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Drug-Induced Toxic Epidermal Necrolysis with Rare Pneumomediastinum in Children: A Case Report

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ABSTRACT

Background:Toxic Epidermal Necrolysis (TEN) is a life-threatening dermatologic emergency. While primarily a cutaneous disease, severe cases may involve the respiratory epithelium, leading to rare complications such as pneumomediastinum and subcutaneous emphysema, which signify a poor prognosis. Pneumomediastinum complicating pediatric TEN is exceptionally rarely reported, giving this case notable educational and clinical value. This case report describes the clinical approach and successful multidisciplinary management of a pediatric patient with drug-induced TEN complicated by rare air-leak syndromes and sepsis.Case Report: A 9-year-old boy presented with widespread blistering and epidermal detachment involving more than 30% of the total body surface area (TBSA) following amoxicillin administration (ALDEN score +2, possible). The condition rapidly progressed to TEN with extensive mucosal involvement and a SCORTEN of 2 (predicted mortality 12.1%) was determined on admission. Patient's condition in Pediatric Intensive Care Unit (PICU) was complicated by sepsis, bilateral pneumonia, pneumomediastinum, and subcutaneous emphysema. Because of clinical deterioration under first-line corticosteroids, immunomodulatory therapy was escalated in a stepwise manner within a multidisciplinary intensive care setting. Significant clinical improvement followed, characterized by complete cessation of new lesion formation, progressive re-epithelialization, and radiological resolution of the pneumomediastinum. The patient was discharged after 17 days with near-complete skin healing and resolved systemic complications. Conclusion: Pediatric TEN complicated by pneumomediastinum and sepsis requires careful, multidisciplinary intensive care with early recognition of respiratory deterioration and prompt escalation of immunomodulatory therapy. In selected severe pediatric TEN cases, this approach may contribute to favorable clinical outcomes.

1. INTRODUCTION

Systemic drug reactions involving the skin can present emergency conditions, among which Stevens–Johnson syndrome (SJS) and Toxic Epidermal Necrolysis (TEN) are the most severe manifestations. TEN is one of the most severe forms of severe cutaneous adverse reactions (SCARs) and is defined by extensive keratinocyte apoptosis triggered by a cytotoxic immune response, leading to substantial separation of the epidermis involving more than 30% of the total body surface area, accompanied by variable mucosal involvement (Frantz et al., 2021; Surowiecka et al., 2023). Disruption of the epidermal barrier results in profound fluid loss, impaired thermoregulation, electrolyte imbalance, malnutrition, secondary infection, and sepsis, thereby placing patients at high risk of multiorgan dysfunction and death (Surowiecka et al., 2023; Labib and Milroy, 2023). Despite being uncommon, with an estimated yearly incidence of 0.4 to 1.9 cases per million people, TEN is a true dermatological emergency requiring intensive monitoring and multidisciplinary management involving dermatologists, pediatricians, intensivists, ophthalmologists, nutritionists, and other relevant specialists, because mortality remains high, particularly among patients with sepsis, respiratory involvement, or multiorgan failure (Surowiecka et al., 2023; Karanam et al., 2025).

While TEN can affect individuals of all ages, the pediatric population presents distinct epidemiological, physiological, and therapeutic challenges. TEN is considerably less common in

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children than in adults, with an estimated incidence of approximately 6.3 cases per 100,000 hospitalized children annually (Jain et al., 2021). Epidemiological analyses indicate that while SJS/TEN occurs more frequently among adolescents aged 11–15 years, in-hospital mortality risks are disproportionately higher in younger children, particularly those under five years of age. Although as many as half of the survivors experience long-term sequelae, reported mortality rates range from 0–3.6% for SJS and approximately 7% for TEN in pediatric cohorts (Hsu et al., 2016). Children generally have more favorable survival than adults; however, their greater body surface-area-to-mass ratio, limited physiological reserves, and age-specific fluid and nutritional requirements increase their susceptibility to dehydration, electrolyte imbalance, malnutrition, and infection during the acute phase (Milheiro Silva et al., 2017). Furthermore, age-specific physiological characteristics and the limited evidence supporting systemic immunomodulatory therapies make therapeutic decision-making particularly challenging in pediatric TEN. Although medications remain the principal cause of TEN, infections such as Mycoplasma pneumoniae and viral illnesses are proportionally more frequently implicated in pediatric mucocutaneous disease than in adults, further complicating diagnostic evaluation (Hu et al., 2015; Labib and Milroy, 2023). In the local Indonesian setting, retrospective data from RSUD Dr. Soetomo Surabaya (2019–2021) showed that children aged 6–10 years comprised 7.1% of all epidermal necrolysis admissions (Banjarnahor et al., 2023).

The majority of TEN cases are drug-induced, accounting for approximately 80–95% of cases. The reaction is generally idiosyncratic and dose-independent. Drugs most strongly associated with TEN include aromatic anticonvulsants, sulfonamide antibiotics, allopurinol, and oxicam-derived non-steroidal anti-inflammatory drugs, although penicillins, cephalosporins, and fluoroquinolones have also been reported as potential triggers (Labib and Milroy, 2023; Karanam et al., 2025; Canhão et al., 2022; Isaac et al., 2021). Drug-induced TEN most commonly develops within 4–28 days after treatment initiation, whereas symptoms may occur more rapidly following previous exposure to the same medication (Canhão et al., 2022; Hama et al., 2024). Early symptoms are often non-specific, including fever and malaise, followed by rapid progression to erythematous macules, blister formation, and widespread epidermal detachment involving the skin and mucous membranes (Labib and Milroy, 2023). Prompt identification and immediate withdrawal of the suspected culprit drug are essential because delayed discontinuation has been associated with poorer clinical outcomes and increased mortality (Garcia-Doval et al., 2000). In pediatric patients, causality assessment may be particularly challenging because antibiotics, antipyretics, anticonvulsants, and analgesics are frequently administered concurrently during the prodromal phase (Nuswantoro et al.. 2025).

Beyond widespread mucocutaneous detachment, severe systemic complications can arise from epidermal barrier breakdown, including homeostatic dysfunction, profound electrolyte derangement, dehydration, and sepsis. Furthermore, internal organs with an epithelial lining can be directly targeted by the necrolytic process, leading to critical conditions such as tracheobronchial epithelial sloughing and gastrointestinal epithelial necrosis (Surowiecka et al., 2023). Respiratory involvement has been reported in approximately 25–30% of patients with TEN and is associated with a substantially poorer prognosis (Supono et al., 2022). Acute respiratory manifestations include pneumonia, pulmonary edema, acute respiratory distress syndrome (ARDS), respiratory failure, and tracheobronchial epithelial necrosis (Supono et al., 2022; Chen et al., 2024). Sloughing of the tracheobronchial epithelium may obstruct the airways with mucosal debris, resulting in air trapping and increased intra-alveolar pressure. Subsequent alveolar rupture allows air to dissect along the peribronchovascular sheaths into the mediastinum through the Macklin phenomenon, producing pneumomediastinum and, in some cases, subcutaneous emphysema. Although pneumomediastinum may resolve with conservative management, it remains an exceptionally rare air-leak complication of TEN, particularly in pediatric patients, and may indicate severe airway involvement. Together with sepsis, severe respiratory complications are among the leading causes of mortality in patients with TEN.

Published reports of pediatric TEN complicated by pneumomediastinum remain exceedingly limited. Jain et al. (2021) described a child with SJS complicated by pneumomediastinum and cerebral venous sinus thrombosis, whereas Bruce-Hickman et al.

(2019) reported bilateral pneumothoraces and pneumomediastinum in an adolescent with SJS. Liu et al. (2023) further demonstrated that severe pediatric TEN may result in chronic pulmonary sequelae such as bronchiolitis obliterans requiring prolonged respiratory support. To our knowledge, reports of drug-induced pediatric TEN complicated by pneumomediastinum remain scarce worldwide and are particularly limited in Indonesia.

Evidence regarding systemic immunomodulatory therapy in pediatric TEN remains limited. Although systemic corticosteroids and intravenous immunoglobulin are frequently used, their effectiveness and optimal timing remain controversial. Cyclosporine has emerged as a promising therapeutic option because it inhibits T-cell activation and cytotoxic pathways involved in keratinocyte apoptosis; however, evidence supporting its use in children is still predominantly derived from observational studies and case reports (Del Pozzo-Magaña et al., 2017; Hama et al., 2024). This case report describes the diagnostic evaluation, clinical progression, development and conservative management of pneumomediastinum, therapeutic response following cyclosporine administration, and clinical outcomes in a child with drug-induced TEN complicated by sepsis. This report provides additional clinical insight into early culprit-drug withdrawal, multidisciplinary management, comprehensive respiratory evaluation, and conservative treatment of a rare air-leak complication in pediatric TEN.

2. METHOD

Case report

A 9-year-old boy was referred from Hospital E to Prof. Dr. Margono Soekarjo General Hospital (RSMS) on March 6, 2026, with a chief complaint of widespread blistering and skin detachment involving almost the entire body. He had no previously documented drug allergy or underlying chronic illness. Five days prior to admission, the patient initially experienced vertigo without other accompanying symptoms. One day later, he developed a high-grade fever up to 39°C, accompanied by sore throat, nausea, and three episodes of vomiting. He was treated at a primary care facility and received amoxicillin, paracetamol, dexamethasone, dexchlorpheniramine maleate, antacids, and domperidone.

Following the initiation of the medication, mucocutaneous lesions rapidly manifested within one day. Three days prior to referral, the patient developed ocular dryness, facial exanthema, and excruciating oral erosions that progressed to blistering over the face, trunk, and genital area. Upon admission, he appeared severely ill but remained fully conscious with a Glasgow Coma Scale (GCS) score of 15 (E4V5M6). Although hemodynamically stable with a blood pressure of 109/73 mmHg, vital signs were notable for tachycardia (heart rate 125 bpm), tachypnea (respiratory rate 24/min), and mild hypoxemia (SpO2: 93% on room air). Anthropometry on admission showed a body weight of 33 kg and height of 125 cm (BMI 20.1 kg/m^2), corresponding to weight-for-age at the 50th–75th, height-for-age at the 5th–10th, and BMI-for-age at the 85th–90th percentile based on the CDC 2000 growth charts, consistent with an overweight nutritional status. Physical examination revealed subcutaneous crepitus, bilateral pulmonary crackles, and multisite mucosal involvement affecting the oral (hemorrhagic crusting and painful erosions), ocular (dryness, later evolving into bilateral blepharoconjunctivitis), and genital mucosae. Respiratory mucosal involvement was suspected given the subsequent development of pneumomediastinum and subcutaneous emphysema. Dermatological evaluation confirmed Toxic Epidermal Necrolysis (TEN) features, characterized by flaccid bullae on an erythematous base with crusting and desquamation, estimated at more than 30% of the total body surface area (TBSA). Epidermal detachment predominantly involved the face, ears, and the anterior and posterior trunk, whereas the extremities showed discrete erythematous lesions without frank bullae (Figure 1). Stevens–Johnson syndrome was excluded by epidermal detachment exceeding 30% TBSA, staphylococcal scalded skin syndrome by the extensive multisite mucosal involvement, and pemphigus vulgaris by the acute drug-related onset. No skin biopsy was performed.

Additional investigations were performed to evaluate the severity of the disease. Initial laboratory tests revealed leukopenia with marked lymphopenia (absolute lymphocyte count

230/µL), hyponatremia, elevated transaminases and normal renal function (Table 1). A SCORTEN of 2 was determined to assess disease severity based on a heart rate greater than 120 beats per minute and epidermal detachment involving more than 10% of the total body surface area. The remaining criteria were not met because the patient was younger than 40 years, had no malignancy, and had a serum urea level of 25.1 mg/dL, bicarbonate level of 21.4 mmol/L, and glucose level of 131 mg/dL, forecasting a 12.1% mortality rate (Widaty et al., 2017). Drug causality was assessed using the Algorithm of Drug Causality for Epidermal Necrolysis (ALDEN). Amoxicillin obtained a total score of +2 (possible), the highest among the co-administered drugs, and was therefore identified as the most probable culprit. A diagnosis of community-acquired pneumonia, sepsis, and electrolyte imbalance-complicated drug-induced Toxic Epidermal Necrolysis (TEN) was made.

3. RESULT AND DISCUSSION

Result

The patient was admitted to the PICU for supportive care, including oxygen therapy, fluid resuscitation, and central venous catheterization. Because of a high risk of cross-reactivity to penicillins and cephalosporins, empirical vancomycin was selected in place of beta-lactam antibiotics, and methylprednisolone (62.5 mg/day) was commenced as first-line immunomodulation. Supportive management included intravenous paracetamol for analgesia, gastric protection, and topical skin care with a compounded emollient ointment applied to eroded areas, preceded by saline (NaCl 0.9%) compresses. Nutritional support was escalated enterally with high-calorie oral formula. Nasogastric tube placement was offered but declined by the patient. His condition deteriorated on day 3, with fever (38.5°C), tachypnea, and worsening tachycardia (heart rate 146 bpm). Chest radiography demonstrated bilateral pneumonia together with pneumomediastinum and extensive subcutaneous emphysema involving the chest and abdominal walls, both axillae, and the supra- and infraclavicular regions, without evidence of pneumothorax or pneumopericardium. Chest CT was not performed because the diagnosis was considered sufficiently established based on the radiographic findings and the patient's clinical presentation (Figure 2). Based on these clinical findings, together with the radiographic evidence of bilateral pneumonia and extensive epidermal barrier disruption, the patient was diagnosed with sepsis. Inflammatory biomarkers, including C-reactive protein and procalcitonin, as well as blood cultures, were not obtained, while sputum cultures were negative and no causative organism was isolated.

Methylprednisolone was discontinued and cyclosporine A (100 mg/day, ≈3 mg/kg/day) was initiated as rescue immunomodulation; after two days it was discontinued and therapy was escalated to high-dose corticosteroid (intravenous methylprednisolone 500 mg/day, followed by dexamethasone 15 mg/day). From day 5, no new bullae developed and progressive re-epithelialization followed. The pneumomediastinum and subcutaneous emphysema were managed conservatively, positive-pressure ventilation was avoided and chest physiotherapy was provided. Serial chest radiographs showed interval resolution between days 6 and 8. Multidisciplinary care involved dermatology, ophthalmology (bilateral blepharoconjunctivitis treated with topical levofloxacin, lubricant drops, and gentamicin ointment), thoracic surgery, rehabilitation medicine, and nutrition. On day 9, meropenem was used to escalate antibiotics according to the clinical evaluation. He was transferred to the general ward on day 10. Serial laboratory (Table 1) monitoring showed early improvement in transaminases, consistent with resolving sepsis-related hepatic involvement, while hypoalbuminaemia and persistent hyponatraemia reflected protein and fluid–electrolyte loss through the denuded skin and were addressed with nutritional and electrolyte support. As corticosteroids were tapered, re-epithelialization continued. The patient was discharged in good condition after the skin lesions were almost completely healed on day 17 (March 23, 2026). At discharge, the patient was scheduled for routine outpatient review. At the outpatient visit on day 25 (31 March 2026), the skin had re-epithelialized with residual post-inflammatory hyperpigmentation, although no structured, protocolized long-term follow-up was undertaken (Table 2).

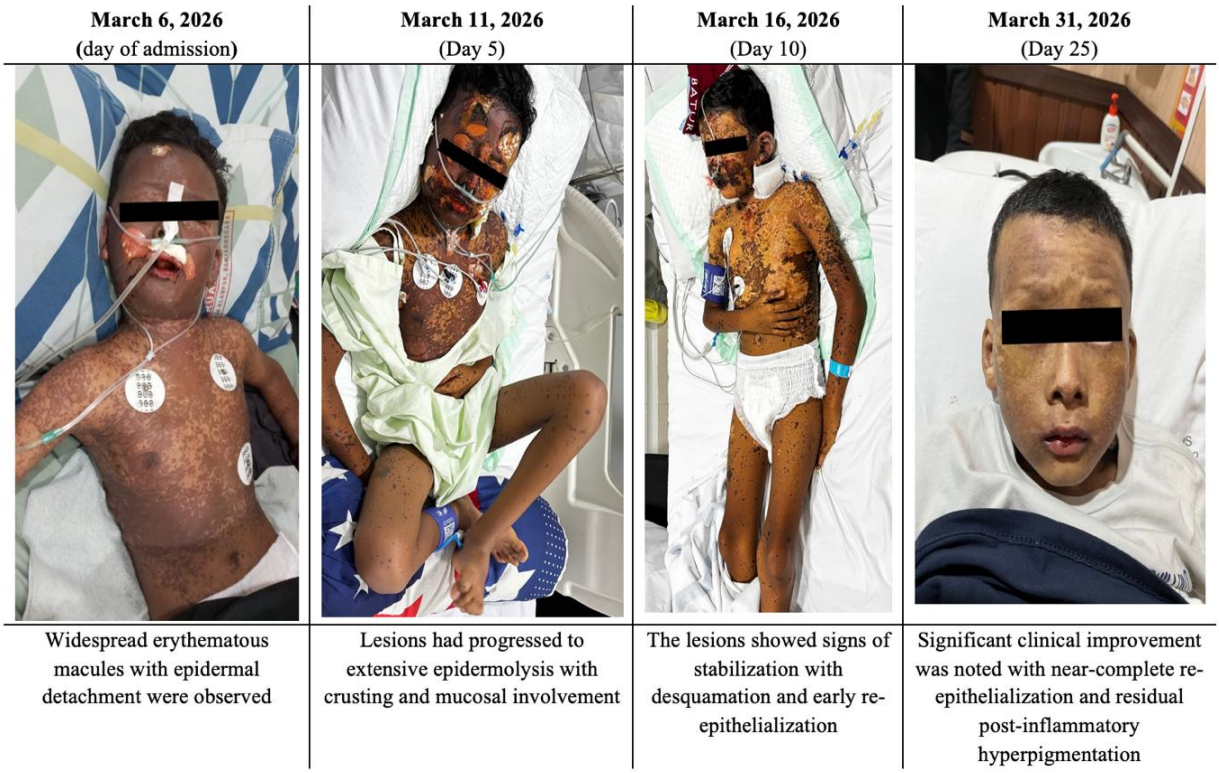

Figure 1. Clinical development of the patient with toxic epidermal necrolysis (TEN)

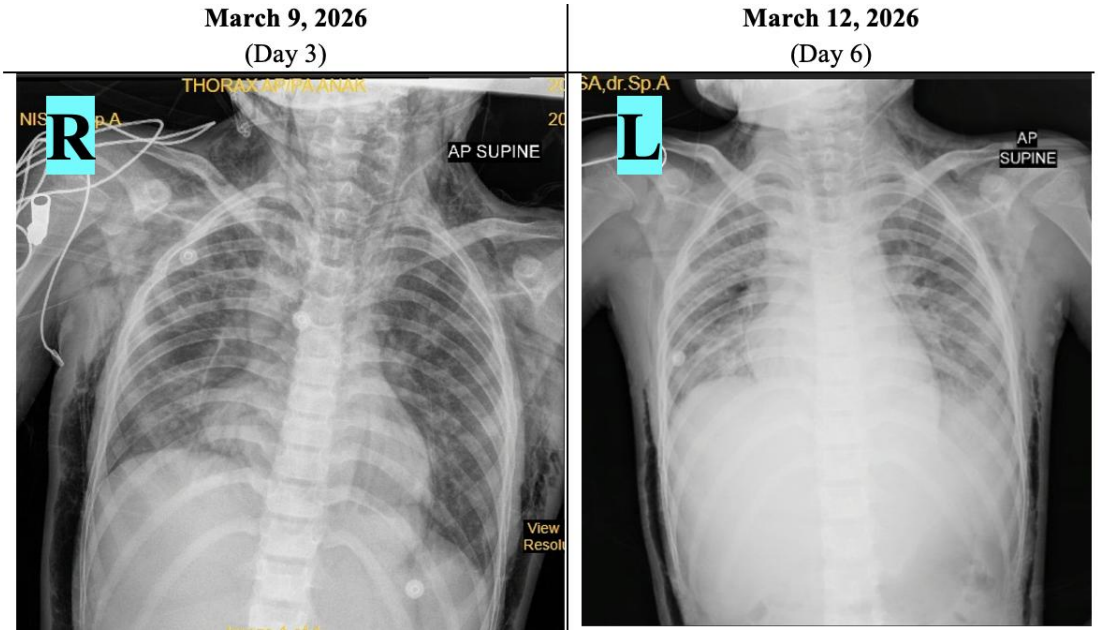

Figure 2. Serial chest radiographs with pneumomediastinum (R) to resolution (L)

Table 1. Serial laboratory result of patient

Examination	06-03-2026	08-03-2026	09-03-2026	10-03-2026	Reference Range
Hemoglobin (g/dL)	11.7	–	–	–	10.8–15.6
Leukocytes (/µL)	4.190	–	–	–	4.500–13.500
Hematokrit (%)	37	–	–	–	33–45
Platelets (/µL)	189.000	–	–	–	181.000–521.000
Neutrophils (%)	82.3	–	–	–	25.0–60.0
Lymphocytes (%)	5.4	–	–	–	25.0–60.0
AST (U/L)	149	–	78	–	<50
ALT (U/L)	246	–	230	–	<41
Albumin (g/dL)	–	–	2.65	–	3.97–4.94
Ureum (mg/dL)	25.1	–	–	–	15.0–36.0
Creatinine (mg/dL)	0.34	–	–	–	0.0–0.73
Random Glucose (mg/dL)	131	137	–	130	80–139
Sodium (mmol/L)	129	–	128	–	136–145
Potassium (mmol/L)	3.6	–	4	–	3.5–5.1
Chloride (mmol/L)	95	–	92	–	97–107
Calcium (mg/dL)	–	–	8.1	–	8.6–10.3
pH	–	7.44	–	–	7.35–7.45
pO_2 (mmHg)	–	75.4	–	–	71.0–104.0
pCO_2 (mmHg)	–	32 ↓	–	–	35.0–46.0
HCO_3 (mmol/L)	–	21.4	–	–	21–28
O_2 Saturation (%)	–	96.9	–	–	94–98
Sputum Culture	–	–	–	Negative	Negative

Table 2. Summary of Clinical Monitoring During Hospitalization

Hospital day	Skin lesions	Temperature / Respiratory	Laboratory / Imaging
1	>30% TBSA epidermal detachment with oral and ocular mucosal involvement	T 36.8°C, HR 125 bpm, RR 24/min, SpO_2 93% (room air)	Sodium 129 mmol/L, AST 149 U/L, ALT 246 U/L
3	Progressive epidermal detachment	T 38.5°C, HR 146 bpm, RR 29/min	Mild hypocapnia on ABG
4	Active skin detachment	Persistent fever	Chest radiograph: bilateral pneumonia, pneumomediastinum, and subcutaneous emphysema
6–8	No new bullae; re-epithelialization began	Afebrile; respiratory status improved	Chest radiograph showed resolving pneumomediastinum
9–10	Continued healing	Stable on room air	Improving laboratory abnormalities
17	Near-complete re epithelialization	Stable vital signs	Laboratory abnormalities improved

Discussion

This case demonstrates the successful resolution of severe pediatric Toxic Epidermal Necrolysis (TEN) complicated by rare air-leak syndromes within 17 days through a multidisciplinary intensive care approach. Its primary clinical significance lies in highlighting that the necrolytic process in TEN is not limited to the integumentary system but can extend to the tracheobronchial epithelium, necessitating advanced respiratory monitoring and timely immunomodulatory escalation. This aggressive disease progression was clearly observed in our patient, whose clinical deterioration on day 3, marked by fever (38.5°C), sepsis, and the emergence of pneumomediastinum and subcutaneous emphysema, required a pivotal shift in therapeutic strategy. Pneumomediastinum is an exceptionally rare complication of TEN, particularly in children, with only a few comparable cases reported in the literature (Bruce-Hickman et al., 2019; Jain et al., 2021; Noureldin and McKell, 2025). The presence of pneumomediastinum in our patient therefore adds to the limited evidence describing severe respiratory involvement in pediatric TEN. Similar to the cases reported by Jain et al. (2021) and Bruce-Hickman et al. (2019), our patient developed pneumomediastinum following rapid clinical deterioration. However, unlike the cases reported by Bruce-Hickman et al. (2019) and Liu et al. (2023), which progressed to bilateral pneumothoraces or required prolonged ventilatory support with subsequent bronchiolitis obliterans, our patient achieved complete clinical recovery with conservative respiratory management and stepwise immunomodulatory therapy. In contrast to several reported cases in which the culprit was an anticonvulsant, the reaction here was attributed to amoxicillin, and recovery was achieved without invasive airway support.

On day 3, the patient experienced a rapid systemic deterioration with tachycardia and tachypnea, which was a direct result of substantial keratinocyte and epithelial apoptosis. The presence of subcutaneous emphysema and pneumomediastinum suggests that the cytotoxic injury had extended beyond the skin to involve the respiratory epithelium. As documented by Hama et al. (2024), the underlying mechanism of TEN involves a type IV delayed-type hypersensitivity reaction, where natural killer (NK) cells and cytotoxic CD8+ T lymphocytes secrete granulysin, the primary effector molecule that causes widespread cell death. When necrolysis extends to the tracheobronchial epithelium, epithelial sloughing may obstruct the airways with mucosal debris, resulting in air trapping and increased intra-alveolar pressure. Subsequent alveolar rupture allows air to dissect along the bronchovascular sheaths into the

mediastinum through the Macklin phenomenon, producing pneumomediastinum and, occasionally, subcutaneous emphysema (Bruce-Hickman et al., 2019; Kouritas et al., 2015). Respiratory involvement has been reported in approximately 25–30% of patients with TEN and is associated with a substantially poorer prognosis (Supono et al., 2022). From a clinical standpoint, the progression of such extracutaneous injuries significantly raises the risk of mortality (Hsu et al., 2016).

Objective severity assessment is crucial in light of this intricate clinical picture. Based on the patient's tachycardia (HR > 120 bpm) and an initial epidermal detachment exceeding the 10% BSA prognostic threshold, a SCORTEN of 2 was determined upon admission, indicating a 12.1% mortality rate according to standard criteria (Widaty et al., 2017). In order to reinforce the association between the suspected trigger and the skin reaction, the algorithm of Drug Causality for Epidermal Necrolysis (ALDEN) was utilized. With an intermediate ALDEN score of +2, amoxicillin was recognized as a possible cause and achieved the highest score among the co-administered drugs. Although the interval between amoxicillin exposure and the onset of mucocutaneous lesions was relatively short (approximately one day), this temporal relationship was incorporated into the overall ALDEN assessment together with the drug's established association with TEN. These clinical findings indicate the profound systemic inflammatory response and homeostatic disruption characteristics of severe epidermal necrolysis, which frequently necessitates intensive care management (Surowiecka et al., 2023). This systemic involvement was further reflected by the laboratory abnormalities observed during hospitalization. Elevated AST and ALT suggested hepatic injury secondary to systemic inflammation, while hypoalbuminemia and persistent hyponatremia reflected capillary leakage, transepidermal protein loss, and ongoing metabolic stress commonly observed in severe TEN (Labib and Milroy, 2023; Surowiecka et al., 2023). Serial laboratory monitoring demonstrated early improvement in transaminase levels whereas hypoalbuminaemia and hyponatraemia persisted during the acute phase, reflecting continuing protein and fluid–electrolyte losses despite clinical improvement.

A central therapeutic challenge in this case was the choice of immunomodulation alongside intensive supportive care. While systemic corticosteroids typically serve as the first-line option, methylprednisolone (62.5 mg/day) was initiated on admission, however, their efficacy can be limited in cases marked by rapid progression or concurrent sepsis. Consequently, Cyclosporine A (3 mg/kg/day, or 100 mg daily) was introduced on day 3 for our patient as a critical rescue intervention. The decision to initiate cyclosporine was supported by evidence suggesting reduced mortality through inhibition of the nuclear factor of activated T-cells (NFAT) pathway, thereby suppressing granulysin release, a key mediator of keratinocyte apoptosis (Hama et al., 2024; Zhou et al., 2024).

This therapeutic escalation is consistent with recent international management changes that favor cyclosporine's early initiation in steroid-resistant pediatric instances to stop epidermal detachment and lower mortality rates (Shah et al., 2024). In our patient, cyclosporine was initiated because of persistent progression of epidermal detachment despite corticosteroid therapy, accompanied by systemic deterioration and a SCORTEN of 2, indicating the need for more targeted immunomodulation. After two days, cyclosporine was discontinued and treatment was escalated to high-dose corticosteroid therapy consisting of intravenous methylprednisolone (500 mg/day) followed by dexamethasone (15 mg/day). No new bullae developed thereafter, and progressive re-epithelialization was observed. Because multiple immunomodulatory agents were administered sequentially, the individual contribution of cyclosporine to the favorable outcome cannot be determined. Preserved renal function supported the safe administration of cyclosporine. Intravenous immunoglobulin (IVIG) was not administered because its clinical benefit in TEN remains controversial (Shah et al., 2024).

Tumor necrosis factor-α inhibitors such as etanercept, although increasingly reported as a promising steroid-sparing option in SJS/TEN, were not used owing to their limited availability in our setting and the limited paediatric evidence supporting their use (Zhou et al., 2024). Successful recovery, however, was not attributable to immunomodulatory therapy alone but also to comprehensive supportive care. Fluid resuscitation and electrolyte correction were essential

to maintain hemodynamic stability and compensate for ongoing transepidermal fluid loss, while early enteral nutrition helped preserve gastrointestinal mucosal integrity and reduce the risk of bacterial translocation during the hypercatabolic phase of TEN (Labib and Milroy, 2023; Surowiecka et al., 2023; Canhão et al., 2022).

Meticulous wound care using 0.9% saline compresses followed by topical emollient application minimized further epidermal trauma and reduced the risk of secondary infection. In addition, dedicated ophthalmic management with topical levofloxacin, lubricant eye drops, and gentamicin ointment was provided to prevent long-term ocular sequelae (Labib and Milroy, 2023; Surowiecka et al., 2023; Canhão et al., 2022). The extensive loss of the epidermal barrier eliminated a critical defence against microbial invasion, providing a portal for bacterial colonization and translocation that predisposed the patient to systemic infection. The development of sepsis likely further amplified systemic inflammation through the release of pro-inflammatory cytokines, perpetuating keratinocyte apoptosis and contributing to ongoing epidermal injury. Prompt recognition of sepsis and timely escalation to meropenem on day 9 were therefore critical not only for infection control but also for interrupting this vicious cycle of inflammation and tissue damage, ultimately contributing to stabilization of the patient's hemodynamic and respiratory status (Hama et al., 2024; Surowiecka et al., 2023).

Positive-pressure ventilation was intentionally avoided because it may aggravate alveolar rupture and worsen existing air-leak syndromes, provided that adequate oxygenation and ventilation can be maintained using less invasive supportive measures (Labib and Milroy, 2023). Instead, a rehabilitation medicine team provided chest physiotherapy to facilitate airway clearance and optimize pulmonary function. Conservative management was considered appropriate because the patient remained hemodynamically stable without evidence of tension pneumomediastinum, esophageal injury, or progressive respiratory compromise requiring invasive airway support.

This multidisciplinary approach likely contributed to the gradual radiological resolution of pneumomediastinum between days 6 and 8. Serial chest radiographs demonstrated interval reduction of pneumomediastinum and subcutaneous emphysema without progression to pneumothorax, supporting the decision to continue conservative management. Although bilateral pulmonary infiltrates initially increased, the overall radiological evolution was consistent with gradual resolution of the underlying air-leak syndrome following treatment of the precipitating airway injury (Bruce-Hickman et al., 2019; Kouritas et al., 2015). Compared with previously reported pediatric cases, some of which required prolonged ventilatory support or developed chronic pulmonary sequelae such as bronchiolitis obliterans (Liu et al., 2023), our patient showed favorable recovery with conservative respiratory management. Clinically, this case highlights the importance of early evaluation for airway involvement in patients with TEN who develop respiratory symptoms or subcutaneous emphysema. Prompt recognition of air-leak syndromes may allow appropriate conservative management before respiratory deterioration necessitates invasive intervention.

Beyond the acute phase, survivors of TEN remain at risk of long-term sequelae, including chronic ocular complications, cutaneous dyspigmentation and scarring, and delayed respiratory disease such as bronchiolitis obliterans, underscoring the importance of structured, multidisciplinary post-discharge surveillance, particularly ophthalmologic and pulmonary follow-up. Despite the favorable outcome and discharge on day 17, this report has several limitations. Bronchoscopy was not performed to directly confirm tracheobronchial epithelial sloughing. In addition, chest computed tomography was not performed because the diagnosis of pneumomediastinum was considered sufficiently established based on the radiographic findings and clinical presentation. The findings from a single case cannot be generalized. In addition, causality between cyclosporine administration and clinical improvement cannot be definitively established because of the observational nature of a single-case report. Although short-term outpatient review demonstrated satisfactory skin re-epithelialization with residual post-inflammatory hyperpigmentation, structured long-term pulmonary and ophthalmologic follow-up was unavailable, precluding assessment of delayed sequelae such as bronchiolitis obliterans or chronic ocular complications. Prospective multicenter studies are therefore needed to better

define standardized management strategies for extra-cutaneous complications, including air-leak syndromes, respiratory support, and immunomodulatory therapy in pediatric TEN.

4. CONCLUSION

This case highlights that early recognition of drug-induced pediatric Toxic Epidermal Necrolysis (TEN), prompt withdrawal of the suspected culprit drug, intensive supportive care, and timely escalation of immunomodulatory therapy collectively contributed to a favorable clinical outcome despite the presence of pneumomediastinum and sepsis. Although pneumomediastinum is an exceptionally rare complication of pediatric TEN, it should be considered in patients who develop respiratory symptoms or subcutaneous emphysema because delayed recognition may worsen the prognosis. Further case reports and multicenter studies are needed to strengthen the evidence regarding the optimal management of pediatric TEN complicated by rare air-leak syndromes such as pneumomediastinum.

5. ACKNOWLEDGE

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