, acyclovir, and moxifloxacin could lead to seizure[9,10]. Moxifloxacin, which is administered to treat urinary tract infection, has been reported to cause TEN as well as seizures. According to previously reported cases, the seizures stopped after moxifloxacin was discontinued[10]. In this case, the seizures continued despite the withdrawal of moxifloxacin, the possibility of the seizure being induced by moxifloxacin was low.

Although cases of TEN due to antiepileptics are common, cases of seizures during treatment of TEN have not been reported. Herein, we report a rare case of TEN with seizure in a patient without any personal or family history of seizure. As TEN is a life-threatening disease, the possibility of seizure should be considered in patients with TEN.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

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