


## Report

# Oropharyngolaryngeal manifestations in severe toxic epidermal necrolysis: a single-center's retrospective case series

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**Abstract**

**Background** Toxic epidermal necrolysis is a rare and life-threatening mucocutaneous disease. Although mucosal ear, nose, and throat (ENT) involvement is common, little is known about the characteristics, treatment modalities, and outcomes of these lesions. The aim of this study was to evaluate ENT mucosal lesions in severe toxic epidermal necrolysis patients and analyze their characteristics, treatment modalities, and outcomes, as well as proposing a management algorithm to prevent long-term debilitating sequelae of these lesions.

**Methods** This is a retrospective review of toxic epidermal necrolysis cases treated at the tertiary burns unit of the Lausanne University Hospital CHUV, Switzerland, between 2006 and 2019.

**Results** Out of 19 patients with severe toxic epidermal necrolysis, 17 (89%) underwent a complete ENT examination at admission and 14 (82%) had ENT mucosal involvement. Five (26.3%) patients died during the stay in the intensive care unit. Of the 16 patients who received maximal care, 13 (81%) required orotracheal intubation for a median time of 16 (IQR: 14) days. Out of the 14 patients who survived, four (29%) had long-term ENT complications consisting of synechiaes necessitating subsequent endoscopic procedures. Those four patients all required mechanical ventilation with an orotracheal tube and suffered from hypopharyngeal synechiaes as well as oral and endonasal synechiaes in individual cases.

**Conclusion** This study suggests a high prevalence of ENT synechiaes in patients with severe toxic epidermal necrolysis and requiring orotracheal intubation. Periodic ENT examination could prevent mature synechia formation in these patients. We propose an algorithm to prevent long-term sequelae in ENT mucosal involvement.

**Introduction**

Stevens–Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) or Lyell's syndrome are rare, severe mucocutaneous conditions most often resulting from adverse reaction to drugs (ARD), through a delayed-type of hypersensitivity.<sup>1</sup> The difference between SJS and TEN is the total body surface area (TBSA) involved, defined by the detached or detachable surface area: <10% for SJS and >30% for TEN, with an SJS and TEN overlap (SJS/TEN) from 10 to 30% TBSA. The underlying pathophysiology is not fully understood, but it implies a type IV hypersensitivity reaction, with different hypotheses on the exact pathogenesis.<sup>2</sup> Following an ARD, a T-cell response is generated, which leads to a keratinocyte apoptosis followed by a full-thickness epidermal necrosis in 5–28 days.<sup>3</sup> The diagnosis of

SJS and TEN relies on clinical signs and skin biopsy. As symptoms can appear up to 8 weeks after the first dose of the causative drug, in 15–30% of cases, the causative agent remains unknown.<sup>4</sup> Erythema multiforme (EM), which shares histologic similarities with SJS and TEN, is the main differential diagnosis. Unlike SJS and TEN, EM is mostly triggered by infections, its skin lesions have different characteristic/distribution, and it involves mucosal membranes in its major form. SJS and TEN universally involve skin and mucous membranes, such as in oral cavity, ocular surface, genitals, respiratory, and gastrointestinal tract.<sup>5</sup> There seems to be a slightly higher prevalence of the disease in female patients (ratio 1.5 : 1).<sup>4</sup> Cutaneous involvement appears as erythematous lesions, mainly on the trunk and the face, progressing to confluent erythematous areas with dusky centers, flaccid blisters with a positive Nikolsky's

sign, and sheet of denuded epidermis.<sup>6</sup> In up to 80% of cases, there is also mucosal involvement consisting of mucositis and ulceration,<sup>4,7</sup> with two or more sites involved but involvement of the oral cavity is found in almost all cases.<sup>4,5</sup>

The SCORTEN score<sup>8</sup> is used to assess the severity and the prognosis of the disease, and patients with SCORTEN  $\geq 2$  or a detachment  $>10\%$  TBSA should preferably be managed in specialized centers or burn intensive care units, as it could decrease the mortality.<sup>9</sup> Rapid withdrawal of the causative drug and supportive care are the mainstay of the management involving multiple specialties (intensive care unit, dermatology, immunology, ophthalmology, gynecology, and ENT). Adjunctive therapies, such as corticosteroids, intravenous immunoglobulin, and cyclosporine are utilized, although there is still no consensus on their efficacy.<sup>4,10</sup> Proper wound care and sterile handling are important to prevent infections and prophylactic antibiotic treatment is not recommended.<sup>9</sup> Surgical wound debridement of the necrotic area is generally discouraged for a more conservative “antishear” approach; the detached/detachable epidermis is left in place and silver-releasing wraps/dressings are applied. Pain management can be extremely challenging and some patients require general anesthesia and mechanical ventilation, especially in case of concomitant acute respiratory failure.

The mortality rate of TEN remains high at around 25–35% (1–5% for SJS)<sup>3</sup> and surviving patients can experience severe sequelae resulting from skin and mucosal lesions. The rarity of TEN explains the paucity of evidences regarding the optimal management of these patients, and the high mortality keeps focus of TEN-related literature to resuscitation and extensive skin lesions. There is very little information on ENT involvement of SJS and TEN, with only one case series published until now,<sup>11,12</sup> and only a few long-term ENT sequelae in severe cases.<sup>11,12</sup>

Our study aims at evaluating the characteristics, treatment modalities, and outcomes of ENT mucosal lesions in severe TEN patients and propose an algorithm to prevent long-term debilitating sequelae of these lesions. Given the rarity of TEN and the paucity of evidence regarding its optimal management, our study seeks to address this gap in knowledge and contribute to the development of more effective treatment strategies for this severe condition.

## Material and methods

This is a retrospective case series from the tertiary burn unit of the Lausanne University Hospital CHUV, Switzerland. The study has been authorized by the local ethic committee (CER-VD 2018-02268).

All patients treated between 2006 and 2019 with the diagnosis TEN (TBSA involved  $\geq 30\%$ ) were included in the study. We excluded one case of SJS and one of SJS/TEN overlap, both of which were briefly hospitalized in our burn unit during this period. The electronic medical record of each patient was reviewed to gather all available information. Demographic

data (age, gender), TEN characteristics (TBSA involved, SCORTEN, etiology), length of stay in the burn unit, immunosuppression factors, tracheal intubation, tracheotomy, nasogastric tube, ENT involvement (oral cavity, ear, nasal cavity, pharynx, and larynx), treatments of ENT lesions, and ENT sequelae (stenosis, synechiae) were extracted when available.

Continuous variables are expressed as mean (standard deviation) or median (interquartile range) when appropriate and qualitative variables as numbers or percentage.

A multidisciplinary team consisting of the intensivists, ENT surgeons, speech and swallow therapists, dental surgeons, and skin specialists evaluated patients with oral, oropharyngeal, and cutaneous lesions. In our management protocol, an ENT evaluation is mandatory at admission. Frequency of the follow-up visit is then at the discretion of the consultant.

## Results

Between 2006 and 2019, 19 patients were admitted at our burn unit with the diagnosis of TEN. The median age was 56 years (20.5) with 42% female patients (58% male). A causative agent was identified in 89.5% of cases. The mean percentage of TBSA involved at presentation was 58.4 (23.6) with a median SCORTEN-Score at admission of 3 (1.5). In 17 (89%) patients, the causative drug was identified and is listed in Table 1.

Five patients died during their hospitalization in the intensive care, resulting in a mortality rate of 26.3%. For three of them (16%), all in advanced oncologic situations, a withdrawal of care was decided early after admission. Sixteen patients received maximal care, however, two of them (12.5%) died during the ICU stay. Both cases died in the context of a septic shock, which was followed by a multiorgan failure in one patient and caused peripheral necrosis of all four limbs in the second patient followed by treatment withdrawal.

All 16 patients remained in the burn unit for a median time of 19 days (13.3), including both patients with a fatal outcome (days until death). Thirteen (81%) patients required orotracheal intubation for a median time of 16 days (14). Tracheostomy

**Table 1** Causal drug in the 19 patients

Drug involved	N (%)
Lamotrigine	3 (16)
Phenytoin	3 (16)
NSAIDs	4 (21)
Allopurinol	2 (11)
Carbamazepine	1 (5)
Ciprofloxacin	1 (5)
Sulfamethoxazole-trimethoprim	1 (5)
Loperamide	1 (5)
Docetaxel	1 (5)
Unknown	2 (11)

was performed in 3/16 (19%) who benefited from maximal treatment, and were performed at, respectively 7, 17, and 27 days following intubation. All 19 patients had nasogastric feeding tubes during their stay at the ICU.

Of the 19 patients, 17 (89%) had an examination of the oral cavity, bilateral nasal endoscopy, and direct pharyngolaryngoscopy with a McIntosh laryngoscope and Hopkins rod optics of different angles. In all cases, the initial ENT exam was performed in the first days after admission. Fourteen of seventeen patients (82%) showed ENT lesions, mostly consisting of mucosal erosions, bullous or fibrinous lesions and their site(s) are summarized in Table 2. The patients received treatment in the intensive care, and specific ENT management consisted of oral nursing, hygiene, and application of dexamethasone ointment. Topical symptomatic treatment in extubated patients, as bicarbonates mouthwash, have not been documented. There was no documentation of the lower airway.

In 78% of the female cases (7/9), gynecological lesions were documented and 74% (14/19) of the patients had concomitant ocular lesions.

Of the 14 patients who survived, six patients (43%) were transferred to the referring hospitals as soon as they did not require specialized care at our institution. During the follow-up,

**Table 2** Demographic data of 19 patients with TEN treated in the ICU between 2006 and 2019 and their head and neck mucosal involvement

Variable	Median (IQR), mean (SD) or count (%) N = 19
Age (median)	56 (20.5)
Sex (female)	8 (42%)
Mortality	5 (26%)
Withdrawal of care early after admission	3 (16% <sup>a</sup> )
Mean TBSA (%), mean)	58.4 (23.6)
SCORTEN score at admission	3 (1.5)
Documented ENT examination	17 (89%)
Documented ENT lesions	14 (82% <sup>b</sup> )
Oral lesions	14 (100% <sup>b</sup> )
Endonasal lesions	3 (18% <sup>b</sup> )
Pharyngeal lesions	10 (59% <sup>b</sup> )
Laryngeal lesions	5 (29% <sup>b</sup> )
Gynecological lesions	7 (78% <sup>c</sup> )
Ocular lesions	14 (74%)
Intubation	13 (81% <sup>d</sup> )
Duration of intubation (days, mean)	15.8 (8)
Tracheostomy	3 (23%)
Prior duration of intubation	7–27 days
Complications (synechiaes)	4 (29% <sup>e</sup> )

<sup>a</sup>Patients in palliative oncologic situations.

<sup>b</sup>N = 17, based on the number of ENT examinations.

<sup>c</sup>N = 9, female patients.

<sup>d</sup>N = 16, the three patients who refused intubation were excluded.

<sup>e</sup>N = 14, patients who survived.

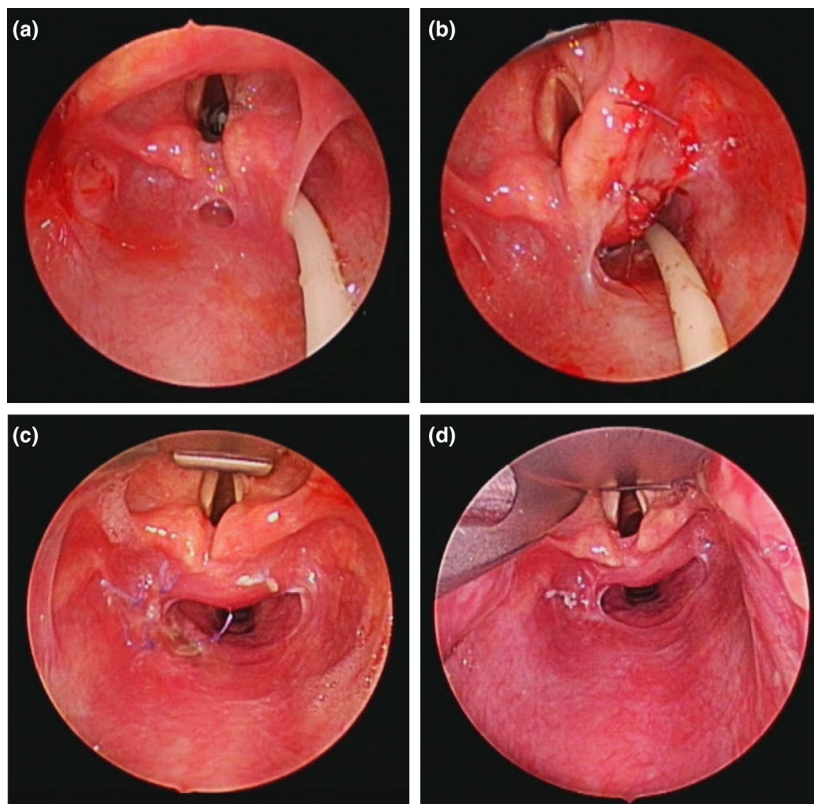
one of these patients complained of major dysphagia and was diagnosed with severe hypopharyngeal synechiaes with severe dysphagia and is published by the referring center as a case report.<sup>12</sup> Long-term follow-up was not available in the remaining five patients.

Four patients (including the one in ref. 12) of the 14 (29%) have documented long-term complications with synechiaes necessitating subsequent endoscopic procedures. Their mean TBSA involved were similar to the patients without ENT sequelae (65% vs. 58%) as well as their SCORTEN-score (median: 2.5 [1.75] vs. 3 [1.5]). Three were intubated for at least 2 weeks (15, 25, and 27 days), and one had a tracheostomy performed at day 7 because of repeated pulmonary toilet. The case illustrated in Figure 1 had a tracheostomy at day 27. Two patients were intubated because of respiratory distress, one for analgesia, and the last one for analgesia and extent of ENT lesions (case in Figure 1).

They all suffered from hypopharyngeal synechiaes. Three of them were diagnosed at 3, 4, and 10 months after the diagnosis of TEN because they were complaining of persistent dysphagia. In the last case (Figure 1), the laryngoscopy performed in the context of the tracheostomy at day 27 revealed the subtotal hypopharyngeal synechiaes. In this same case, evolution of the oral and oropharyngeal mucosal lesions led to multi-site mucosal synechiaes between the epiglottis and the base of the tongue, between the floor of the mouth and the tongue, as well as severe gingivolabial adhesions (Figures 1 and 2). This same case also presented a retrocricoid fistula. A second patient had gingivolabial synechiaes with limited symptoms. Another patient complained of epiphora and nasal obstruction caused by severe endonasal adhesions.

All patients required endoscopic treatment for their hypopharyngeal synechiaes with a successful outcome for the dysphagia and subsequent normal oral intake. In all cases, a combination of synechiaes lysis/resection with the CO<sub>2</sub> laser (continuous mode, between 1 and 2 Watts), plus balloon/bougie dilation was performed. The patient with more severe synechiaes necessitated a more complex treatment and is detailed below (Figure 1). All other patients did not show any recurrence after the first endoscopic treatment.

Endonasal adhesions of the third patient were released endoscopically, with placement of silicone sheet for 1 week to prevent recurrence. Epiphora was treated with an adhesiolysis, endoscopic dacryocystorhinostomy (DCR) on the right side, and a bicanalicular probe placement on the left side. One patient with severe gingivolabial adhesions was treated with multiple adhesiolysis and local application of betamethasone-gentamicin ointment. The patient further needed several local mucosal grafts placements to prevent recurrence and optimize oral compliance during feeding and speech. One patient who was diagnosed with gingivolabial synechiaes during the endoscopy for hypopharyngeal adhesions did not receive any treatment because of lack of symptoms.



**Figure 1** Hypopharyngeal synechiae and postoperative result. *Clinical case:* 37-year-old patient for which a complete endoscopic examination was performed in the context of the tracheostomy (27 days of intubation) and showed severe gingivolabial synechiae, synechiae between the epiglottis and the base of the tongue, and hypopharyngeal synechiae. Synechiae have been manually treated especially at the base of tongue. (a) Endoscopy 10 days after the tracheostomy: Severe hypopharyngeal synechiae with complete closure of the left sinus piriformis and adhesions of both arytenoids with posterior pharyngeal wall. Vocal cord mobility was preserved. (b) Partial section of the adhesion with the CO<sub>2</sub> laser and endoscopic suture of the mucosa to prevent a recurrence. (c) CO<sub>2</sub> laser section and endoscopic suture of the residual adhesions. (d) Long-term results (after three endoscopic treatments) in a patient with no residual dysphagia

## Discussion

To our knowledge, this is only the second case series reporting ENT lesions and their complications in adult patients with toxic epidermal necrolysis. Bequignon et al.<sup>5</sup> were the first to publish a case series of 49 patients who suffered of SJS or TEN and ENT mucosa involvement, and few others reporting hypopharyngeal stenosis.<sup>11,12</sup>

In Bequignon's case series,<sup>5</sup> only 16% of the patients were treated with mechanical ventilation (vs. 81% in our case series) and had a significantly lower mean TBSA involved (20% vs. 58%) and median SCORTEN-score (1 vs. 3). The prevalence of gynecological and ocular involvement was similar to that reported in the literature.<sup>13–15</sup> ENT involvements were comparable with most lesions located in the oral cavity (94%). Nasal lesions were found in 53% of the cases and 29% of the patients had severe pharyngolaryngeal lesions, but only 59% of their patients required nasogastric feeding tube. At 1-year follow-up, 98% of the patients did not show any long-term sequelae and

no synechiae were described at any time. Only one patient showed a persistent bullous lesion on the palate at 7 months without further complications.

In the present series, one out of five patients showed long-term ENT sequelae after prolonged intubation. Our patients had more severe forms of TEN than in Bequignon's case series, as illustrated by the mean TBSA involved, the median SCORTEN score or the number of patients requiring mechanical ventilation. This is explained by our patient selection which was limited to the severe TEN patients admitted in our burn unit.

Comparing our case series with Bequignon's, there seems to be an association between prolonged intubation and mucosal synechiae, especially in the hypopharynx. Unfortunately, due to the low number of patients, a statistical analysis is not meaningful. A nasogastric tube (NGT) placement may cause potentially serious complications in these patients, and the tube size, type (soft, hard), and its placement (traumatic/attraumatic) will play a role. Cases of severe ulceration of the posterior pharyngeal wall are widely described, even retrocricoid ulceration





**Figure 2** Severe gingivolabial synechiae of the upper lip. Same patient as in Figure 1, which had similar scarring at the lower lip and between the floor of the mouth and the tongue, limiting its mobility

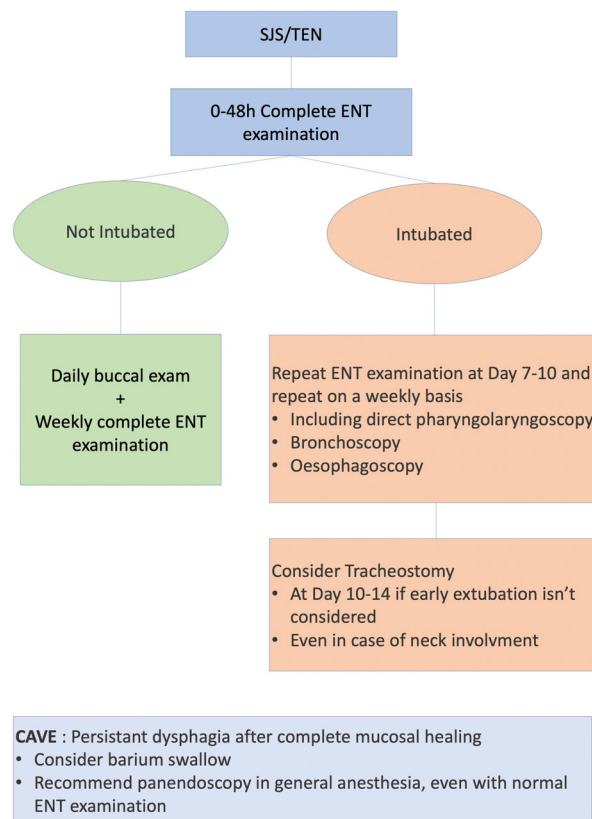
leading to vocal cord immobility.<sup>16</sup> One can therefore imagine that intubation combined with the nasogastric tube in place can trigger and/or worsen the lesions already present in the context of TEN. The lack of mobilization of the oro-pharyngolaryngeal musculature and the unconsciousness preventing the patient to complain of pharyngeal symptoms that would otherwise warrant an early ENT examination probably also contributes to the development of ulcerations and their evolving into synechiae.

Prolonged intubation is known to be a major cause of laryngo-tracheal trauma resulting in laryngotracheal stenosis.<sup>17,18</sup> In an inflammatory situation with mucosal fragility such as in TEN, one would expect to find cases of laryngotracheal stenosis. However, our cohort shows no short- or long-term laryngeal sequelae, although patients were intubated for an average of 15 days and even up to 27 days in one case. In prolonged intubation, tracheostomy has been demonstrated to be an effective way to reduce sedation and accelerate weaning from mechanical ventilation.<sup>19,20</sup> Smailes et al.<sup>21</sup> showed that even in patients with severe burns, early tracheostomy (<10 days) is associated with earlier active exercise, results in fewer days of ventilation, and shorter length of hospital stay. The pathophysiology in TEN patients may be different than in burn patients, but the reason tracheostomy is often delayed in both (cervical burns) pathologies is because the neck skin in these patients is more prone to infections. In patients with limited neck involvement, early tracheostomy should be considered.<sup>22</sup> In TEN patients with neck skin involvement, a tracheostomy during the necrolysis period, which usually progresses for 5–7 days,<sup>23</sup> should be strictly avoided.

During the re-epithelialization period, which lasts between 1 and 3 weeks, the tracheostomy should be considered if early extubation is not possible. All our patients with hypopharyngeal synechiae were intubated for 15, 25, and 27 days. In this context, performing the tracheostomy earlier (day 10–14) seems reasonable to prevent pharyngolaryngeal synechiae, not to mention the potentially positive effect on weaning from sedation and ventilation, which we will not dwell on since it is not the subject of this article. It seems reasonable to advocate laryngo-hypopharyngoscopy immediately after placement of the tracheostomy to diagnose and treat potential aero-digestive lesions.

All patients with SJS or TEN should have a dedicated ENT examination, as no correlation has been shown between the TBSA involved and mucosal involvement.<sup>23</sup> It seems reasonable to recommend a complete ENT examination in intubated TEN patients, to detect and ensure early treatment against potentially debilitating oral and oropharyngeal synechiae. The French national diagnosis and care protocol (PNDS; protocole national de diagnostic et de soins) recommends daily examination of accessible mucosae including the outer ear and once a week a complete specialized ENT examination.<sup>10</sup>

To avoid unnecessary bleeding and iatrogenic lesions, repeated examination should be avoided during the necrolysis



**Figure 3** ENT mucosal management algorithm in SJS/TEN patients

period (5–7 days). After this period, a direct pharyngolaryngoscopy with a McIntosh laryngoscope and high-quality optics should be performed once a week in order to prevent the formation of mature synechiae by manually releasing adherences while they are in formation. Thereby, a management algorithm of TEN patients with ENT involvement is described in Figure 3, which seems to be consistent with the French national diagnosis and care protocol.<sup>10</sup> Until now, the literature seemed to show that lesions of the oral cavity heal without complications,<sup>5</sup> but our series shows that two patients suffered of gingivolabial adhesions and one had cicatricial adhesions between the tongue and the floor of the mouth. In our clinical case, the severity of the oral adherences was probably caused by insufficient nursing and could have been prevented. In this case, daily manual digital mobilization with steroid ointments (betamethasone) of the lips and tongue could avoid the above-mentioned sequelae.

Our cohort possibly underestimates the rate of ENT sequelae in severe TEN patients who necessitated a mechanical ventilation. Out of the 14 patients who survived, 71% were transferred in other hospitals or ICUs as soon as they were stable enough. The lack of long-term follow-up is one of the main weaknesses of our study. Other limitations are the small number of patients and the retrospective nature. Because of the rarity of the disease, there are very few large cohorts that have been published about SJS and TEN. The first multicenter (18 centers) large cohort in the United States has been published in 2018 with a retrospective recruitment of 377 patients between 2000 and 2015 (Micheletti et al. 2018), with 89 patients necessitating an intubation and only includes 79 TEN patients (which corresponds to the proportion of severe cases; compared to 19 severe TEN cases and 13 necessitating an intubation in our case series). This study, like the majority of the few large retrospective cohorts, focuses on the general management and resuscitation of those patients and makes no description of the ENT involvement or its management.<sup>24,25</sup>

Almost all patients have initially been evaluated by residents with variable experience and therefore possibly over- or under-estimating the mucosal lesions. Unfortunately, the tracheo-bronchial tract was not documented in the ENT examination. In addition, due to the long recruitment period, patients did not receive the same systemic treatments, which may potentially influence the overall long-term prognosis and the intubation duration.

Despite these limitations, this study is the largest series to document ENT lesions in severe TEN patients. To our knowledge, it is the only study which documented multiple cases of long-term sequelae, especially hypopharyngeal synechiae. Further studies are needed to validate the proposed algorithm for preventing long-term sequelae in this patient population.

## Conclusion

TEN is a rare severe disease with high mortality and potentially high morbidity. There seems to be an association between

synechiae of the ENT region, especially in the hypopharynx, in severe TEN patients and prolonged intubation. In intubated patients, once the necrosis period is over, a periodic ENT examination to see the evolution of mucosal lesions seems reasonable. Endobuccal synechiae should be prevented with daily digital mobilization of the immature scar and application of topical corticosteroids. In awake patients, slight dysphonia, stridor, or dysphagia warrants an early ENT examination.

In case of mature hypopharyngeal synechiae, endoscopic CO<sub>2</sub> laser treatment seems to be a safe and effective procedure if performed by an experienced team.

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## References

- 1 Lerch M, Mainetti C, Terzicoli Beretta-Piccoli B, Harr T. Current perspectives on Stevens-Johnson syndrome and toxic epidermal necrolysis. *Clin Rev Allergy Immunol*. 2018;**54**:147–76. <https://doi.org/10.1007/s12016-017-8654-z>
- 2 Hasegawa A, Abe R. Recent advances in managing and understanding Stevens-Johnson syndrome and toxic epidermal necrolysis. *F1000Res*. 2020;**9**:612. <https://doi.org/10.12688/f1000research.24748.1>
- 3 Harr T, French LE. Toxic epidermal necrolysis and Stevens-Johnson syndrome. *Orphanet J Rare Dis*. 2010;**5**:39. <https://doi.org/10.1186/1750-1172-5-39>
- 4 Frantz R, Huang S, Are A, Motaparthy K. Stevens-Johnson syndrome and toxic epidermal necrolysis: a review of diagnosis and management. *Medicina (Kaunas)*. 2021;**57**:895. <https://doi.org/10.3390/medicina57090895>
- 5 Bequignon E, Duong TA, Sbidian E, Valeyrie-Allanore L, Ingen-Housz-Oro S, Chatelin V, et al. Stevens-Johnson syndrome and toxic epidermal necrolysis: ear, nose, and throat description at acute stage and after remission. *JAMA Dermatol*. 2015;**151**:302. <https://doi.org/10.1001/jamadermatol.2014.4844>
- 6 Grünwald P, Mockenhaupt M, Panzer R, Emmert S. Erythema multiforme, Stevens-Johnson syndrome/toxic epidermal necrolysis – diagnosis and treatment. *J Dtsch Dermatol Ges*. 2020;**18**:547–53. <https://doi.org/10.1111/ddg.14118>
- 7 Hsu DY, Brieva J, Silverberg NB, Silverberg JI. Morbidity and mortality of Stevens-Johnson syndrome and toxic epidermal necrolysis in United States adults. *J Invest Dermatol*. 2016;**136**:1387–97. <https://doi.org/10.1016/j.jid.2016.03.023>
- 8 Fouchar N, Bertocchi M, Roujeau J-C, Revuz J, Wolkenstein P, Bastuji-Garin S. SCORTEN: a severity-of-illness score for toxic epidermal necrolysis. *J Invest Dermatol*. 2000;**115**:149–53. <https://doi.org/10.1046/j.1523-1747.2000.00061.x>
- 9 Palmieri TL, Greenhalgh DG, Saffle JR, Spence RJ, Peck MD, Jeng JC, et al. A multicenter review of toxic epidermal necrolysis treated in U.S. burn centers at the end of the twentieth century. *J Burn Care Rehabil*. 2002;**23**:87–96. <https://doi.org/10.1097/00004630-200203000-00004>
- 10 Ingen-Housz-Oro S, Duong T-A, Bensaid B, Bellon N, de Prost N, Lu D, et al. Epidermal necrolysis French national diagnosis and care protocol (PNDS; protocole national de diagnostic et de soins). *Orphanet J Rare Dis*. 2018;**13**:56. <https://doi.org/10.1186/s13023-018-0793-7>

- 11 Barrera JE, Meyers AD, Hartford EC. Hypopharyngeal stenosis and dysphagia complicating toxic epidermal necrolysis. *Arch Otolaryngol Head Neck Surg.* 1998;**124**:1375–6. <https://doi.org/10.1001/archotol.124.12.1375>
- 12 Vourexakis Z, Heymans F. Hypopharyngeal synechiae in laryngeal syndrome (toxic epidermal necrolysis). *Otolaryngol Head Neck Surg.* 2015;**153**:152–3. <https://doi.org/10.1177/0194599815580981>
- 13 Morales ME, Purdue GF, Verity SM, Arnoldo BD, Blomquist PH. Ophthalmic manifestations of Stevens-Johnson syndrome and toxic epidermal necrolysis and relation to SCORTEN. *Am J Ophthalmol.* 2010;**150**:505–510.e1. <https://doi.org/10.1016/j.ajo.2010.04.026>
- 14 O'Brien KF, Bradley SE, Mitchell CM, Cardis MA, Mauskar MM, Pasieka HB. Vulvovaginal manifestations in Stevens-Johnson syndrome and toxic epidermal necrolysis: prevention and treatment. *J Am Acad Dermatol.* 2021;**85**:523–8. <https://doi.org/10.1016/j.jaad.2019.08.031>
- 15 Saeed HN, Chodosh J. Ocular manifestations of Stevens-Johnson syndrome and their management. *Curr Opin Ophthalmol.* 2016;**27**:522–9. <https://doi.org/10.1097/ICU.0000000000000312>
- 16 Sofferman RA, Haisch CE, Kirchner JA, Hardin NJ. The nasogastric tube syndrome. *Laryngoscope.* 1990;**100**:962–8. <https://doi.org/10.1288/00005537-199009000-00010>
- 17 Sandu K. Laryngotracheal complications in intubated COVID-19 patients. *Clin Med Insights Case Rep.* 2021;**14**:11795476211020590. <https://doi.org/10.1177/11795476211020590>
- 18 Shinn JR, Kimura KS, Campbell BR, Sun Lowery A, Wootten CT, Garrett CG, et al. Incidence and outcomes of acute laryngeal injury after prolonged mechanical ventilation. *Crit Care Med.* 2019;**47**:1699–706. <https://doi.org/10.1097/CCM.0000000000004015>
- 19 Hosokawa K, Nishimura M, Egi M, Vincent JL. Timing of tracheotomy in ICU patients: a systematic review of randomized controlled trials. *Crit Care.* 2015;**19**:424. <https://doi.org/10.1186/s13054-015-1138-8>
- 20 Szakmany T, Russell P, Wilkes AR, Hall JE. Effect of early tracheostomy on resource utilization and clinical outcomes in critically ill patients: meta-analysis of randomized controlled trials. *Br J Anaesth.* 2015;**114**:396–405. <https://doi.org/10.1093/bja/aeu440>
- 21 Smailes S, Spoons C, da Costa FM, Martin N, Barnes D. Early tracheostomy and active exercise programmes in adult intensive care patients with severe burns. *Burns.* 2022;**48**:1599–605. <https://doi.org/10.1016/j.burns.2021.10.005>
- 22 Smailes ST, Ives M, Richardson P, Martin RV, Dziewulski P. Percutaneous dilational and surgical tracheostomy in burn patients: incidence of complications and dysphagia. *Burns.* 2014;**40**:436–42. <https://doi.org/10.1016/j.burns.2013.07.011>
- 23 Estrella-Alonso A, Aramburu JA, González-Ruiz MY, Cachafeiro L, Sánchez Sánchez M, Lorente JA. Toxic epidermal necrolysis: a paradigm of critical illness. *Rev Bras Ter Intensiva.* 2017;**29**:499–508. <https://doi.org/10.5935/0103-507X.20170075>
- 24 Kridin K, Brügggen M-C, Chua S-L, Bygum A, Walsh S, Nägeli MC, et al. Assessment of treatment approaches and outcomes in Stevens-Johnson syndrome and toxic epidermal necrolysis. *JAMA Dermatol.* 2021;**157**:1182–90. <https://doi.org/10.1001/jamadermatol.2021.3154>
- 25 Micheletti RG, Chiesa-Fuxench Z, Noe MH, Stephen S, Aleshin M, Agarwal A, et al. Stevens-Johnson syndrome/toxic epidermal necrolysis: a multicenter retrospective study of 377 adult patients from the United States. *J Invest Dermatol.* 2018;**138**:2315–21. <https://doi.org/10.1016/j.jid.2018.04.027>