Corneal histopathology in Stevens-Johnson syndrome: A case report and review of literature

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Research Article

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Abstract

Stevens-Johnson syndrome is a life-threatening, immune-mediated, acute inflammatory disorder of the mucocutaneous membranes. It affects people of almost any age and has a high mortality and morbidity rate. Therefore, histopathological confirmation of the diagnosis is essential. Ocular involvement occurs in more than 50% of the affected patients. Here, we report a case of Stevens-Johnson syndrome with ocular involvement in a 10-year old boy that presented with complaints of pain, burning, stinging in both eyes, and decreased vision. Histopathological findings were consistent with the changes due to the syndrome. Stevens-Johnson syndrome affects various mucous membranes along with the skin. Ocular involvement may manifest both acutely and chronically and causes morbidities. Therefore, a careful clinical and histopathologic examination is required in order to give the correct diagnosis.

Introduction

Stevens-Johnson syndrome (SJS) is a life-threatening, immune-mediated, acute inflammatory disorder of the mucocutaneous membranes. Its counterpart, toxic epidermal necrolysis (TEN), is considered the most severe variant with a high mortality rate of up to 30% [1]. The disease is mostly drug-induced; however, some microbiological agents such as *Mycoplasma pneumoniae* have proven to be etiological factors. It is frequently seen in adults, and the children might also be affected, but they usually have better outcomes [2].

Depending on the severity of the disease, clinical manifestations change, including sepsis, respiratory dysfunction, and multiple organ failures. In addition, ocular involvement occurs in more than 50% of the patients, starting with ocular surface inflammation in the acute phase and moving on to corneal and conjunctival defects as it becomes chronic, which may result in visual impairments [3].

Herein, we report a pediatric case report with a history of ongoing SJS that manifested ocular complications, and we aim to discuss the specific histopathological changes.

Case Presentation

A 10-year old boy presented with complaints of pain, burning, stinging in both eyes, and decreased vision. He had been diagnosed as SJS with a skin biopsy performed six months ago on the history. He had been given 2gr/kg intravenous immunoglobulin for an initial diagnosis of Kawasaki disease and also with amoxicillin-clavulanate and then cefdinir for high fever. However, he had not benefited from amniotic membrane graft, and topical treatment with the biological agent bevacizumab and systemic therapy with prednisolone/cyclosporine had been started.

Physical examination revealed oral lesions and scars of old skin lesions, including nummular plaques on the face, trunk, and extremities and occasional hyperpigmented maculae with central scars and conjunctival hyperemia in both eyes. His blood tests showed leucocytosis and neutrophilia. The immunoglobulin levels were within normal limits. A corneal biopsy was obtained. Microscopical findings

revealed epithelial regeneration, necrotic keratinocytes, and perivascular lymphohistiocytic infiltrate [Figure 1]. In addition, there were Goblet cells present in the corneal epithelium [Figure 2]. This finding was confirmed with PAS stain histochemically [Figure 3]. The histopathologic findings were consistent with the changes due to SJS.

Conclusions

SJS is an acute immunological mucocutaneous disorder with a high mortality and morbidity rate that may affect patients at any age. However, the children are known to be affected less severely, and the mortality rate is around 7.5%. SJS and TEN are considered two similar entities of the same disease spectrum, differing only in the severity of skin detachment. The distinction is mainly based on the involved body surface area [4].

The most known cause of the disease is the usage of drugs, accounting for approximately 80% of the cases. Even though the pathogenesis of the disease is not fully understood, it is now known that it happens as a result of a cumulative effect of the drug's structure and the patient's genetic predisposition. There are many defined genetic associations between the drugs, Human Leukocyte Antigen (HLA) alleles, cytochrome p450 (CYP) pathways, and various ethnicities [5]. In a study that reviewed the causes of SJS and TEN in children by Ferrrandiz-Pulido et al., it was stated that the drugs that cause SJS vary, and the main ones are sulphonamides and anticonvulsants, followed by penicillins and nonsteroidal anti-inflammatory drugs. Mycoplasma and herpes virus infections are also common causes in childhood [2].

The diagnosis of SJS is confirmed by the histopathologic examination of a biopsy of the characteristic skin lesions that are diffuse erythematous macules with purpuric, necrotic centers with blisters. The hypersensitivity reaction results in widespread inflammation of the epidermis, leading to necrosis, blistering, and sloughing of the tissue. In early lesions, scattered necrotic keratinocytes are seen in the epidermis with mild superficial perivascular mixed inflammatory dermal infiltrate, and as the blisters start to form in later stages, full-thickness epidermal necrosis is seen with basal vacuolar change, subepidermal bullae, and mild superficial perivascular mixed inflammatory dermal infiltrate [6, 7].

There is an involvement of mucous membranes in approximately 90% of the affected patients, and the lip, oral cavity, conjunctiva, nasal cavity, urethra, vagina, gastrointestinal tract, and/or respiratory tract may be affected as lesions develop. Ophthalmic involvement is common and develops in approximately 50–60% of hospitalized patients [8]. In a retrospective analysis by Chang et al., 60% of the patients with SJS/TEN developed ocular involvement during the acute phase of the disease [9]. Clinically, acute and extensive ocular surface inflammation occurs with the pseudomembranous formation and corneal or conjunctival epithelial defects resulting in dry eye disease, corneal and conjunctival scarring, and symblephera formation. The most common ocular feature of SJS is the loss of corneal epithelial stem cells located in the limbal area, which is confirmed by the loss of palisades of Vogt. With the loss of the stem cells during the acute phase of the disease, the corneal epithelium stops regenerating, resulting in

“conjunctivalization,” which can be defined as a conjunctival epithelial invasion into the cornea [3]. This feature can be indicated histopathologically by the presence of the Goblet cells in the cornea.

In a study by Lopez-Garcia et al., histopathologic and cytologic changes were recorded during the acute phase and then six months later. They concluded that epithelial cell squamous metaplasia was related to ocular involvement severity in the acute phase and conjunctival cytological samples showed a marked decrease in goblet cell density as the lesions subsided [10].

Corneal involvement then may result in cicatricial, sclerotic changes of the ocular surface and changes such as neovascularization, opacification, keratinization, and even ulceration and perforation. After the acute phase, some of these changes may subside; however, there may be permanent visual impairment and conjunctival inflammation that prolong at the chronic stage [3].

Detailed clinical information and histopathological appearance constitute the strengths of the case.

In conclusion, Stevens-Johnson syndrome affects various mucous membranes along with the skin. Therefore, ocular involvement is an essential factor that causes morbidities, and a careful clinical and histopathologic examination is required in order to give the correct diagnosis.

Declarations

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Code availability: Not applicable.

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Figures

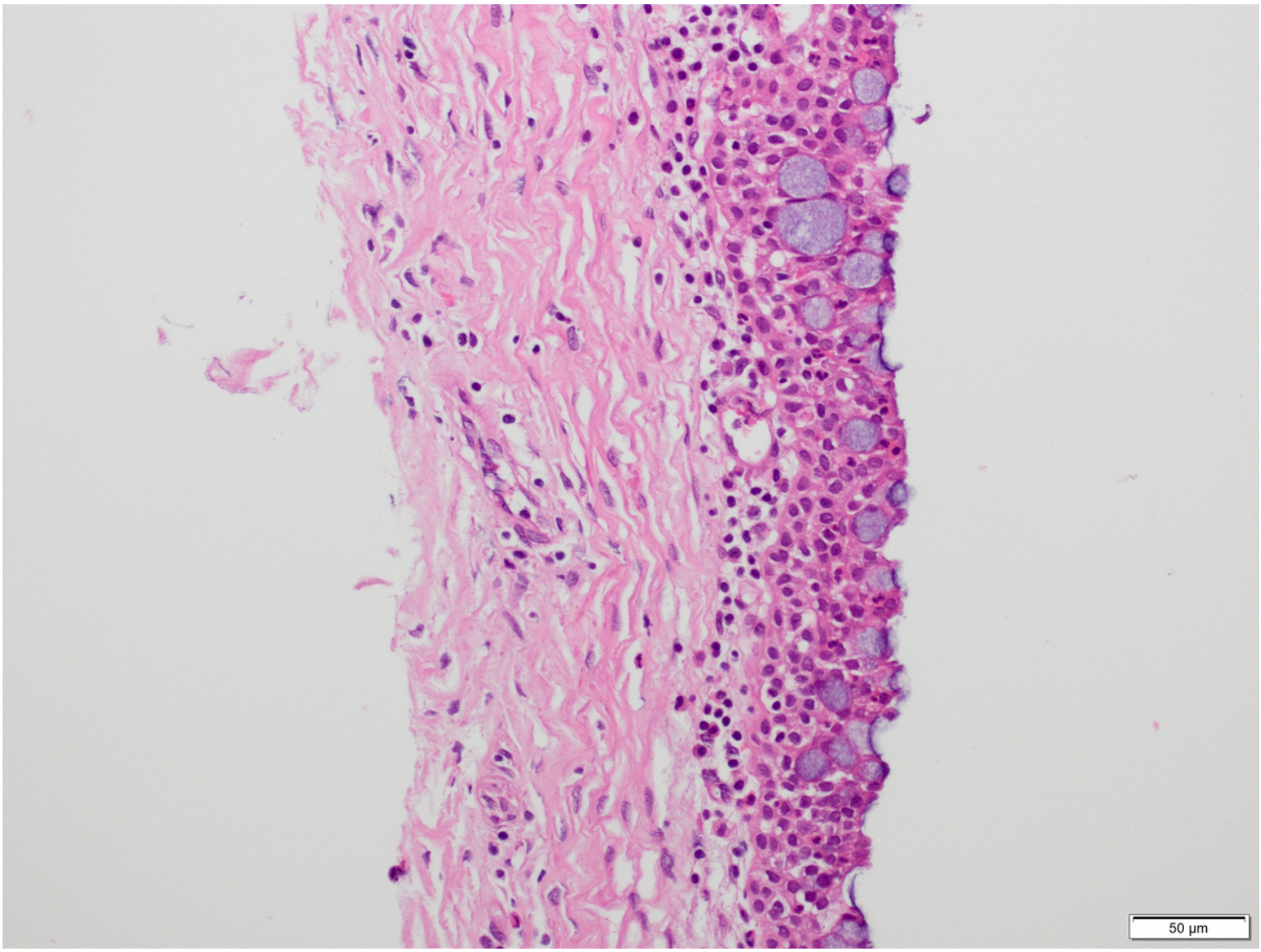

Figure 1

Epithelial regenerative changes and perivascular inflammatory infiltrate is seen. (H&E, 20x)

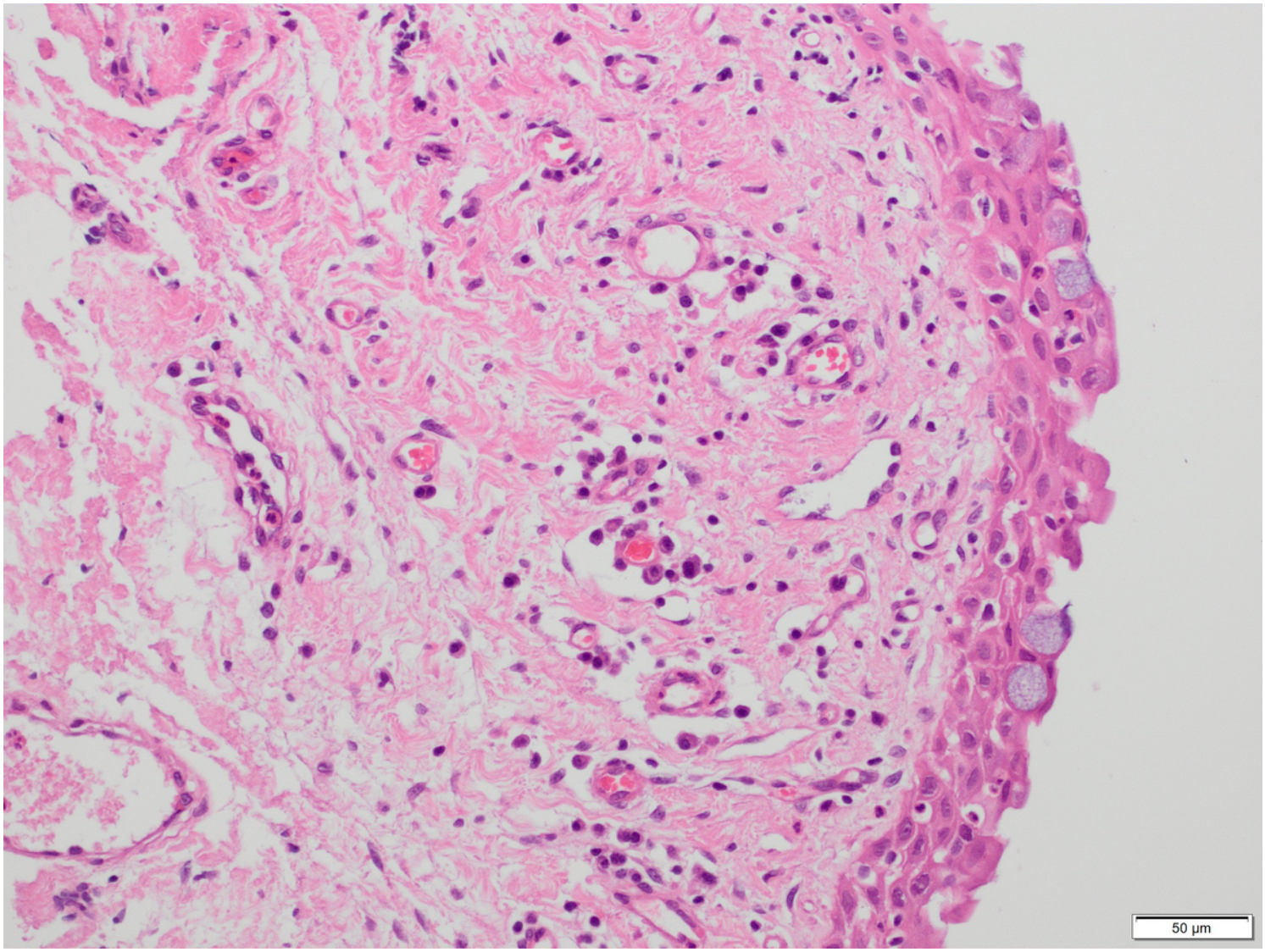

Figure 2

Goblet cells are seen in the corneal epithelium. (H&E 20x)

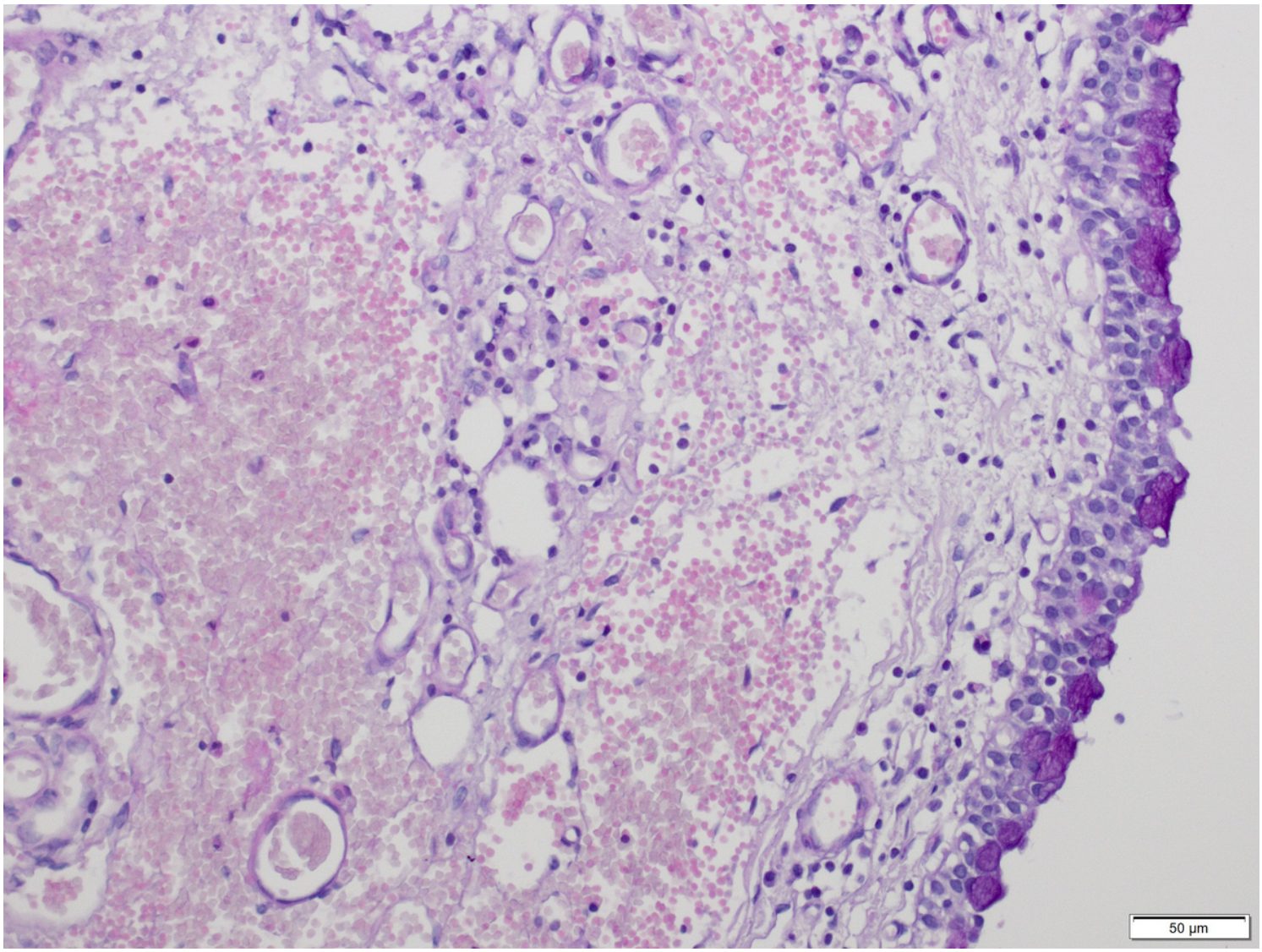

Figure 3

Goblet cells in the corneal epithelium are identified with PAS stain

Supplementary Files

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