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International Journal of Pharmaceutical Research & Allied Sciences, 2022, 11(1):29-34
https://doi.org/10.51847/K833tMZjQP

Review Article

ISSN : 2277-3657
CODEN(USA) : IJPRPM

An Overview on the Evaluation and Management of Stevens-Johnson Syndrome/Toxic Epidermal Necrolysis

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ABSTRACT

One of the rare dermatological illnesses that might cause a medical emergency is SJS/TEN. SJS/TEN trigger an aggressive immune reaction to destroy the epithelium of the skin and mucous membranes. They are life-threatening mucocutaneous responses with death rates as high as 30% and a wide range of acute and chronic morbidities. Therefore, early detection and adequate and early treatment can save the patient's life. To review the evaluation of SJS/TEN clinical manifestations and the different aspects of the management. PubMed database search engine was the preferred method for data selection, and the following keys were used in the mesh ((“Stevens-Johnson Syndrome/Toxic Epidermal Necrolysis"[Mesh]) AND (“evaluation”[Mesh]) OR (“management"[Mesh])). While there is no test or set of criteria that can determine whether or not an individual has Steven-Johnson syndrome or Toxic epidermal Necrolysis, a skin biopsy can assist in determining other illnesses that have clinical manifestations.
Provided there is no effective approach to treat SJS/TEN, presently the best approach is to have a great doubt for the syndrome, early clinical diagnosis, immediate discontinuation of suspected causing substance, supportive therapy, and close monitoring for and treatment of high morbidity complications like infection and ophthalmologic sequelae. Moreover, pain control is crucial to retain a sense of the mental and physical well-being of the patients.

Key words: *Stevens-Johnson syndrome, Diagnosis, Management, Evaluation*

INTRODUCTION

SJS/TEN are rare disorders that trigger an aggressive immune reaction to destroy the epithelium of the skin and mucous membranes [1, 2]. Stevens-Johnson syndrome has a national incidence of 6.3 per 100,000, Stevens-Johnson syndrome/toxic epidermal necrolysis overlap syndrome had a national incidence of 0.7, and toxic epidermal necrolysis had a national incidence of 0.5 [3].

This illness is frequently misdiagnosed. This can occur as a result of manifestations that are similar to those seen in primary care, such as upper respiratory tract infection, adverse medication response, conjunctivitis, viral exanthem, and so on. It is also easy to mix it up with more uncommon medical illnesses like bullous pemphigoid and autoimmune blistering diseases such as pemphigus Vulgaris [4].

One of the rare dermatological illnesses that might cause a medical emergency is SJS/TEN. SJS/TEN are life-threatening mucocutaneous responses with death rates as high as 30% and a wide range of acute and chronic morbidities. Therefore, early detection and adequate and early treatment can save the patient's life [1, 5]. We aim in this article to provide an overview of the evaluation and management of SJS/TEN.

MATERIALS AND METHODS

PubMed database search engine was the preferred method for paper selection, and the following keys were used in the mesh ((“Stevens-Johnson Syndrome/Toxic Epidermal Necrolysis"[Mesh]) AND (“evaluation” [Mesh]) OR (“management"[Mesh])).

The inclusion criteria were selected from the following topics: Stevens-Johnson Syndrome/Toxic Epidermal Necrolysis. Exclusion criteria were all other articles, except topics that did not have one of the inclusion criteria.

Around 179 publications were chosen as the most clinically relevant out of 1054 articles indexed in the last decade, and their full texts were evaluated. A total of 20 of the 179 were included after a thorough examination. Additional research and publications were found using reference lists from the recognized and linked studies. Expert consensus recommendations and commentary were added where relevant to help practicing physicians assess cirrhosis most simply and practically possible.

RESULTS AND DISCUSSION

F.C. Johnson together with A.M. Stevens originally identified SJS reported in two infants with, stomatitis, eruptive fever, and ophthalmia in 1922. Then, A. Lyell initially created the term TEN in nineteen sixty-five, when he described 4 individuals who had ‘‘burning sensation in a clinical presentation that is closely related to a toxic eruption which it gives rise in the patient’’ [6].

When it comes to identifying SJS/TEN from clinical mimics, a skin biopsy is frequently required. Full-thickness epidermal necrosis is the most common pathologic feature [6, 7]. While 5–20% are assumed to be idiopathic, SJS/TEN are likely to be caused by a mix of immunological vulnerability and external triggers like medicine or infection that cause epithelial cell death. Depending on the demographic studied, medication exposure is linked to 50–95% of instances. SJS/TEN are more likely to occur in people who have particular HLA serotypes, or abnormalities related to assimilation capabilities, disseminate to tissues, process, or excrete drugs [8].

Clinical presentation and evaluation

While there is no test or set of criteria that can determine whether an individual has steven-Johnson syndrome or Toxic Epidermal Necrolysis, a skin biopsy can help determine other illnesses that have clinical manifestations. A dermis-containing shave biopsy or punch biopsy is the best way to collect the material. Formalin is where the sample should be collected, on suspicion in the diagnosis of SJS/TEN should be indicated on the associated documentation, and quick processing (a few hours or less) should be requested when preparing it for submission. At the beginning of the clinical presentation, it can be difficult to distinguish SJS/TEN from erythema multiforme, although erythema multiforme will express less widely and redly than SJS/TEN, and erythema multiforme have less involvement of mucosa that typically appears with SJS/TEN [8, 9].

Drug-related TEN usually begins with a fever and flu-like symptoms 1 to 3 weeks following the administration of the suspected drug. In up to 90% of cases, indications appear one to three days later in the membrane of the mucosa, including the eyes, mouth, nose, and genitalia. Generalized macules with purpuric cores characterize skin lesions. The macules grow into enormous confluent blisters with eventual epidermal peeling, although the hair is never involved. Separation of the epidermis occurs during the next 3 to 5 days, resulting in vast denuded patches. Intense discomfort, enormous protein loss together with fluid, bleeding, evaporative heat loss with consequently decreased body temperature, and infection result from the vast wound area [10, 11].

The epidermis, extracutaneous epithelium, and mucous membranes are all separated on histopathology at the dermal-epidermal junction of the skin. A positive Nikolsky sign, which presents with slight rubbing of skin results in exfoliating of the outermost layer with inspecting finger, can be used to diagnose this. Unlike full-thickness burns, the epidermal glands are mostly complete, allowing for epithelium formation without scarring. The epidermis begins to re-epithelialize around a week after the commencement of skin responses and can take up to three weeks.

The mouth and esophagus, as well as the small bowel and colon, are commonly involved in gastrointestinal disease. TEN patients seldom develop a paralytic ileus, allowing for early enteral feeding. Involvement in the

gastrointestinal system can result in obstruction or strictures, as well as long-term problems such as dysphagia and ileus. Vaginal stenosis or strictures can occur as a result of vulvovaginal involvement [12, 13].

Hyper- and hypopigmentation affect almost all children, and while they lessen over time, they seldom go away completely. Scarring and hypertrophic alterations to the skin are uncommon. Fingernails and toenails are also affected in the long run, then frequently the nail beds and loss of the nails become inflamed on the acute phase of TEN. Nails can acquire abnormalities that are often painless and without causing considerable functional impairment. When dyspnea, bronchial hypersecretion, a normal chest X-ray, and decreased oxygen level are seen at the onset of the disease, pulmonary edema, and progressive respiratory failure emerge, as well as extensive ulcerations and epithelial necrosis of the bronchial epithelium must be suspected. Intubation and mechanical ventilation may be necessary, and this is linked to a greater risk of death. Barotrauma and ventilator-induced lung damage can be avoided with permissive hypercapnia and mild respiratory acidosis. Nitric oxide inhalation therapy may be beneficial. After receiving low-dose inhaled nitric oxide, the PaO2/FIO2 ratio improved by 162%, while nonsurvivors had a substantially less favorable first reaction. Even if they did not require mechanical ventilation, patients that survived from SJS/TEN can experience long-term breathing complications including a loss in CO diffusion ability of up to Thirty-five percent–forty percent below normal [10, 11].

Ophthalmic problems are found in roughly 30% of surviving children and up to 74 percent of adults, with serious complications occurring in 25% of cases. Inflamed and reddish eyelids, bacteria caused conjunctiva inflammation, suppurative keratitis, or endophthalmitis characterize the acute stage of ocular involvement, which lasts 2 to 6 weeks. Topical steroids can help minimize the circle of cicatrization and eyelid abnormalities if there is a lot of irritation. Scarring in the epithelium of the conjunctiva, membranous or pseudomembranous conjunctiva inflammation, ankyloblepharon, or symblepharon, together with other issues such as entropion or lagophthalmos, causes severe dry eye syndrome or vision loss [10, 14, 15].

Management

Provided there is no effective approach to treat SJS/TEN, presently the best approach is to have a great doubt for the syndrome, immediate clinical intervention, early discontinuation of suspected causing substance, supportive therapy, and close monitoring for and treatment of high morbidity complications like infection and ophthalmologic sequelae. If a patient has mild systemic symptoms, has limited skin involvement, and is progressing slowly, care can be provided in a non-specialized setting; however, all other patients should be admitted to an ICU or burn unit, as individuals who receive attention in burn units have a better morbidity and mortality outcome. In all suspected cases, a dermatologist should be consulted [8, 16, 17].

Supportive management

Tachypnea and hypoxia can suggest respiratory alkalosis from respiratory involvement, therefore taking vital signs is a crucial initial step in evaluating a patient with suspected SJS or TEN. Because fluid loss leads to hypotension secondary to hypovolemia, hypoalbuminemia, electrolyte abnormalities, and renal dysfunction, severe fluid loss from the lesion of the skin should be treated with vigorous fluid resuscitation. While significant doses of intravenous fluids are given, because of the lack of interstitial edema in SJS/TEN, lesser quantities than those used for burns can be given. Hemodynamic monitoring and stabilization, antimicrobial prophylaxis, nutritional supplementation and/or substitution, control of temperature, numbness, and meticulous skin, eye, and membrane of the mucosa care are all common supportive therapy in these instances. Infectious problems manifest initially, and as sepsis is the leading source of death in SJS/TEN, instant treatment is recommended [18].

Staphylococcus aureus and Pseudomonas spp. are the most typically found infectious agents. Because noncutaneous Enterobacteriae are found in one-third of positive blood cultures in these individuals, bacterial passage change from the GI tract is likely to be a prevalent mode of contamination. Prophylactic antibiotics are not recommended, aside from a daily mouth rinse with an antiseptic or antifungal solution. Instead, emphasis should be placed on aseptic procedures. Skin, blood, and urine cultures should be acquired regularly [19]. Surgical wound debridement is not advised since it might exacerbate skin lesions; nonetheless, the optimum procedures for treating cutaneous lesions and improving skin care have yet to be discovered [20].

An ophthalmologist should evaluate ocular lesions daily. Early in the illness course, preservative-free emollients, antiseptic or antibiotic eye drops, and vitamin A are the therapies advised reducing the development of problems. If these therapies are given sooner, they are more likely to be successful [21]. Individuals suffering from ocular sequelae of SJS/TEN who were treated with scleral lenses had less photophobia and discomfort, according to a retrospective study [8].

Skin treatment

In the acute phase of SJS/TEN, skin involvement is well reported, and the manifestation of the skin includes purpuric macules or target lesions that are not typical with blisters and erosions in 100% of SJS/TEN patients [22]. Cutaneous lesions start symmetrically on the face and upper torso and spread quickly throughout the whole body, mostly on the trunk and proximal limbs, with lesions reaching their maximum extent in 2–3 days. TEN is characterized by a sheet-like loss of epidermis in areas affected by confluent erythema [5, 23].

The severity of the disease is determined by the degree of skin involvement, which is measured in the percentage of total body surface area. This should be done regularly, especially during the first week after the commencement of the condition. When the skin's barrier function is destroyed, as in burn injuries, homeostatic systems are disrupted. Fluid and loss of electrolytes, hypovolemia, infection vulnerability, poor thermoregulation, changed immunologic processes, high energy expenditure, and reduced rate of utilizing substrate are all possible outcomes. The severity of these side effects is related to the degree of epidermal loss. In the acute phase, there are several techniques for skincare, with little evidence to favor one over the other.

To protect the underlying dermis, a conservative technique entails aspirating blister fluid while keeping the separated outermost layer unaltered. If the dermis is exposed, adequate bandaging is done to decrease the loss of fluid, prevent infection from microbial colonization, and promote re-epithelialization by maintaining a moist wound environment. Debridement of the separated epidermis is performed surgically, followed by wound closure with synthetic dressings, allograft, or xenograft. This method eliminates any infectious material from the skin's surface [24].

In terms of long-term morbidity, however, there is currently no indication that one technique is more successful than the other. The majority of skin involvement goes away on its own with no long-term consequences, however, pigmentation irregularities and scarring can develop. Long-term abnormalities of the fingernails might result from the involvement of the paronychium and nail plate during the acute phase. Hair loss has also been recorded in the first six months after discharge from the hospital, with the scalp, eyebrows, and eyelashes being the most typically afflicted locations [25]. Pigmentary alterations, scarring, and nail dystrophy are frequent long-term integumentary system sequelae, but they are usually not severe [26]. In a recent study, 88% of patients with SJS/TEN exhibited long-term cutaneous sequelae such as post-inflammatory skin changes, scars, milia, and urticaria after a mean follow-up duration of 51.6 ± 74.7 months. A dermatologist or a burn/plastic surgeon should handle these complications. To avoid post-inflammatory hyperpigmentation, explicit instructions on sun protection and the use of sunscreens should be given upon discharge [22, 25].

Management of pain

In SJS/TEN, pain control is crucial. In the acute and subacute stages of the disease, Steven-Johnson syndrome/Toxic epidermal syndrome is marked by significant skin discomfort, and patients may require intense sessions of pain medication [22]. In the acute phase of the condition, combination therapy is frequently used. When necessary, oral nonsteroidal anti-inflammatory medications and opioid-based regimens are recommended. The use of opioid-based regimens at large dosages and for lengthy periods is common, mandating respiratory monitoring [27].

Dressing changes and other operations necessitate further analgesia or supplementation. The pain was monitored on a ten-point visual analog scale (VAS) every four hours in one trial of SJS/TEN patients, and the pain control regimen was changed based on the VAS score. Patient-controlled analgesia (PCA) methods were used to start morphine if the VAS score was higher than 4. Patients with SJS/TEN who are unable to employ PCA mechanisms for pain medication administration may require infusions of opioid medicines or derivatives, even though Patient-controlled analgesia devices are effective throughout the recuperation duration [28].

While pain management is critical, the high dosages used during protracted hospital stays can develop addiction and dependency after release. Patients require pain control to retain a sense of mental and physical well-being, as well as to be useful members of society; nevertheless, they cannot be discharged from the hospital on narcotic medicine that exceeds a certain threshold level, since they risk becoming addicted. Any patient who is unable to wean off pain medication as discharge planning approaches should visit a pain management team member and be closely monitored after release. In the subacute and chronic phases of SJS/TEN, long-acting opiates like methadone can be used to reduce pain, and gabapentin can be used to treat neuropathic pain in the chronic phase [22].

CONCLUSION

While there is no test or set of criteria that can determine whether or not a patient has SJS or TEN, a skin biopsy can help rule out other illnesses that have clinical manifestations.

Given the lack of a proven effective cure or treatment for SJS/TEN, the best approach based on current data is to have a high suspicion for the syndrome, early clinical diagnosis, immediate discontinuation of suspected causing substance, supportive therapy, and close monitoring for and treatment of high morbidity complications like infection and ophthalmologic sequelae. Moreover, pain control is crucial to retain a sense of the mental and physical well-being of the patients.

ACKNOWLEDGMENTS : None

CONFLICT OF INTEREST : None

FINANCIAL SUPPORT : None

ETHICS STATEMENT : None

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