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Case Report

Toxic Epidermal Necrolysis following Antiepileptic Therapy: A Case Report and review of Supportive Care Strategies

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Abstract:

Background: Toxic Epidermal Necrolysis (TEN) is a rare, life-threatening mucocutaneous reaction, most commonly triggered by medications. Characterized by widespread epidermal detachment and mucosal involvement, TEN closely resembles severe burn injuries in both clinical presentation and pathophysiology, including risks of fluid loss, sepsis, and multi-organ failure.

Case Report: We report a case of a 36-year-old female with a known history of epilepsy, who developed TEN following the administration of Carbamazepine, an antiepileptic drug introduced after a recent seizure episode. Within days, the patient presented with high-grade fever, facial edema, and painful, fluid-filled skin lesions that rapidly progressed across the body, along with mucosal and ocular involvement. Laboratory findings revealed leukocytosis, elevated CRP and ESR levels, and electrolyte imbalances.

Discussion: The patient was treated with a multidisciplinary approach including immediate withdrawal of the offending drug, immunosuppressive therapy with intravenous dexamethasone, symptomatic relief, intensive wound care, ocular protection, electrolyte correction, nutritional support, and psychiatric evaluation. Gradual improvement was noted, and corticosteroids were tapered and discontinued after one week. The comprehensive supportive care approach led to stabilization and eventual recovery.

Conclusion: This case underscores the importance of early identification and withdrawal of the causative drug in suspected TEN cases, followed by aggressive supportive care. Although specific pharmacological treatments such as corticosteroids are used, their efficacy remains controversial, and supportive management remains the cornerstone of therapy. A coordinated, interprofessional approach is essential for improving patient outcomes in TEN.

Keywords: TEN, Carbamazepine, Drug induced reaction, multi faceted management approach

Introduction

Toxic epidermal necrolysis [TEN] is potentially life-threatening condition characterized by extensive exfoliation of the epidermis and mucous membrane which may result in sepsis and death. It is typically drug induced mucocutaneous disease. It is clinically characterized as a widespread sloughing of the skin and mucosa including both external and internal surfaces . TEN is also called as LYELLS SYNDROME. TEN is a severe T cell mediated type IV (delayed) hypersensitivity reaction (1).

In the United States, the annual frequency of TEN is reported to be 0.22- 1.23 cases per 100000 population. In 1992 the cumulative incidence of TEN and SJS in Germany was 1.9 cases per million populations. In the HIV positive population, the incidence of TEN increases to 1 case per 1000 year. Most studies report that Asian and black patients are more susceptible compared to the white population.in general adult cases are mainly drug induced, while infections are the main cause in children. Many recent studies highlighted the association between different HLA alleles and the development of TEN, especially in the southern Asian population (2 & 3).

The majority of toxic epidermal necrolysis (TEN) cases result from a hypersensitivity reaction to medications. Other potential triggers include infections such as *Mycoplasma pneumonia*, dengue virus, and cytomegalovirus, as well as exposure to contrast media. TEN has also been reported following measles, mumps, and rubella (MMR) vaccination. Most cases are believed to stem from idiosyncratic drug reactions. Although over 220 medications have been implicated, only a few are frequently associated with the condition.

- Antibiotics such as sulfonamides (particularly trimethoprim \ sulfamethoxazole), beta lactamase inhibitors, tetracyclines and quinolones (especially ciprofloxacin).
- Anticonvulsants such as phenytoin, phenobarbital and carbamazepine.
- Antiviral such as abacavir, oseltamivir.
- NSAIDS like oxicam, piroxicam

According to the 2008 Euro SCAR study, the drugs with a high risk of TEN are lamotrigine, carbamazepine, phenytoin, nevirapine, phenobarbital, sulfonamides, sulfasalazine, allopurinol and oxicam -NSAIDS (4). TEN is considered to be related to Fas – Fas ligand or granulysin mediated apoptosis . More recent studies suggested the reactive oxygen species (ROS) as the initiating factor for keratinocyte damage and that it precedes the activation of the before mentioned apoptic systems . Fas is a membrane bound protein responsible for the initiation of programmed cell death through a series of intracellular events. Fas ligand (FasL) is usually produced by cytotoxic T (CTL)and natural killer(NK) cells. Granulysin is a pro apoptic protein that was also detected in TEN blisters .its is also secreted bt CTL and NKL cells that lead to cell mediated cytotoxicity . OXIDATIVE STRESS is one of the proposed theories of TE .Glutatione S transferase p (GST -p) is a biomarker of oxidative stress in keratinocytes .the culprit drug may interfere with the detoxification pathways resulting in the accumulation of reactive oxygen species (ROS) , triggering programmed cell death (5).

TEN typically begins within 4 weeks of drug exposure. First symptoms are typically non specific. Early symptoms may include headache, rhinitis, cough, sore throat, or myalgias. At this stage, it is important to have a broad differential as patients are misdiagnosed initially with erythema multiform, Phemphigous Bulloid; characteristically cutaneous lesions first appear in the presternal region as well as the face, palms and soles of the feet. Mucosal involvement occurs in more than 90% of patients, predominantly affecting the mouth, genitalia, and / or ocular region. In some cases the respiratory system and gastrointestinal tract are also affected, ocular involvement are frequent. During the course of the disease the lesions rapidly coalesce and become tense bullae .the degree of skin involvement is a highly important prognostic factor. A classification system for TEN is according to the skin detachment has been suggested (6).

TEN cause painful, blistering, peeling skin on at least 30%of the body leading to open erosions, these erosions may lead to dangerous complications such as sepsis, organ failure, infections or death. TEN requires immediate medical attention. Loss of the epithelial barrier increases the risk of infection and septicaemia. Tis may evolve to septic shock and multiorgan failures in long term the involved skin may show hypo or hyper pigmentation. TEN also can lead to stenosis, vulvar adenosis and dyspareunia. In

male phimosis is the most common complications (7). Ocular complications are the one of the most common and serious sequalae of TEN. Corneal ulcer, xerophthalmia, meibomian gland dysfunction, panophthamitis or even blindness is some of the reported complications. Respiratory complications include pulmonary embolism, adult respiratory distress syndrome (ARDS) and pneumonia. Gastrointestinal complications in the form of extensive bleeding from the affected mucosa, gingival synechua and xerostomia due to the affection of the salivary glands (8).

Case Report

A female patient of 36 years old visited Mamatha General hospital with the complaints of dark fluid filled lesions over upper limbs , lower limbs ,posterior side of the body and face since 6 days, painful red lesions appeared over abdomen and complained of fever since 6 days. Patient is a known case of epilepsy since 3 years and she was on phenobarbitone for the first 2 years and 1 year back due to an episode of seizure activity she was advised with the alternate drug tab phenytoin and she was on phenytoin for the past 1 year (Antiepileptic drug). Patient was apparently asymptomatic since 1 week back and upon the stoppage of the drug she developed seizures and she was treated with INJ CARBAMAZEPINE. Latter she developed high grade fever with chills of sudden onset and associated with swelling of face and lips, and then she developed painful fluid filled lesions initially over the upper limbs which are progressed to lower limbs, posterior side and abdomen. She also complained of blisters all over the body, itching, and burning sensation over blisters. The patient was advised for CBP, CRP, ESR, CLINICAL BIOCHEMISTRY REPORT, USG and LFT. The reports shown an elevation in the WBC count (leucocytosis), hyponatremia and hypokalaemia and increased CRP and ESR levels, adonexial lesions in ovaries and the remaining reports were found to be normal among the performed laboratory tests. On the first day the patient was treated with inj. dexamethasone, inj. pantop, clonate ointment, moisture x soft lotion, dologel, kenocortoro paste, momate F cream, tab avil, sypmucaine gel and IVF NS. On the second day same treatment was continued along with the injmidaz .on the third day ,the patient still complained of itching and burning sensation over blisters and also complained of body pains ,so the patient was advised with the same drugs along with tab pheniramine maleate , amorphous hydrogel wound dressing with colloidal silver,white soft paraffin +light liquid paraffin ,choline salicylate, benzalkonium chloride, lignocaine HCl gel , inj lorazepam, lubimoist, moxifloxacin eye ointment and inj. Tramadol, kenocortoro paste was used to treat mouth ulcers .To prevent the skin from clinging to the cotton bed the patient was forced to adjust her position on a sterile sheet, ocular lubrimoist solution, moxifloxacin eyedrops were used to treat ocular lesions .supportive care include protein supplements for maintaining nutrition, and a stringent diet was prescribed by a nutritionist for the first 10 days until she switched to conventional regimen after the lesions began to heal. Review at psychiatry OPD at the time of discharge. DEXAMETHASONE dose was gradually reduced and then discontinued after 7 days.

Discussion

Toxic epidermal necrolysis (TEN) is indeed a severe and potentially life-threatening condition that requires prompt recognition and treatment. Let's break down the key aspects of TEN based on the discussion:

Etiology and Causative Agent:

The temporal association between the administration of carbamazepine and the onset of symptoms strongly implicates this antiepileptic medication as the causative agent. Carbamazepine is among the most frequently reported drugs associated with TEN, alongside others such as phenytoin, allopurinol, sulfonamides, and NSAIDs. This patient had previously tolerated phenobarbitone and phenytoin, but TEN symptoms developed shortly after carbamazepine was introduced following a seizure episode.

TEN is often caused by idiosyncratic, immune-mediated hypersensitivity reactions, typically occurring 1–3 weeks after drug exposure, though rapid-onset cases are not uncommon with re-exposure or in individuals with particular susceptibility. Genetic predispositions such as HLA-B*1502 in Asian populations are well-known risk factors for carbamazepine-induced SJS/TEN.

Clinical Presentation:

The clinical manifestations in this patient are consistent with classic TEN:

- **Initial symptoms**: High-grade fever with chills, facial and lip swelling, and generalized malaise.
- **Skin lesions**: Painful, fluid-filled bullae and erythematous macules, initially appearing on the upper limbs and rapidly spreading to involve lower limbs, posterior trunk, face, and abdomen.
- **Mucocutaneous involvement**: Painful oral ulcers and ocular involvement, both hallmarks of TEN.
- **Systemic symptoms**: Severe itching, burning sensation, and body pain indicated extensive epithelial necrosis and systemic inflammatory response.

This patient exhibits Toxic Epidermal Necrolysis (TEN) symptoms through high-grade fever along with facial swelling and painful bullae and mucosal ulceration and rapid epidermal detachment. The laboratory examination strengthened the clinical assessment enabling proper medical care decisions. Systemic inflammatory responses along with subsequent bacterial infections commonly occur because skin barriers become compromised during TEN. The high inflammatory state became more evident through increased levels of C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR). The clinical situation of TEN patients requires immediate management of hyponatremia and hypokalemia because they appear from fluid losses through skin erosion which leads to fatigue and muscle weakness and heart instability and requires appropriate treatment. The adnexal lesions discovered through imaging proved to be non-significant for the current evaluation because they appeared incidentally.

The complete clinical range of TEN requires intensive supportive care since its diagnostic symptoms include mucosal involvement and oral and eye lesions together with extensive painful bullae skin clusters and body-wide itching as well as systemic indications of fever and fatigue. The therapy combined specific treatments which directed their action toward both immune dysfunction and symptoms control. Dexamethasone delivered through high-dose intravenous administration acted as the main treatment for controlling immune response and preventing disease spread before doctors tapered the doses to minimize inflammatory returns. Skin healing and protection in addition to minimizing infection risk were achieved through colloidal silver hydrogel dressings and emollients while painful ulcers were eased by kenocortoro paste and mucaine gel application. The patients' discomfort received treatment from systemic analgesics (tramadol) while anxiolytics (lorazepam) and antihistamines (pheniramine maleate) managed both anxiety and pruritus symptoms. Lubricating drops combined with antibiotic drops served as the treatment method for TEN-related eye involvement to avoid conjunctival scarring while preserving vision.

Critical to the patient's recovery was starting a high-protein nutritionally supervised diet since their metabolic needs sharply rise when healing extensive skin damages. The patient’s treatment success through improvement alongside immunosuppressant dose reduction demonstrates the value of early drug offending identification followed by drug withdrawal as well as multidisciplinary care approach. Clinical evidence shows the vital importance to link medical laboratory data with whole-body symptoms which enables practitioners to select precise therapeutic approaches that save lives for patients with TEN.

Treatment and Management with Clinical Correlation

Precise medical care for Toxic Epidermal Necrolysis (TEN) by implementing a broad multidisciplinary method that utilized immunosuppressive treatments together with supportive methods and wound treatments along with nutritional and psychiatric care designed to match the patient's complex medical features. Doctors started an early administration of intravenous dexamethasone as an immunosuppressive medication to stop the immune attack on epidermal tissue that typifies TEN. A rapid deterioration of her lesions and mucosal damage led to the necessity of early steroid therapy for preventing further skin detachment along with systemic inflammatory reactions. Symptomatic and supportive treatments managed the complete range of symptoms which included body pain combined with itching sensation along with gastrointestinal distress and anxiety. Both Tramadol treated the severe body pain and blister discomfort through analgesia effects yet the patient needed Pheniramine maleate to control the itchiness and pantoprazole protected mucosal tissue from systemic steroid damage. Lorazepam and midazolam acted as anxiolytics to reduce anxiety together with restlessness while treating severe symptoms that potentially worsened because of her shallow electronic status epilepticus and epilepsy.

Mucocutaneous lesions received treatment with topical agents including kenocortoro paste together with momate-F cream and dologel and mucaine gel to achieve anti-inflammatory effects and aid epithelial healing and minimize pain in the oral region when feeding and hydration were compromised. Wound care with amorphous hydrogel dressings containing colloidal silver and emollients (white soft paraffin and liquid paraffin) provided essential functions for TEN patients because they maintained a moist wound environment and prevented superinfection and fostered skin re-epithelialization.

Eye preservation required the combination of lubricating drops (lubrimoist) and antibiotic preparations (moxifloxacin) to lessen the risk of ocular complications which could result in conjunctivitis or corneal ulceration or symblepharon leading to visual impairment. The patient required thorough nutritional care because skin loss along with mucosal ulceration increased his metabolic needs while making it difficult to consume food by mouth. A high-protein nutritional diet with clinical supervision appeared as part of the treatment plan to help body tissues heal and keep systemic well-being stable throughout the initial 10 days.

Medical care professionals understood how a disfiguring painful condition like TEN would affect emotional well-being of this patient with chronic epilepsy therefore they arranged psychiatric support. Care for her mental health and evaluation of any neuropsychiatric effects between corticosteroid medicine and hospital stay duration were addressed by psychiatric consultation. The treatment strategy combined strategies to manage acute manifestations of TEN while emphasizing patient recovery in addition to quality of life to match established best practices in severe cutaneous adverse drug reactions.

Conclusion

Patients who develop Toxic Epidermal Necrolysis (TEN) require rapid recognition of this severe condition alongside the removal of carbamazepine because this is the drug responsible for their condition after they used antiepileptic medications. The proper and successful treatment of this patient demonstrates the need for complete multidisciplinary interprofessional medical care. Extensive burn injury patients share the same complications with TEN patients including severe fluid loss and the risk of sepsis and multi-organ dysfunction that required comprehensive monitoring and management in this individual case. The application of corticosteroids through dexamethasone constitutes an exception but medical professionals still doubt their overall effectiveness because research findings remain

inconclusive. The base of managing TEN effectively depends on thorough supportive care which should incorporate microsurgical wound care and treatment of fluid and electrolyte imbalance with infection prevention protocols and nutritional support as well as psychological care. Clinical care demands both medication surveillance and swift medical intervention to obtain better patient outcomes after administering high-risk prescription medications.

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