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Toxic Epidermal Necrolysis with Sepsis: Early Recognition and Intervention in a Critical Case

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ABSTRACT
Toxic epidermal necrolysis (TEN) is a rare but life-threatening skin condition, often caused by adverse immune responses to certain drugs, with a high mortality rate of 30%. The case report aims to detail the comprehensive management of a patient with TEN and sepsis. Case. A 66-year-old male with some flaccid bullae with erosions appeared on his body and epidermal detachment is more than 30% of the total body surface area with a positive Nikolsky sign. He took the medication, including Carbamazepine, Paracetamol, and Gabapentin, 3 days ago. Upon examination, he has high a temperature with work of breathing. The Glasgow Coma Scale 14, Mean Arterial Pressure 80 mmHg and laboratory examination shows platelets 70x10^3/µl and creatinine enzymatic 1.49 mg/dl. The patient showed signs of TEN with sepsis. The treatment was given meropenem for sepsis, stopping patient's medications, fluids replacement, administering blood transfusions, electrolyte replacement and wound care for TEN. After being treated for 2 days, the patient was fully conscious, vital signs were normal, the laboratory results returned to normal. TEN is a severe cutaneous adverse reaction characterized by widespread epidermal necrosis and detachment. Sepsis is a critical complication in TEN due to the extensive loss of skin integrity. Supportive care, including fluid resuscitation, electrolyte replacement, and nutritional support is the cornerstone of TEN. Antibiotics is crucial for the management of TEN with sepsis. Thus, the antibiotics option must be chosen with caution. Patients with TEN and sepsis must receive immediate treatment. However, the medication regimen administered needs to be carefully considered, as it may potentially worsen the progression of the disease.

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INTRODUCTION

Toxic epidermal necrolysis (TEN) is a severe, life-threatening condition characterized by extensive epidermal detachment, typically affecting more than 30% of the total body surface area (BSA) and often associated with high morbidity and mortality rates. The disorder is most commonly triggered by adverse drug reactions, with anticonvulsants, antibiotics, and nonsteroidal anti-inflammatory drugs (NSAIDs) being the main culprits.1 Although rare, TEN has a significant fatality rate, ranging from 25-30%, and patients often experience serious complications, including sepsis and multi-organ failure.2 Due to its rapid onset and the severity of symptoms, early recognition and immediate medical intervention are crucial in improving patient outcomes.

The pathophysiology of TEN involves immune-mediated destruction of keratinocytes, largely driven by cytotoxic T cells and massive release of pro-inflammatory cytokines. This leads to extensive epidermal necrosis and a breakdown of the skin's protective barrier, significantly increasing the risk of secondary infections.4 Sepsis is one of the most frequent and life-threatening complications in patients with TEN, often developing as a result of bacterial translocation through the compromised skin barrier. The management of TEN with sepsis is particularly challenging, requiring careful consideration in

selecting antibiotics, as certain medications can exacerbate the condition or trigger additional hypersensitivity reactions.3,4

Meropenem, a broad-spectrum carbapenem antibiotic, has demonstrated efficacy in treating severe infections, including sepsis caused by multidrug-resistant organisms. Its favorable safety profile and wide-ranging activity against gram-positive, gram-negative, and anaerobic bacteria make it a valuable alternative in cases where conventional antibiotics may be contraindicated due to drug hypersensitivity.5 While the use of meropenem in TEN patients is not widely documented, its role as a treatment option in sepsis management is gaining attention due to its low cross-reactivity with other antibiotics commonly associated with adverse drug reactions.6

This case report aims to detail the comprehensive management of a patient with TEN and sepsis and to highlight the successful use of meropenem as an alternative antibiotic in a patient with both TEN and sepsis. Given the high risk associated with the use of antibiotics in TEN patients, this case underscores the importance of careful antibiotic selection and offers evidence supporting meropenem's potential as a safe and effective option in managing sepsis in these complex cases.

CASE ILLUSTRATION

A 66-year-old male presented to the emergency department with erythematous skin lesions on his chest and upper arms that had worsened over the past few hours. He complained of increasing pain, skin peeling, bilateral conjunctivitis, oedema of lips and eyelids, along with mild shortness of breath and excessive tearing. The patient had a history of trigeminal neuralgia and had been taking Carbamazepine, Gabapentin, Paracetamol for neuralgia for 3 days ago, with the last dose taken the night before admission. Initial examination revealed a weak general condition, with a Glasgow Coma Scale (GCS) of 15, blood pressure of 156/81 mmHg, heart rate of 94 beats per minute, respiratory rate of 20 breaths per minute, a high temperature of 37.8°C, and an oxygen saturation of 98%. Cardiovascular and respiratory examinations were unremarkable, and initial laboratory tests showed hematocrit at 36.5% (low), lymphocytes at 10.9% (low), and monocytes at 10.3% (high). Liver enzymes, particularly SGOT, were elevated at 90 U/L, while electrolytes were low. A chest X-ray and electrocardiogram (ECG) were normal. The patient received fluids replacement, wound care and immediate cessation of suspected culprit medication. The patient received intravenous fluids Ringer's lactate of 1500 mL/24 hr, Methylprednisolone injection of 80 mg/day, and Paracetamol 3 × 500 mg orally.

Figure 1. Bullae appear all over the body on the 3rd day.

By the third day of hospitalization, the patient started getting blisters spreading all over her body, bilateral conjunctivitis, oedema of lips and eyelids, haemorrhagic crusts of the lips and body accompanied by pain in swallowing. The skin efflorescence was multiple blisters filled with clear fluid and loose walls, without any pus with positive Nikolski's sign reater than 30% of the body surface area (BSA) is involved. The patient's had deteriorated, showing increasing confusion and restlessness. The

family reported disorientation, with the patient often forgetting he was in the hospital. Objective assessment revealed worsening consciousness with a GCS score of 14, a blood pressure of 120/60 mmHg, heart rate of 100 beats per minute, respiratory rate of 24 breaths per minute, and temperature of 39.4°C, Mean Arterial Pressure 80 mmHg. Laboratory examination shows Hemoglobin 5,1 g/dl (low), leukocytes 1,00x10^3/µl (low), platelets 70x10^3/µl (low), hematocrit 15,3% (low) and creatinine enzymatic 1.49 mg/dl (high), albumin 3.24 gr/dl (low) and natrium 122 mmol/L (low). Signs of sepsis had emerged, with significant skin lesions and signs of TEN (Figure 1.), confirmed by a consultation with dermatology specialists. The patient was treated with intravenous Meropenem for sepsis, alongside electrolyte correction with NaCl 3%, albumin replacement for hypoalbuminemia, and blood transfusions. The patient was isolated to prevent secondary infection, and continuous monitoring of vital signs, bilateral conjunctivitis were managed with eye drops and fluid balance was initiated.

Figure 2. Generalized major erythema multiforme involving widespread skin lesions

By day 5, the patient's fever had reduced to 36.3°C, and his overall condition showed slight improvement. However, he remained weak with persistent erythema and skin lesions (Figure 2). Blood pressure was stable at 120/70 mmHg, respiratory rate of 18 breaths per minute and heart rate was 90 beats per minute. Laboratory examination shows Hemoglobin 15.8 g/dl, leukocytes 5.84x10^3/µl, platelets 264x10^3/µl, hematocrit 45,5% and creatinine enzymatic 1.09 mg/dl, albumin 3.17 gr/dl (low) and natrium 133.5 mmol/L. Although still under close monitoring for sepsis, the treatment regimen of Meropenem and supportive care was maintained.

By day 7, the patient had regained full consciousness but reported persistent pain and burning sensations throughout his body. His vital signs remained stable, with normal temperature and blood pressure. The erythematous lesions began to heal, and the patient's overall condition showed significant improvement; however, the clinical diagnosis of TEN remained, compounded by a history of sepsis and renal impairment. Further treatment focused on maintaining electrolyte balance, wound care, and the continued administration of meropenem to mitigate the risk of infection.

RESULT AND DISCUSSION

TEN is a severe cutaneous adverse reaction characterized by widespread epidermal necrosis and detachment, frequently triggered by medications such as anticonvulsants and antibiotics, with a high mortality rate reported at 30%.7 Anticonvulsants, particularly carbamazepine, are often the primary treatment for painful trigeminal neuralgia, despite their association with hypersensitivity reactions, including TEN. Research indicates that anticonvulsants like diphenylhydantoin, barbiturates, and carbamazepine have an 11% to 15% relative chance of causing SJS or TEN.8

In this case, the patient presented with classic signs of TEN, including flaccid bullae, epidermal detachment, and a positive Nikolsky sign, after exposure to carbamazepine and gabapentin all well-documented triggers for this life-threatening reaction. The immune mechanism underlying TEN involves drug-specific CD8+ cytotoxic T cells that release pro-apoptotic molecules such as granulysin,

leading to keratinocyte apoptosis.4 The extent of epidermal detachment, affecting more than 30% of the patient's body surface area, along with a positive Nikolsky sign, confirmed the diagnosis of TEN.

Sepsis is a critical complication in TEN due to the extensive loss of skin integrity, which facilitates bacterial invasion and infection.9 In this patient, the development of sepsis was marked by altered mental status, fever, and lab findings indicating renal impairment, hyponatremia, and hypoalbuminemia. These lab results, including creatinine levels at 1.09 mg/dl and albumin at 3.17 g/dl, are consistent with sepsis-related kidney dysfunction and protein loss. Hypoalbuminemia has been recognized as a poor prognostic marker in sepsis, with studies showing increased mortality in patients with serum albumin below 35 g/L.10 In addition, sepsis-related hyponatremia is frequently observed, particularly in severe cases, and is associated with higher mortality rates due to the loss of sodium regulation in critical illness.11 Endothelial dysfunction, vasodilation, and increased capillary permeability are all brought on by dysregulation of cytokine release in sepsis. This leads to cellular leakage syndrome, which disrupts fluid management and results in intravascular hypovolemia, cellular malfunction, and ultimately tissue death. Electrolyte abnormalities, including hyponatremia, are caused by the dysregulation of intra- and extra-vascular volumes.12

Anemia is another common finding in septic patients, often caused by inflammation, hemolysis, and disrupted iron metabolism.13 Although initial hemoglobin levels may not show significant differences, rapid declines occur in sepsis, which exacerbates the patient’s overall condition and complicates treatment.14 This patient's anemia likely contributed to their longer recovery, emphasizing the multifactorial challenges of managing TEN with sepsis.

Meropenem, a broad-spectrum carbapenem antibiotic, was chosen for the management of sepsis in this patient. It is effective against a wide range of pathogens, including gram-negative organisms and multi-drug-resistant bacteria, which are common in hospitalized patients with severe infections. The choice of meropenem is supported by its efficacy in treating severe sepsis in critically ill patients, particularly those with comorbidities or a compromised immune system.15 Given the critical nature of the patient's condition, broad-spectrum antibiotic coverage is crucial until specific cultures can guide therapy.

Tocco-Tussardi et al. had emphasizes the role of antibiotics to treat infections in immunocompromised patients. The study underscores that a significant portion of TEN patients received empiric antibiotic therapy, often including meropenem. While empiric antibiotic use, including meropenem, may have had a beneficial effect in preventing some infections, broad-spectrum antibiotic use is generally not recommended without clear indications due to concerns about triggering further complications. This is particularly important because certain antibiotics, like sulfamethoxazole/trimethoprim, are commonly associated with the development of SJS/TEN.16

On the other hand, Sameed M et al. reported different results where meropenem was implicated in the development of TEN. The patient, who initially received meropenem for a suspected infection, developed erythematous rash and desquamation after several doses, consistent with TEN. The case highlights the importance of recognizing drug-induced SJS/TEN, particularly with antibiotics like meropenem, which are listed as potential causes of severe cutaneous adverse reactions (SCARs) in post-marketing data. Although carbapenems, including meropenem, are sometimes used when other beta-lactam antibiotics cause hypersensitivity reactions, this case underscores the need for caution, as meropenem itself may trigger or exacerbate SCARs.17

Therefore, while meropenem is a potent broad-spectrum antibiotic often used in severe infections, including in patients with SJS/TEN, its safety profile in these cases is contentious. On one hand, meropenem may be necessary to manage life-threatening infections in immunocompromised patients. On the other hand, it has been implicated in causing or worsening SJS/TEN in rare cases, and thus should be used with extreme caution, especially in patients with a history of antibiotic

hypersensitivity reactions. The decision to use meropenem should be based on a thorough assessment of the risks and benefits, considering alternative antibiotics, the patient's history, and microbiological findings to guide therapy.

Management of TEN hinges on the immediate discontinuation of the causative drug, which in this case was carbamazepine. Early drug withdrawal is critical to halting progression. Supportive care, including fluid resuscitation, electrolyte replacement, and nutritional support, is the cornerstone of TEN management.3,18 In this case, the patient received systemic corticosteroids (methylprednisolone) and broad-spectrum antibiotics (meropenem) to manage inflammation and prevent secondary infections. Although the role of corticosteroids remains controversial due to potential immunosuppression, recent studies support their early use in severe TEN to reduce mortality and accelerate recover.2

The patient's recovery, characterized by stabilization of vital signs, improvement in laboratory parameters, and gradual healing of skin lesions, highlights the importance of multidisciplinary management in TEN with sepsis. The successful outcome in this case emphasizes the need for early diagnosis, withdrawal of the offending drug, appropriate antibiotic therapy, and careful supportive care. This case underscores the importance of selecting the appropriate antibiotics in managing sepsis complicating TEN. Meropenem's efficacy in this context, coupled with the use of corticosteroids, contributed to the patient's recovery. The management of this case aligns with current therapeutic strategies for TEN and sepsis and serves as an example of the complexity involved in treating such severe, drug-induced skin reactions.19

CONCLUSION

This case highlights the therapeutic challenges of managing TEN complicated by sepsis, particularly in choosing appropriate antibiotics while avoiding hypersensitivity reactions. The use of Meropenem as an alternative broad-spectrum antibiotic in a patient with TEN and sepsis proved to be effective and safe. Supportive care, including fluid resuscitation, electrolyte replacement, Supportive care, including fluid resuscitation, electrolyte replacement, blood tranfusion and managing hypoalbumin is also important for this case. It underscores the need for prompt intervention in such critical cases, emphasizing the importance of early identification of offending drugs, aggressive supportive care, and the cautious selection of antibiotics in patients with severe cutaneous adverse reactionsinduced TEN with sepsis.

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