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CASE REPORT

A CASE REPORT ON GABAPENTIN INDUCED TOXIC EPIDERMAL NECROLYSIS

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ABSTRACT
Toxic epidermal necrolysis (TEN) and SJS are fatal skin reactions characterized by full-thickness epidermal necrosis which is caused by medicines or their metabolites . Both are most commonly caused by drugs and are most likely to develop in the first few weekspost-administration/ingestion of the medication . In this case report, we present a case of gabapentin induced TEN and its management at our Pharmacovigilance center in a tertiary care hospital.

KEYWORDS: Toxic epidermal necrolysis, Stevens-Johnson syndrome, Erythema, multiforme, Nikolsky sign, Neuropathic pain.

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INTRODUCTION
Toxic epidermal necrolysis (TEN) is a mucocutaneous skin reaction characterized by extensive, full-thickness epidermal necrosis, which is most commonly caused by medicinesor their metabolites. The shedding of epidermis leaves the exposed and irritated dermis which makes the patient vulnerable to infection, significant fluid changes, loss of thermoregulation, and electrolyte imbalance repetition . As a result, TEN has a high death rate and significant long-term morbidity[1].
The pathophysiology of TEN was identified as circulating toxins selectively targeting the epidermis, causing necrosis. TEN and erythema multiforme were first assumed to be on the same spectrum as a single drug hypersensitivity illness based on these early descriptions of the lesions .[2]TEN is present on the same clinical spectrum as Stevens-Johnson Syndrome (SJS) as a more severe variant with widespread systemic rash, persistent fever, buccal mucosal inflammation, and conjunctival inflammation[3-5]. The classification of SJS and TEN is based on a continuum of body surface areas affected by epidermal exfoliation:[3,4]

1. SJS The total body surface area included in SJS is < 10%
2. SJS/TEN involve body surface area between 10% and 30%
3. TEN involves> 30% body surface area

Malaise, fever, and a respiratory tract infection are the first signs and symptoms of TENs. Atypical targets or purpuric macules on the face, upper chest, and limbs are the first lesions; which grow in size and consolidate as the disease spreads swiftly into vesicles or fluid blisters. The skin is detachable, and gentle pressure causes the epidermis to detach from the dermis (known as a positive Nikolskysign)[5]. Drugs are the most common cause of TENs, and occurs most frequently in the first few weeks after taking the medications.[6] SJS/TEN has been linked to various medications, including anti-infectives,allopurinols, antiepileptics carbamazepine, phenobarbital, nevirapine, lamotrigine, gabapentin, phenytoin, and oxicam-nonsteroidal anti-inflammatory drugs(NSAIDs).[7,8]Females are 1.5 times more likely than males to be affected[9].

Severity of illness score for toxic epidermal necrolysis (SCORTEN SCORE)

The prognosis for TEN can be assessed rapidly in the early stages of the disease using the Toxic Epidermal Necrosis Severity Scale (SCORTEN). SCORTEN is a validated evaluation tool based on seven easily derived clinical and laboratory factors as shown in Table.[5]Mortality increases from 3.2% for a score of 0-1 to >90% for a score of 5 or higher.

Prognostic factors	Score 0	Score 1
Age	< 40 years	>40 years
Tachycardia	< 120 bpm	>120 bpm
Malignancy	No	Yes
Body surface area detached	< 10 %	>10 %
Serum urea nitrogen	< 28 mg/dL	>28 mg/dL
Serum glucose	< 252 mg/dL	>252mg/dL
Serum bicarbonate	< 20 mmol/L	>20 mmol/L

Early diagnosis and identification of the culprit drug, followed by its discontinuation, is a key principle in the treatment of TEN.[5] Because of the disease's immunological nature, immunosuppressive therapies are supposed to help with treatment. Many case reports have documented positive results with a variety of treatment regimens involving different drugs combination including corticosteroids, IVIg (Intravenous immune globulin), cyclosporine, and Tumor Necrosis factor (TNF)-alpha inhibitors[10,11]. Short-term dexamethasone medication appears to be effective when started early. At an early stage of the reaction, short-term dexamethasone medication (1.5 mg/kg/day) on three consecutive days may reduce mortality without affecting healing time[12].

CASE REPORT

A 65-year-old female patient with a known case of rheumatoid arthritison treatment came to the emergency department of our hospital with complaints of rashes associated with skin lesions all over the body, more of ulcerative superficial lesion over face, mouth and body since 8-10 days, arthralgia with old deformities, and low grade fever since 1 day. Initially patient developed swelling over face associated with itching on 24 october 2021, which suddenly increased all over the body, patient was taking tablet (Tab.) Folitrax, Tab. Tolperitas, Tab. Flugesic SR, Tab. Gabapentin. She was initially admitted to the ward on 2nd November 2021, however, in view of increasing skin lesions and worsening general condition, she was shifted to ICU on 6th November 2021. Investigations done revealed: Hemoglobin- 11.3 g/dl, TLC: 7390 c/cumm, platelet: 249000 c/cumm, ESR: 37 mm/hr, peripheral smear microcytes present, urea:79 mg/dl, creatinine: 1.3 mg/dl, uric acid: 9.2 mg/dl, calcium: 8.0 mg/dl, sodium: 136 mEq/L, potassium:3.9 mEq/L, HbA1C: 6.0 %, bilirubin total/direct: 0.3/0.2, protein: 5.7 g/dl, albumin: 3.2 g/dl, SGOT/SGPT: 42/14, ALP: 85 U/L, GGT: 17 U/L. RA factor:67.34 IU/ml (positive), Anti CCP:>200 RU/ml (positive), ANA:positive, aerobic blood culture: sterile, aerobic urine culture: sterile, HPE(Epidermis tissue from skin lesion): completely necrotic epidermis, calcium ionized:1.07 mmol/L , PT-INR: 11.8/1.0, APTT: 27.5 sec. Chest x-ray showed diffuse osteopenia, bilateral apical pleural thickening, arotic knuckle calcification noted and bilateral CP angles blunted , pleural effusion, pleural thickening.

Based on the physical and laboratory findings, the patient was diagnosed as having toxic epidermal necrolysis . On the day of admission, the drug gabapentin was withheld, and she was symptomatically managed with IV fluids, corticosteroids, antibiotics, IV immunoglobulins, topical agents and other supportive measures. As the patient's general condition improved, she was shifted back to ward on 20th November 2021. By excluding other factors of TENs, it was confirmed as gabapentin induced toxic epidermal necrolysis . Patient was discharged on 27th November 2021 in hemodynamically stable condition.

DISCUSSION

Toxic epidermal necrolysis is a hypersensitive reaction that causes skin and mucous membrane epithelial damage. SJS is characterized by epidermal detachment of less than 10%, but toxic epidermal necrolysis (TEN) is characterized by a ≥ 30% involvement of total body surface area[13].TEN is a serious dermatologic emergency with a high rate of morbidity and mortality. There is a broad differential diagnosis that needs to be

examined early in the disease course, and a quick diagnosis is crucial in achieving the best outcomes[14].Medications are the most common cause of SJS, but diseases like cytomegalovirus, herpes simplex virus and mycoplasma pneumonia have all been linked to the syndrome. The patient in this situation had recently been prescribed gabapentin . Gabapentin is an antiepileptic medication that is also used to treat neuropathic pain[15].

Our patient had a history of rheumatoid arthritis and was on Gabapentin 300 mg twice day. After one week on gabapentin, the patient suffered rashes and itching, and ulcerative superficial lesions appeared on the face, lips, and body, prompting admission to our hospital. On the first day of admission, Gabapentin was withdrawn and symptomatically treated. Later, the lesions healed and the pain from them subsided. After 28 days in the hospital, the patient's clinical condition had improved and she was discharged in hemodynamically stable condition.

CONCLUSION

In conclusion, TEN is a potentially fatal immune-mediated medication adverse reaction with a high rate of morbidity and fatality. Although the underlying processes of the disease are unknown, granulysin is widely believed to be the key mediator of CTL-induced keratinocyte death. The mainstay of disease treatment is early diagnosis and identification of the culprit substance. Early diagnosis, discontinuation of the offending substance, and a focus on supportive care remain the gold standard. Since toxic epidermal necrolysis is a rare and fatal medical condition, immediate medical attention is recommended if the patient exhibits symptoms.

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