Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/burns

Review

Complications of Stevens–Johnson syndrome beyond the eye and skin

Hajirah Saeed [a], *Iason S. Mantagos* [b], *James Chodosh* [a,*]

[a] *Department of Ophthalmology, Massachusetts Eye and Ear Infirmary, Harvard Medical School, 243 Charles St., Boston, MA 02114, USA*

[b] *Department of Ophthalmology, Boston Children's Hospital, Harvard Medical School, 300 Longwood Ave, Boston, MA 02115, USA*

ARTICLE INFO

Article history:
Accepted 20 March 2015

Keywords:
Stevens–Johnson syndrome
Toxic epidermal necrolysis

ABSTRACT

Introduction: Ocular and cutaneous disease are common chronic sequelae of Stevens–Johnson syndrome/toxic epidermal necrolysis (SJS/TEN) and have been well described in the literature. Long-term complications affecting other organ systems have not been so well described. The purpose of this review article is to highlight non-ocular and non-cutaneous chronic complications of SJS/TEN.

Methods: The PubMed database was searched for the keywords "Stevens–Johnson syndrome" and "toxic epidermal necrolysis" through September 1, 2014. Relevant articles were then reviewed in full.

Results: 138 articles in the English language were found that described chronic sequelae of SJS/TEN. Our search revealed six affected organ systems other than the eyes and integument, with chronic sequelae from SJS/TEN: respiratory, gastrointestinal/hepatic, oral, otorhinolaryngologic, gynecologic/genitourinary, and renal. Complications involving these organs systems appeared likely to reduce the quality of life for SJS/TEN survivors.

Discussion: SJS/TEN is a multi-organ disease requiring multidisciplinary care from a variety of specialists. Affected patients have complex hospital stays, and their quality of life may be severely impacted by multiple long-term complications. We believe that preventative care in the acute setting might limit the development and progression of many of the sequelae described above.

Contents

* *Corresponding author at*: 243 Charles St., Boston, MA 02114, USA. Tel.: +1 617 573 6398; fax: +1 617 573 4324.
E-mail addresses: Hajirah_Saeed@meei.harvard.edu (H. Saeed), Jason.Mantagos@childrens.harvard.edu (I.S. Mantagos), James_Chodosh@meei.harvard.edu (J. Chodosh).

Abbreviations: SJS, Stevens–Johnson syndrome; TEN, toxic epidermal necrolysis; AM, amniotic membrane; EM, erythema multiforme.

http://dx.doi.org/10.1016/j.burns.2015.03.012

1. Introduction

Stevens–Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) together form a spectrum of delayed-type hypersensitivity reactions triggered by drugs, and less commonly by infections. This mucocutaneous disease is typified by an acute febrile illness associated with prodromal target lesions, followed by skin detachment and involvement of at least 2 mucous membrane sites [1]. SJS is on the less severe end of the spectrum, constituting <10% of epidermal detachment and with a 1–5% mortality. The more severe TEN involves ≥30% of the epidermis and has a 25–35% mortality. Epidermal detachment between 10 and 30% constitutes SJS-TEN overlap [2]. The classification of SJS/TEN and other mucocutaneous diseases have long been debated, with initial descriptions categorizing erythema multiforme, SJS, and TEN as diseases on one spectrum. In 1993, Bastuji-Garin et al. developed a classification of bullous mucocutaneous diseases based on patterns of the skin lesions in addition to degree of skin involvement, classifying erythema multiforme as a clinically distinct disease from SJS/TEN [2]. Later papers further supported this categorization, and EM is now considered a clinically, etiologically, and epidemiologically distinct condition from SJS/TEN [2–4].

SJS/TEN is a rare disease, affecting between two and seven cases per million people per year [5–10]. The acute sequelae of SJS/TEN, however, are well documented [11]. SJS/TEN is typically severe and potentially fatal in the acute phase due to the associated necrosis of external and internal body surfaces which predispose the patient to life-threatening complications including sepsis and multi-organ failure [12]. SJS/TEN also results in significant long-term morbidity involving various organ systems. Ocular and cutaneous sequelae are the two most common and have been well described in the literature. The diffuse epithelial necrosis in SJS and TEN can lead to severe chronic conjunctivitis, pseudomembrane formation, trichiasis, and extensive corneal damage leading to blindness [3,13,14]. Long-term cutaneous sequelae include nail deformities, pigmentation abnormalities, and dermatitides [15]. Long-term complications affecting other organ systems have not been so well described.

As the chronic complications of SJS/TEN in the skin and eye are well known, in this study, we sought to create a comprehensive review of published complications of SJS/TEN across other organ systems, based on a systematic review of the published literature. We hope this will aid physicians in all disciplines in understanding the history and extent of systemic involvement, and caring for patients with this rare but multi-organ disease process.

2. Methods

A literature search was conducted on PubMed for all publications related to SJS/TEN through September 1, 2014. The search terms used were ''Stevens–Johnson syndrome'' and ''toxic epidermal necrolysis.'' The title and abstract (if available) of every publication in the search results were reviewed for relevance, and relevant articles were then reviewed in full. Only those articles in the English language were used. The reports were considered by organ system and in chronologic order.

3. Results

A total of 4944 publications were returned with the keywords ''Stevens–Johnson syndrome'' and ''toxic epidermal necrolysis.'' 138 were found to be relevant to the chronic sequelae of SJS/TEN and in English. Forty three were not in English and were not reviewed. This comprehensive search revealed six organ systems, other than the eyes and integument, with chronic sequelae from SJS/TEN: respiratory, gastrointestinal/hepatic, oral, otorhinolaryngologic, gynecologic/genitourinary, and renal.

4. Discussion

4.1. *Respiratory*

The first reports of pulmonary involvement in SJS/TEN were in 1945 and 1947. The respiratory involvement described was acute in nature, resolving 2–3 weeks after the onset of the rash, and described as parenchymal infiltration and bronchopneumonia [16–18]. Autopsy reports at that time demonstrated alveoli distended with an exudate of desquamated alveolar and mononuclear cells [19]. Since that time, acute pulmonary involvement in patients with SJS/TEN has been well described, with 10–20% of SJS/TEN patients requiring mechanical ventilation [20].

The cumulative available data support pulmonary function abnormalities as a chronic complication of SJS/TEN, and warrant monitoring of long term pulmonary function, particularly in those who suffered from acute pulmonary complications of SJS/TEN [21,22]. Chronic pulmonary complications of SJS/TEN, were first described in 1983, wherein an 8-year-old girl died of chronic obliterative bronchitis 10 months after the resolution of her rash [23]. Since the