Steven Johnson Syndrome : A Pediatric Case Report

Dr. Mridula Goswami
Professor & H.O.D.

Dr. Mahesh Verma
Professor, Director, Principal

Dr. Geetika Datta
Senior Resident

Dept. of Pedodontics & Preventive Dentistry, Maulana Azad Institute of Dental Sciences, New Delhi

Abstract

Stevens Johnson Syndrome (SJS) is a potentially fatal multiorgan disease associated with many risk factors but is commonly drug related. Physicians and dental practioners must therefore consider SJS syndrome as a potential complication of treatment, especially when use of medication is questionable. The multiorgan aspect of the condition is best addressed by early involvement of medical specialists. The ophthalmic sequelae are dramatic, while cutaneous sequelae are unsightly. These sequelae have marked repercussions on the social and professional integration of the patients.

Keywords: Steven Johnson Syndrome, Erythema Multiforme, Dental features and management.

Introduction

Steven Johnson Syndrome is an array of potentially fatal acute mucocutaneous reactions that are most often elicited by drugs and occasionally by infections. This condition presents as an acute emergency in dermatological practice. [1] First described by Steven and Johnson in 1922, this condition manifests itself as a vesiculo-bullous eruption mainly on the skin and mucosal surface and is commonly associated with multiorgan involvement. Symptomatic treatment and early identification of the offending drug is necessary for early withdrawal and prevention of fatal recurrence in future. However, the high morbidity, incapacitating sequelae and associated mortality represent a high emotional and economical cost.[2] This case report highlights the clinical features, various drastic sequelae of Steven Johnson Syndrome and the dental management of such patients.

Case Report

A 6 year old patient reported to the Department Of Pedodontics, Maulana Azad Institute of Dental Sciences with a chief complaint of pain in the decayed teeth in the right lower back tooth region. The patient had hyper- pigmented patches all over the body, with complete loss of vision and a typical symblepharon affecting the right eye. (Fig 1)

The patient was earlier diagnosed as suffering from STEVEN JOHNSON SYNDROME. The disease began as a prodrome of high grade fever, for which he was being treated with antimalarial (Larigo), antibiotics (Ofloxacin), and NSAID (Nimesulide). Within 12 hours of receiving the above drugs, the entire body surface was covered with macular rashes, areas of diffuse erythema, which first appeared on the face and lips and then gradually spread all over the body , finally forming sheets of necrotic epithelium, giving a clinical picture of a severe burn . He was treated in the intensive care unit as a burn patient with massive cutaneous injuries and the concomitant systemic effects. The denudation of the body surface area was followed by shedding of finger nails and toe nails, (Fig 2 and 3) as well as loss of hair from scalp, eyebrows and cilia. The cutaneous rash was accompanied with mucous membrane involvement of the entire body especially oral, bulbar conjunctiva and anogenital mucosa. Though the acute symptoms regressed over a period of time, but the sequelae which are common features of late phase of SJS, developed slowly. Bilateral conjunctivitis, corneal ulcerations were followed by corneal opacity,conjuctival granulomatous hypertrophy and ultimately blindness. Episodes of seizures due to severe electrolyte imbalance, epistaxis followed by dysphagia, dysuria due to formation of strictures were among the few late complications.

Oral Features

In the acute phase of the disease massive hemorrhagic crusting of the lips was seen. Burning sensation of the buccal mucosa was followed by edema, erythema and blisters, which ruptured to form extensive hemorrhagic dull red erosions covered by grayish white psuedomembrane. Oral lesions were severely painful causing eating difficulties and hypersalivation, which later progressed to xerostomia due to damage to salivary glands.

Clinical examination revealed underlying xerostomia, increased acidic Ph and low buffering capacity of saliva and inability of the patient to maintain oral hygiene, lead to multiple carious teeth. Loss of enamel and dentin gave a typical yellowish brown appearance to the dentition (Fig 4) .The disintegration of the tooth substance in some teeth was severe enough to lead to pulpal exposure in a few deciduous teeth and even in permanent molars. (Fig 5) Follow up visits showed a hyper pigmented parchment like areas on the healing oral mucosa, bluish black pigmentation of the tongue, with the complete loss of lingual papillae.(Fig 6) Also localized areas of gingival recession were seen.

Dental Management

With the consent of the physician the carious teeth were restored conservatively, although deep caries management included pulpotomy and extraction of unrestorable teeth with the administration of adrenaline free local anesthesia. The medications were used only after a negative skin test was obtained. Dental medicaments that could cause irritational or allergic reactions to the oral mucosa were avoided. The past physical and mental sufferings, repeated hospitalization due to late developing complications of the disease and the devastating ophthalmic sequelae which leads to the complete loss of vision made dental management a challenging task.

The patient management included careful and slow delivery of instruction regarding each dental procedure. Symptomatic and conservative management was aimed upon. Visually impaired children are more likely to have gingival inflammation because of their inability to see and remove plaque, hence emphasis on oral hygiene maintenance was given and the patient was on a monthly recall preventive strategy.

Discussion

Stevens A. and Johnson F. described a strikingly distinct disease in two children as an "extraordinary, generalized eruption with continued fever, inflamed buccal mucosa and severe purulent conjunctivitis." [3] Stevens - Johnson syndrome (SJS) is an immune-complex mediated hypersensitivity reaction that is a severe expression of erythema multiforme. It is known by some as Erythema Multiforme major, but disagreement still exists in the literature. Most authors and experts consider Stevens-Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN) different manifestations of the same disease.[4] Although Erythema Multiforme is usually a Type III hypersensitivity reaction to an infection caused mostly by Herpes Simplex and is relatively benign, the aetiology of SJS and TEN is mainly drug related. Their consequences are potentially more dangerous than those of Erythema Multiforme.

Typically, the disease process begins with a nonspecific upper respiratory tract infection. This usually is part of a one to fourteen -day prodrome during which fever, sore throat, chills, headache and malaise may be present. Vomiting and diarrhea are occasionally noted as part of the prodrome. Non pruritic mucocutaneous lesions develop abruptly. Clusters of outbreaks last from two-four weeks.[5] A macular, often morbilliform rash appears first on the face, neck, chin and central trunk areas. It may then spread to extremities and the rest of the body.[6] The center of these lesions may be vesicular, purpuric or necrotic.

The typical lesion has the appearance of a 'Target' which is considered pathognomonic. However, in contrast to the typical Erythema Multiforme lesions, these lesions have only two zones of color. The core may be vesicular, purpuric or necrotic and that zone is surrounded by macular erythema. Some have called these 'Targetoid' lesions. Lesions may become bullous and later rupture, leaving denuded skin which is susceptible to secondary infection. [6]

Oral Features

Oral manifestations of SJS range from tender superficial erythematous and hyperkeratotic plaques, to painful deep hemorrhagic bullae and erosions covered by grayish white psuedomembrane.[7] Hemorrhagic crusting over the lips is usually seen. Involvement of oral and/or mucous membranes may be severe enough that patients may not be able to eat or drink.[15]

Although gingival involvement is rare ulcerative gingivitis, recession and mucosal synechiae may be seen. Decreased saliva volume, increased acid pH, low buffering capacity leads to multiple caries and loss of tooth enamel. The more severe dental

abnormalities include agenesia, root dysmorphia, root-building abortion with incomplete root apex closure, shorter root, and microdontia.[8]

Large flaccid blisters which turn necrotic can lead to denudation of basal surface area as much as 10-90%. Sheets of necrotic epidermis slide off the face and pressure points at the back of neck and shoulders. Patients with genitor-urinary involvement may complain of dysuria or an inability to void. In several cases of TEN involvement of skin appendages can lead to shedding of fingernails and toenails.[6] SJS and TEN are variants within a continuous spectrum; detachment of less than 10% of the total body surface area defines SJS, whereas greater than 30% defines TEN. Intermediate cases are called SJS/TENoverlap.[9]

Etiology

Various etiologic factors have been implicated as a cause of Steven Johnson Syndrome, such as:

- Drugs
- Viral infections
- Malignancies
- Vaccines
- Radiological contrasts
- Vaginal suppositories
- Acrylonitrates
- Graft versus host reaction.[1]

Although, StevensJohnson Syndrome has a polyetiologic reaction pattern, the leading cause appears to be the use of medication. The list of causative agents differs from country to country, but the following groups of drugs namely antibacterial sulfonamides, anticonvulsants, NSAIDs are the main causative agents. Antimalarials, allopurinol, and a few others like quinolones & antifungals follow a close second.[6] Hallgren et al reported ciprofloxacin-induced Stevens-Johnson syndrome in young patients in Sweden.[10] In recent years antiretroviral drugs have emerged as an important cause of SJS/TEN. Metry et al reported Stevens-Johnson syndrome in two HIV patients treated with Nevirapine. The authors speculated that the problem may extend to other non-nucleoside reverse transcriptase inhibitors.[11] Often the drugs taken during the prodromal phase, to alleviate symptoms cannot be distinguished from those that actually caused the disease, hence circumstantial evidence serves as the only criteria.[6]

Pathophysiology

The pathophysiology includes epidermolysis as a result of keratinocyte cell apoptosis-an organized series of biochemical reactions leading to cell changes and cell death. The cytotoxic T- lymphocytes found in TEN patients' blister fluid is believed to induce a cascade of intracellular enzymes that results in a rapid, triggered cell death. A strong association between HLA-B*1502 and carbamazepine-induced TEN has been identified.[12]

Stevens-Johnson syndrome is a fatal multiorgan disease.[13] Ocular complications occur in about 70% of patients with Stevens-Johnson syndrome.[14] as symblepharon, synechiae, entropion, ectropion, corneal opacities scarring leading to blindness. Photophobia and a purulent form of conjunctivitis may be present initially, but corneal ulcerations and anterior uveitis can develop. Secondary infection, corneal opacity, and blindness can follow.[6] Late complications include impaired tear production and drainage, aberrant lashes, metaplasia of the conjunctiva, and corneal ulcers. In addition to skin infections, which are associated with high mortality, skin sequelae include scarring, dyscromia (hypo-hyper pigmentation) and nail deformities (anonychia).[2] Pulmonary involvement may first appear as a harsh, hacking cough, [15] and chest x-ray films may show patchy areas of tracheal and bronchial involvement. The stomach and spleen can also be affected, and renal complications can occur in the form of acute tubular necrosis.[6]

Diagnosis relies mainly on clinical signs together with the histological analysis of a skin biopsy showing typical full-thickness epidermal necrolysis due to extensive keratinocyte apoptosis. Differential diagnosis includes linear IgA dermatosis and paraneoplastic pemphigus, pemphigus vulgaris and bullous pemphigoid, acute generalized exanthematous pustulosis (AGEP), disseminated fixed bullous drug eruption and staphylococcal scalded skin syndrome (SSSS). More than 50% of patients surviving TEN, suffer from long-term sequelae of the disease.[1]

Conclusion

SJS and TEN are considered medical emergencies as they are potentially fatal. Prompt diagnosis and management may reduce the morbidity and mortality in SJS/TEN patients.[1] The ophthalmic sequelae of Steven Johnson Syndrome are deemed serious, often leading to blindness, which adversely affect social and functional outcome.[17] Physicians must therefore consider Stevens-Johnson Syndrome as a potential complication for treatment, especially when use of medication is questionable.[18] Medical treatments do little to arrest these problems, and repairing the damage after the acute phase is difficult, if not impossible.[19] Patients should be informed about the potential risks and instructed on preventive oral hygiene measures. As Pediatric dentists we should commit ourselves in providing compassionate dental care and life long oral health to such individuals.

Refrences

1. Sanmarkan AD, Sori T, Thappa DM, Jaisankar TJ. Retrospective analysis of Stevens-Johnson syndrome and toxic epidermal necrolysis over a period of 10 years. Indian journal of dermatology 2011 56;1: 25-29
2. Del Pozzo-Magana BR, Lazo-Langner A, Carleton B, Castro-Pastrana LI, Rieder MJ. A Systematic Review of Treatment Of Drug-Induced Steven Johnson Syndrome And Toxic Epidermal Necrolysis In Children. J Popul Ther Clin Pharmacol March 21, 2011;Vol 18(1):121-133.
3. Stevens A, Johnson F. A new eruptive fever associated with stomatitis and ophthalmia : report of two cases in children . Am J Dis Child 1922; 24:526-53
4. French LE. Toxic epidermal necrolysis and Stevens Johnson syndrome: our current understanding. Allergol Int. Mar 2006; 55(1): 9-16.
5. Steven J Parrillo Catherine V Parrillo Stevens-Johnson Syndrome in Emergency Medicine Clinical Presentation: http://emedicine. medscape.com/article/756523-overview
6. Fritsch PO, Ruiz-Maldonado R. Stevens-Johnson Syndrome toxic epidermal necrolysis. In: Freedberg IM, Eisen AZ, Wolff K, et al, editors. Fitzpatrick's dermatology in general medicine. 5th ed. Vol 1. New York: McGraw-Hill; 1999: P 644-54.
7. Ayangco L, Rogers RS 3rd. Oral manifestations of erythema multiforme. Dermatol Clin. 2003 Jan; 21(1):195-205. Review.
8. Gaultier F, Rochefort J, Landru MM, Allanore L, Naveau A, Roujeau JC, Gogly B. Severe and unrecognized dental abnormalities after drug-induced epidermal necrolysis. Arch Dermatol. 2009 Nov; 145(11):1332-3.
9. Bastuji Garin S, Rzany B, Stern RS, Shear NH, Naldi L,Roujeau JC. Clinical classification of cases of toxic epidermal necrolysis, Stevens-Johnson syndrome, and erythema multiforme. Arch Dermatol 1993; 129:926.
10. Roujeau JC.What is going on in erythema multiforme? Dermatology1994; 188:24950.
11. Assier Bastuji-Garin S, Revuz J, Roujeau JC. Erythema multiforme with mucous membrane involvement and Stevens-Johnson syndrome are clinically different disorderswith distinct causes. Arch Dermatol. 1995 May; 131(5):539-43.
12. Castana O., Rempelos G., Anagiotos G., Apostolopoulou C., Dimitrouli A., Alexakis D.Stevens - Johnson syndrome: A Case Report Annals of Burns and Fire Disasters (ISSN 1592-9566) -Pending Publications
13. Tan YM, Goh KL. Esophageal stricture as a late complication of Stevens-Johnson syndrome. Gastrointest Endosc. 1999 Oct; 50(4):566-8.
14. Power WJ, Ghoraishi M, Merayo-Lloves J, Neves RA, Foster CS.. Analysis of the acute ophthalmic manifestations of the erythema multiforme/ Stevens-Johnson syndrome/toxic epidermal necrolysis disease spectrum. Ophthalmology. 1995 Nov; 102(11):1669-76.
15. Habif TP. Clinical Dermatology. 3rd ed. St Louis: Mosby-Year Book; 1996. p 570-2.
16. Harr T, French LE.Toxic epidermal necrolysis and Stevens-Johnson syndrome. . Orphanet J Rare Dis. 2010 Dec 16;5:39
17. Fellahi A, Zouhair K, Amraoui A, Benchikhi H. [Stevens-Johnson and Lyell syndromes: mucocutaneous and ocular sequels in 43 cases]. Ann Dermatol Venereol. 2011 Feb; 138(2):88-92. Epub 2010 Dec 15.
18. Matthew Smelik. Clinical contributions- Stevens-Johnson Syndrome: A Case Study. www.thepermanentejournal.org/files/ PDF/ Winter 2002. pdf
19. Gregory DG The ophthalmologic management of acute Stevens-Johnson syndrome. Ocul Surf. 2008 Apr; 6(2):87-95.

Legends

Fig 1 Complete loss of vision Post SJS sequelae (Symblepharon and Conjuctival granu-lomatosis)
Fig 2 Complete shedding of finger and toe nails (Anonychia)
Fig 3 Marked areas show discoloration of nails due to Onychomycosis
Fig 4 Atypical yellowish brown appearance of the dentition
Fig 5 Marked Areas of Pulp Exposure Due To Severe Degeneration of Tooth Substance
Fig 6 Tongue With Complete loss of Lingual Papillae

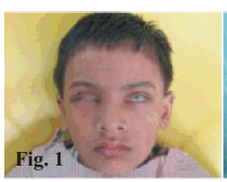
Fig. 1

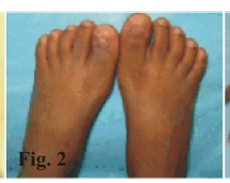
Fig. 2

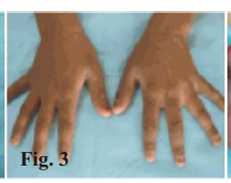
Fig. 3

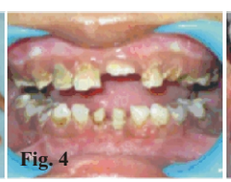
Fig. 4

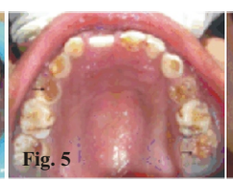
Fig. 5

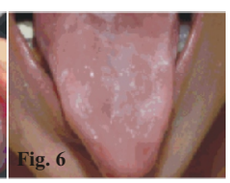
Fig. 6