IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 22, Issue 7 Ser.5 (July. 2023), PP 40-45
www.iosrjournals.org

A Case Report On Antibiotic Induced Stevens Johnson Syndrome

Dr Surajit Bose[1], Dr Sohini Roy Chowdhury[2], Dr Jayanta Chattopadhyay[3]
[1](Assistant Professor, Department of Oral and Maxillofacial Pathology & Microbiology, Kusum Devi Sunderlal Dugar Jain Dental College & Hospital, India)
[2] (Housestaff, Department of Oral and Maxillofacial Pathology & Microbiology, Kusum Devi Sunderlal Dugar Jain Dental College & Hospital, India)
[3] (HOD, Department of Oral and Maxillofacial Pathology & Microbiology, Kusum Devi Sunderlal Dugar Jain Dental College & Hospital, India)

Abstract:
Background: *Stevens-Johnson Syndrome (SJS) Is A Life-Threatening, Acute And Potentially Fatal Mucocutaneous Disorder Due To An Aggressive Immune Response. Majority Of The Cases Are Drug Induced Manifesting As Severe Mucosal Erosions With Widespread Erythematous Cutaneous Macules (Atypical Targets). The Symptoms Appear Shortly After Usage Of A Drug Or A Combination Of Drugs And They Rapidly Deteriorate In A Short Period Of Time. Early Diagnosis And Management Play An Important Role In Stopping The Progression Of SJS.*
Aim: *The Aim Of This Article Is To Record A Case Of Early Diagnosis And Effective Management Of A Patient With Stevens Johnson Syndrome Secondary To A Combination Drug Therapy Of Ofloxacin & Ornidazole Prescribed For Tooth Pain.*
Conclusion: *Dentists Should Be Clinically Oriented Towards Signs And Symptoms Of The Disease, Both Oral And Systemic And Hence They Should Be Able To Effectively Diagnose And Manage Cases Of SJS Which Can Happen Due To The Drugs That Are Commonly Used In Tooth Related Diseases.*
Key Word*: Stevens Johnson Syndrome, Ofloxacin, Ornidazole, Mucocutaneous Disorder*

Date of Submission: 03-07-2023 Date of Acceptance: 13-07-2023

I. Introduction

"A new eruptive fever with stomatitis and ophthalmia" was described as a severe variant of erythema multiforme and it was termed by Steven and Johnson in 1922. By the 1940's it was commonly known as "Stevens-Johnson syndrome (SJS)" [1].

Stevens-Johnson syndrome (SJS) is a life-threatening immune complex mediated hypersensitivity reaction which mainly involves skin and mucous membrane. Patients usually present with mucocutaneous exfoliative lesions involving the oral, ocular, or genital mucosa. Stevens-Johnson syndrome is part of a spectrum of diseases ranging from SJS when presented with less than 10% skin detachment to toxic epidermal necrolysis (TEN) when presented with greater than 30% skin detachment [2]. Stevens-Johnson syndrome, otherwise known as erythema multiforme major, represents a continuum of disease, the most benign type being erythema multiforme, whereas toxic epidermal necrolysis being the most severe [3]. Clinical characteristics of SJS include hemorrhagic erosions, mucocutaneous tenderness and erosion of the mucous membrane, erythematous macules, blisters and denuded skin [4]. Approximately 5–20% of cases remain idiopathic [5], SJS and TEN may develop due to a combination of immune predisposition and exogenous stimuli such as medication [6] or infection that results in apoptosis of epithelial cells [7]. Drug induced cases are found in 50–95% of patients, depending on the population examined [8]. People with certain HLA serotypes, TCR subtypes, or differences in their ability of absorption, distribution, metabolization, or excretion of the medications have a higher likelihood of developing SJS and TEN [7]. SJS is rare and studies reveal that it affects 7.1 per million persons, and as high a ratio as 49 persons per million will develop erythema multiforme [2]. Studies conducted in India showed males predominating the SJS group with a ratio of 1.63:1, whereas females predominating in the TEN group with a ratio of 1:2.57 [9]. SJS has a significant impact on public health in view of its high morbidity and mortality rates.
The most important clinical signs and symptoms of SJS are the following:

- Prodromal signs: 2-3 days of malaise, rash, fever, cough, arthralgia, myalgia, rhinitis, headache, anorexia, and nausea and vomiting, with or without diarrhoea
- Conjunctivitis, usually occurring 1-3 days before the skin lesions appear

- Intense erythema, progressing rapidly to epidermolysis and ceasing in 2-3 days
- Blisters on the skin and mucous membrane
- Erosion of the mucous membrane
- Haemorrhagic crusting of the lips
- Epidermal detachment
- Positive Nikolsky sign
- Target-like lesions
- Extreme pain at the sites of the lesions
- Dehydration, which may lead to hypovolemic shock and death
- Mimicking of the staphylococcal scalded skin syndrome (similar appearance, but blisters rise nearer the skin's surface) [2]

Unfavourable drug reactions can occur by binding of the metabolite to the major histocompatibility complex (MHC) type 1 thus causing SJS. In addition to this, CD8+ cells, CD40 ligand cells and the innate immune system also play a role in the interaction with drugs causing SJS [4]. These T cells can destroy cells using 1 or more mechanisms, including those involving perforin and granzyme, Fas and Fas ligand (FasL), and tumor necrosis factor α (TNF-α). In SJS and TEN, when the tissue is incompatible with a presenting drug or virus, it triggers the production of CD8+ CTLs, which travel to the skin and stimulate keratinocyte cell death (apoptosis). Keratinocytes emerge from the dermis and migrate upward to form squamous cells on the surface of the skin. Apoptosis of keratinocyte causes breakage in the continuity of the skin [10]. With the frequent use of prescribed medications such as antibiotics, anticonvulsants and nonsteroidal anti-inflammatory drugs (NSAIDS), adverse drug reactions leading to SJS represent a continuing challenge for all healthcare providers. Stevens Johnson syndrome (SJS) can also be caused by infection such as herpes simplex virus infection, TB, Mycoplasma pneumoniae, histoplasmosis, coccidioidomycosis, Strongyloides infection, vaccination, autoimmune diseases, malignancy and radiotherapy [7,11,12]

Table no 1 : Ulcerative & Erythematous drug reactions: Representative causative drugs [12]

Analgesics	Aspirin, Codeine, Oxicams, Propionic acid derivatives
Antibiotics	Erythromycin, Penicillin, Streptomycin, Tetracycline, Sulfonamides, Fluoroquinolones
Anticonvulsants	Barbiturates, Phenytoin
Antifungals	Ketoconazole
Anti-inflammatory	Indomethacin
Anti-malarial	Hydroxychloroquine
Cardiovascular	Methyldopa, Oxprenolol
Psychotherapeutic	Meprobamate, Chlorpromazine
Others	Retinoids, Cimetidine, Gold compounds, Local anesthetics

The importance of our case is that it is a case of SJS secondary to drug therapy targeted for the dental pain, consisting of drugs that are very commonly used. The past medical and drug history plays a very important role in planning the treatment of the patient and the dentist should always be cautious about the drug reactions of the medicines being prescribed.

II. Case Report

A 34 years old female reported to a general physician with the complaint of pain in the right upper and lower back teeth region since 2 weeks. The doctor prescribed,

1. Ofloxacin(200mg)-Ornidazole(500mg), twice daily after food for 5 days

2. Paracetamol(650mg), twice daily after food for 3 days followed by sos on pain.

On Day 3, she visited a dental surgeon and complained of a burnt appearance of the lips with severe pain and burning sensation in and around the mouth, inability to eat or drink or open the mouth, since 2 days. The pain was localized, sudden in onset, continuous in nature, and severe in intensity, aggravated on touching, speaking, and eating food, with no relieving factor. The pain was accompanied by a severe burning sensation. A thorough medical and drug history revealed that she had developed oral blisters 2 years back after the intake of Ofloxacin, Ornidazole combination tablet, which she was prescribed for diarrhoea, thereafter the symptoms were relieved within a week after taking anti allergic medications. She has no history of any oral deleterious habits.

The patient was well-oriented and her vital signs were recorded as

- Temperature: 98.8 degrees Fahrenheit
- Heart rate: 100 beats per minute
- Blood pressure: 120/78 mm of hg
- Respiratory rate: 16 cycles/ minute

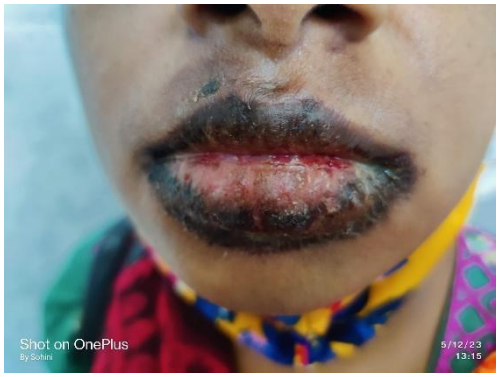

Figure no 1: Haemorrhagic, crusty lips with eroded areas

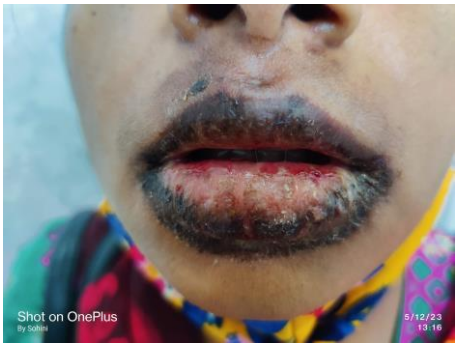

Figure no 2: Inability to open the mouth

- Extraoral: Swelling of the upper and lower lips with haemorrhagic, crusty, eroded areas were noted in and around the vermillion border of the upper and lower lips. The rest of the face, eyes, neck, trunk and extremities showed no abnormalities. Lymph nodes were non-tender and non-palpable.
- Intraoral examination was entirely not possible since the patient was unable to open her mouth beyond a few millimetres. Intraoral blisters were noted in the inner aspect of the lower lip. Her complaint of dysphagia indicated that erosion might have affected her hard and soft palate and the throat. The rest of the face, eyes, neck, trunk and extremities showed no abnormalities. Lymph nodes were non-tender and non-palpable. The oral ulcerations had developed a day after starting the prescribed medications.

The patient was suspected of suffering from Steven Johnson's Syndrome.
Differential diagnosis : Stomatitis Medicamentosa, Pemphigus vulgaris, Bullous Pemphigoid, Staphylococcal Scalded Skin Syndrome,
The patient was subjected to only the hematologic investigation as the patient was already under severe pain & discomfort. Her complete blood picture revealed

- Haemoglobin: 10.3g/dl,
- ESR: 47 mm/1st hour
- Total leucocyte count:11000 cells/mm3
- Platelet count: 1,90,000/mcL.

The patient was asked to immediately stop the drugs previously prescribed and advised alternate medication

1. Tab Prednisolone 40mg, once daily for 1 week followed by a tapering dose.
2. Tab Levocetirizine 10mg, twice daily for 1 week,
3. Triamcinolone 0.1% ointment, for topical application thrice daily for 1 week
4. Clotrimazole 0.1% mouth paint for topical application thrice daily for 2 weeks
5. Chlorhexidine and benzocaine gel for topical application thrice daily for 2 weeks
6. Benzydamine mouthwash, twice daily for 2 weeks
7. Multivitamin capsules, once daily for a month

Patient was recalled for follow-up after 1 week. The haemorrhagic ulcerations had disappeared leaving hyperpigmented healing tissue. Patient was able to eat and drink and speak properly. Intraoral lesions had resolved.

Figure no 3: Healed extraoral lesions

Figure no 4: Ability to open the mouth

Figure no 5: Healed intraoral lesions

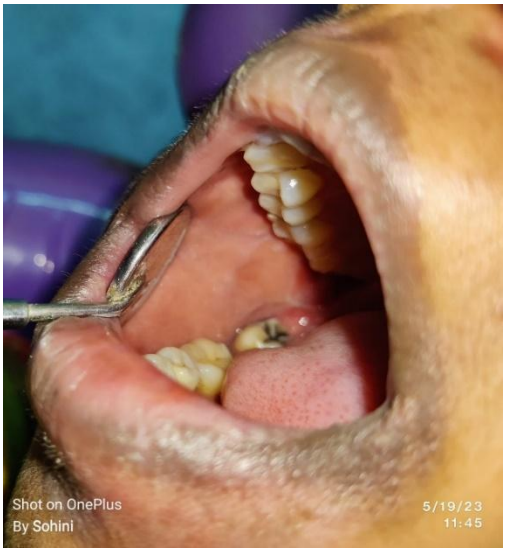

Figure no 6: Healed intraoral lesions

Complete resolution of symptoms was seen within 2 weeks of treatment.

III. Discussion

The patient had taken multiple drugs, like Paracetamol, Ofloxacin and Ornidazole. There are some studies that reveal that all the three drugs can cause SJS several. This patient did not have any other reason for developing SJS other than the addition of Ofloxacin, Ornidazole and paracetamol to his treatment regimen. She had not received any recent immunizations neither did she have a viral infection, graft-versus-host disease, hematologic malignancy, systemic lupus erythematosus, known cerebral tumor and upper respiratory infection. The study carried out by Stephen L Melde revealed that there is very little published information regarding ofloxacin-induced toxic epidermal necrolysis [13]. There are few cases reported with other fluoroquinolones in which they have been associated with toxic epidermal necrolysis. The study conducted by Neki et al. concluded that Acetaminophen is a relatively safe drug devoid of serious side effects, severe hypersensitivity reactions can occur with its usage, which can be potentially life threatening [14]. Study conducted by Junaid et al suggested that Metronidazole (another medicine from the nitroimidazole group, the same as Ornidazole) can lead to severe hypersensitivity reactions such as SJS and TEN even at therapeutic dosages [15]. There are studies showing Ornidazole capable of Fixed Drug Reaction [16]. The study carried out by Purkayastha et al. revealed that Paracetamol is capable of causing such reactions as is evident from earlier reports [17]. It is essential for the clinicians to be aware of the severe undesirable complications that might occur even with drugs that are commonly

used. The study carried out by Lihite et al. revealed that, the antimicrobials, anticonvulsants and antipyretics were commonly reported as an offending group of drugs for SJS/ TEN in patients [18]. Paracetamol (8/45) and Phenytoin (7/45) were commonly reported as offending drugs in the individual drug category. The study carried out by Naveen et al. observed that, Oflaxacin, a commonly used antibiotic in India, has a risk of inducing SJS TEN, which may be fatal. SJS-TEN induced by ofloxacin has a higher morbidity and mortality compared to anticonvulsants [19]. Further research on these drugs are needed for better accomplishment of the results.

IV. Conclusion

It is difficult to confirm exactly which drug is responsible for the SJS. Since the patient's past drug history reveals that she had a skin allergy with blisters all over her mouth after consuming Ofloxacin Ornidazole combination drug two years back, it is hoped that this case of SJS has also developed because of the same two drugs. Hence this case highlights the importance of a thorough drug history of the patient before prescribing any drugs. More importantly every medical and dental practitioner must be aware and alert of the complications that the drugs can cause and hence be acquainted with prompt and effective treatment regimes in case of such undesirable adverse effects.

References

[1]. Deore Ss, Dandekar Rc, Mahajan Am, Shiledar Vv. "Drug Induced - Stevens Johnson Syndrome: A Case Report". Int J Sci Stud. 2014;2(4):84-87.

[2]. Castana O, Rempelos G, Anagiotos G, Apostolopoulou C, Dimitrouli A, Alexakis D. Stevens-Johnson Syndrome: A Case Report. Ann Burns Fire Disasters. 2009 Sep 30;22(3):147-51. Pmid: 21991171; Pmcid: Pmc3188138.

[3]. Smelik M. Stevens-Johnson Syndrome: A Case Study. Perm J. 2002 Winter;6(1):29-31. Doi: 10.7812/Tpp/02.997. Pmid: 30313009; Pmcid: Pmc6220622.

[4]. Al Hathlol Wk, Almeslet A. Early Diagnosis Of Stevens-Johnson Syndrome In The Dental Clinic Setting. Cureus. 2021 Mar 28;13(3):E14160. Doi: 10.7759/Cureus.14160. Pmid: 33936873; Pmcid: Pmc8078824.

[5]. Wolff K, Johnson R, Saavedra Ap, Roh Ek. The Acutely Ill And Hospitalized Patient. In: Fitzpatrick's Color Atlas And Synopsis Of Clinical Dermatology, 8e. New York; 2012.

[6]. Morel E, Escamochero S, Cabanas R, Dias R, Fiandor A, Bellon T. Cd94/Nkg2r Is A Killer Effector Molecule In Patients With Stevens-Johnson Syndrome And Toxic Epidermal Necrolysis. J Allergy Clin Immunol. 2010;125(3):703–710.

[7]. Smith C. Erythema Multiforme, Stevens–Johnson Syndrome, Toxic Epidermal Necrolysis, Staphylococcal Scalded Skin Syndrome. In: Soutor C, Hordinsky Mk, Editors. Clinical Dermatology. New York; 2013.

[8]. Schwartz Ra, Mcdonough Ph, Lee Bw. Toxic Epidermal Necrolysis: Part 1. Introduction, History, Classification, Clinical Features, Systemic Manifestations, Etiology, And Immunopathogenesis. J Am Acad Dermatol. 2013;69(2):173.E1–173.13.

[9]. 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 J Dermatol. 2011 Jan;56(1):25-9. Doi: 10.4103/0019-5154.77546. Pmid: 21572786; Pmcid: Pmc3088929.

[10]. Hanson Lm, Bettencourt Ap. Stevens-Johnson Syndrome And Toxic Epidermal Necrolysis: A Guide For Nurses. Aacn Adv Crit Care. 2020 Sep 15;31(3):281-295. Doi: 10.4037/Aacnacc2020634. Pmid: 32866260; Pmcid: Pmc7539539.

[11]. Breslin Me, Garcia-Lloret M, Braskett M. A Fatal Case Of Drug Reaction With Eosinophilia And Systemic Symptoms (Dress) – Stevens Johnson (Sjs)/Toxic Epidermal Necrolysis (Ten) In The Setting Of Strongyloides Infection: Treatment Considerations. J Allergy Clin Immunol. 2015;135(2):Ab124. Doi: 10.1016/J.Jaci.2014.12.1338.

[12]. Regezi, J.A., Sciubba, J.J. And Jordan, R.C.K. (2011) Oral Pathology: Clinical Pathologic Correlations. 6th Edition, Elsevier Saunders, St Louis, 388.

[13]. Melde Sl. Ofloxacin: A Probable Cause Of Toxic Epidermal Necrolysis. Annals Of Pharmacotherapy. 2001;35(11):1388- 1390. Doi:10.1345/Aph.1z433.

[14]. Neki, Et Al. Paracetamol Induced Steven-Johnson Syndrome-Toxic Epidermal Necrolysis Overlap. International Journal Of Medical And Health Research. 2016;2(12):59-61.

[15]. Ali J, Rahman M, Ahmad A, Khattak Z, Shahzad Ma. Toxic Epidermal Necrolysis Secondary To Metronidazole. Cureus. 2021 Aug 11;13(8):E17101. Doi:10.7759/Cureus.17101. Pmid: 34527487; Pmcid: Pmc8432438.

[16]. Gupta R. Fixed Drug Eruption Due To Ornidazole. Indian J Dermatol. 2014 Nov;59(6):635. Doi: 10.4103/0019- 5154.143591. Pmid: 25484435; Pmcid: Pmc4248543.

[17]. Purkayastha A, Et Al. A Case Report Of Paracetamol-Induced Toxic Epidermal Necrolysis In A Female Patient At A Tertiary Care Hospital In Assam. Asian J Pharm Clin Res. 2016;9(4):7-8.

[18]. Lihite Rj, Et Al. A Study On Drug Induced Sjs, Ten And Sjs-Ten Overlap. J Young Pharm. 2016;8(2):149-53.

[19]. Naveen Kn, Pai Vv, Rai V, Athanikar Sb. Retrospective Analysis Of Steven Johnson Syndrome And Toxic Epidermal Necrolysis Over A Period Of 5 Years From Northern Karnataka, India. Indian J Pharmacol. 2013 Jan-Feb;45(1):80-2. Doi: 10.4103/0253-7613.106441. Pmid: 23543919; Pmcid: Pmc3608301.