Case Report

Lip synechiae: A rare complication of azithromycin-associated Stevens–Johnson syndrome

ABSTRACT

Stevens–Johnson syndrome (SJS) is a severe form of erythema multiforme, is a self-limiting acute inflammatory disease of multifactorial origin, but can also present as a chronic recurrent lesion. It causes a whole plethora of lesions, mostly mucocutaneous. It is a dermatologic emergency that occurs with a spectrum of severity and can result in severe morbidity and mortality. Lip adhesion is an unusual complication of healing in the lesions of SJS, for which only a few cases have been reported till date which not only causes esthetic morbidity but also impairs the proper functioning of the patient. The importance of this lesion also lies in its multifactorial and varied origin, this being the first case to report azithromycin as a causative drug, leading to SJS associated with lip adhesion. In this paper, we present a case report of SJS with lip adhesion, azithromycin being the causative drug, which was treated surgically with chalinoplasty. Along with it, the clinical features, its pathogenesis, the preventive measures, and the treatment modalities for the same including conservative as well as surgical have also been extensively discussed with a review of the existing English literature to date.

Keywords: Azithromycin, lip adhesion, Stevens–Johnson syndrome

INTRODUCTION

Stevens–Johnson syndrome (SJS) is a severe form of erythema multiforme. It is a disease of multifactorial origin. This self-limiting acute inflammatory disease affects the skin and oral mucous membranes, especially the lips due to which speech, eating, and swallowing becomes very difficult and painful.[1]

Its causative agents including various triggering agents such as infections, food, drugs (azithromycin being one of the rarest), immunizations, malignancies, and certain systemic diseases are also implicated in its pathology.[2]

An unusual complication of healing lesions in azithromycin-induced SJS is lip adhesion, and only a few cases have been reported in the World English Literature so far.

CASE REPORT

An 18-year-old female reported to us with restricted mouth opening due to adhesion of lips. On recording the history, it was found out that the patient was treated with azithromycin for common cold 2 months back, following which she developed skin target lesions on her trunk, limbs, and face, mild conjunctivitis, and severe desquamative gingivostomatitis. The patient was diagnosed with SJS that developed due to azithromycin administration [Figure 1] and was successfully managed at a tertiary care center.

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On the day of the presentation to our department, the patient had no systemic disability and the skin lesions were resolving. On examination, the patient was well and had mucosa-lined adhesions close to the corners of her mouth, one on each side, between the upper and lower lips that restricted her mouth opening [Figure 2]. These bands were pink, 0.2 cm in diameter, and about 1 cm in length on either side (at maximal opening). Although her mouth opening was restricted, the interincisal opening was almost 2 cm.

Bilateral chalinoplasty was performed that involved the release of adhesions between the lips at the corners of mouth using a knife under local anesthesia and lips were applied with petroleum jelly so as to prevent re-attachment. The postoperative period was uneventful, with no recurrence of lip adhesions [Figure 3].

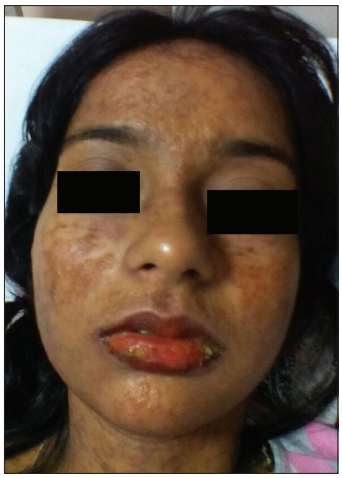

Figure 1: Stevens–Johnson syndrome developed in an 18-year-old female due to azithromycin administration

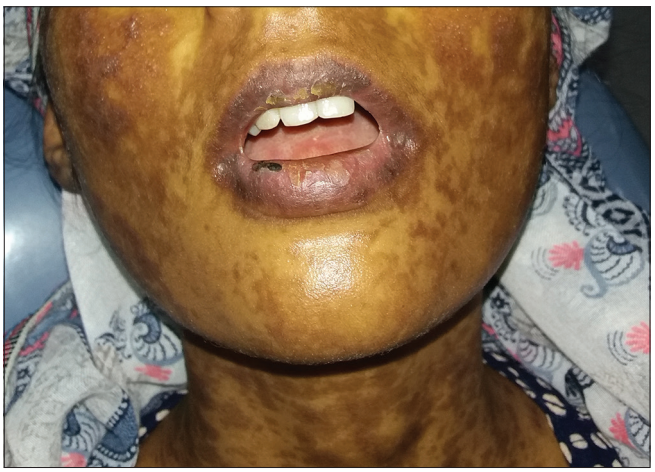

Figure 2: Bilateral lip adhesions after healing of lip lesions

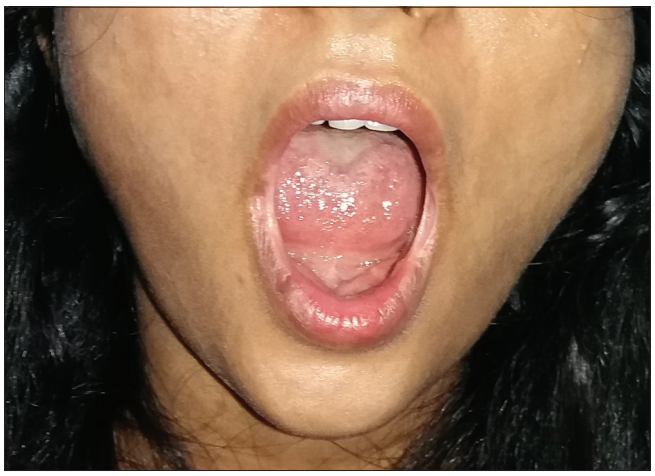

Figure 3: Lips 6 weeks after bilateral chalinoplasty

DISCUSSION

In 1922, Stevens and Johnson described SJS as a combination of symptoms reported in two patients who had continuous fever, inflamed buccal mucosa, and severe conjunctivitis.[3] The various features associated with the syndrome include target lesions of the skin, erosions of the oral mucosa and lips, and formation of pseudomembranous tunica conjunctiva palpebrarum. SJS, also known as erythema multiforme major,[4] is an immune complex-mediated disease which can cause significant morbidity given that it includes the skin and mucous membrane and may even lead to death (10%–34%).[5,6]

The disease usually begins with a nonspecific upper respiratory tract prodrome, which lasts for up to 14 days. Mucocutaneous lesions then develop abruptly, and these may continue to erupt for around 2–4 weeks. Some of the complications that can occur are corneal ulceration, anterior uveitis, panophthalmitis, penile scarring, vaginal stenosis, esophageal webs and strictures, renal tubular necrosis, renal failure, tracheobronchial shedding, respiratory failure, and finally scarring, deformity, and infections that mostly occur in slow-healing ulcers.[7]

The oral mucosal lesions are painful, and the progression of the disease is such that the vesiculobullous lesions rupture soon after their appearance causing the raw exudate to further limit the function.[8]

Wherever broad erosions of the labial epithelium are seen, lip adhesions, although uncommon, may occur in severe cases. This is followed by crusting, which occurs in approximately 2–3 days.[4] The lips often seal at the angle region due to crusting, most probably by the scarred healing of the coalescence of pseudomembranes and oral mucosal ulcers, and so was the scenario in our case.

To the best of our knowledge, five other cases of lip adhesion have been reported previously, out of which three occurred as a complication of erythema multiforme, all of which affected children or adolescents, one of them reported as a complication of a herpetic infection in an adult, and only one case was related to complication of a drug, phenytoin (anticonvulsant).[1,2,9-11]

With a review of the current literature, we can appreciate the rarity of this condition which can also be attributed to the paucity of the reported cases due to lack of awareness because of the multifactorial origin of the disease.

When we talk about the etiology of the cases that have been mentioned in the English literature, we conclude that the causes of angular webbing[9] that have been reported so far are concurrent with the etiological factors mentioned in the literature, including erythema multiforme, infections, and anticonvulsant drugs such as phenytoin;[1] however, ours is the first case that has azithromycin as an etiological factor, which is in fact a very commonly prescribed drug for common cold and hence raises a point of concern for the physician before prescribing it.

Although rare, exposure to azithromycin may result in immune-mediated dermatologic emergency known as SJS. The exact pathogenesis of SJS is not well established so far. Aihara *et al*. measured serum cytokines and eosinophilic cationic protein (ECP) levels at different time intervals in a patient of SJS due to azithromycin. Serum cytokines, ECP, and interleukin-6 levels were increased initially on day 8 and then decreased dramatically on day 28. Based on their findings, they suggested that activated eosinophil might play some role in SJS.[12]

More or less, its management is supportive and symptomatic, and the use of corticosteroids is still a topic of debate. Controversy exists as to whether newer treatments such as intravenous immunoglobulin, plasmapheresis and hemodialysis, cyclophosphamide, cyclosporine, acetylcysteine, and thalidomide actually decrease mortality.[13]

Although lip adhesion is not a serious complication and can be treated appropriately with chalinoplasty which was the treatment of choice, in this case, prevention is always better; hence, precautionary measures can be taken such as application of a lubricant-like petroleum jelly over the lips. Another method to encourage rapid healing is the use of hydrocortisone ointment over the ulcerations.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that her name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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