Drug Induced - Stevens Johnson Syndrome: A Case Report

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Stevens Johnson Syndrome (SJS) is a severe hypersensitive reaction that can be precipitated by infection such as herpes simplex virus or mycoplasma, vaccination, systemic diseases, physical agents, foods and drugs. The drugs that cause SJS commonly are antibacterials (sulfonamides), anticonvulsants (phenytoin, phenobarbital, carbamazepine), non-steroidal anti-inflammatory drugs (oxicam derivatives) and oxide inhibitors (allopurinol).

SJS may present as a nonspecific febrile illness (malaise, headache, cough, rhinorrhea) with polymorphic lesions of skin and mucous membrane characterized by acute blisters and erosions. Stevens-Johnson syndrome, otherwise known as erythema multiforme major, is thought to represent a continuum of disease, the most benign type of which is erythema multiforme, whereas toxic epidermal necrolysis is the most severe. The importance of our case is that it is a case of SJS secondary to drug therapy instituted for...
the dental pain which was consisting drugs that are very commonly and widely used. One should use the common drug regimen also with caution and detailed history of past drug consumptions is required while treating common cases.

**CASE REPORT**

A 21 year old female reported to a dental OPD of MGV dental college & hospital Nashik with a chief complaint fever and extensive rashes on the skin of the face and neck, erythema of conjunctiva, ulceration of eyelid and oral cavity and difficulty in routine oral habits since a day. It was also associated with pain which was sudden in onset, burning type, continuous, localized, and severe in intensity, aggravated on touching, speaking, eating food & there was no relieving factor.

The past dental history of the patient revealed that he had dental pain due to carious tooth in lower left posterior teeth region for which she had been prescribed Tab Ciplox TZ, BD & Tab Voveron 50 mg TDS for 5 days by a general practitioner, which she consumed for 3 days and she developed this type of reaction.

The patient was well-oriented and on examination, had hyperpyrexia, generalized, maculopapular and bullous eruptions on the neck, face, external ear (Figures 1 and 2). The trunk and extremities were having well developed variably sized target like lesions (Figure 3). She also complained of burning micturation. The vaginal lesions were confirmed with examination in department of Venerology.

Intraoral examination revealed ulcerations of the vermilion surface of lips, labile mucosae, tongue and palate (Figure 4). The ulcers were hemorrhagic and tender on palpation. Hemorrhagic crusted erosions were also seen on both the upper and lower lips. Bilateral submandibular lymph nodes were palpable, tender, mobile, firm in consistency. The oral ulcerations were developed one day prior to development of the skin lesions. But she considered them as a routine

Figure 1: Maculopapular rash over the face, forehead and neck (Front View)

Figure 2: Maculopapular rash over the face, forehead and neck (Lateral view)

Figure 3: Round well circumscribed Target like lesions over hand

Figure 4: Ulcerations and bloody crusting lesions of vermilion surfaces of lips
complication of therapy and started with application of glycerin.

Ophthalmic examination showed acute conjunctivitis and subconjunctival hemorrhages. The hemorrhagic ulcerations of the eyelid associated with watering of eyes & pus discharge were also noted (Figure 5).

Based on this our clinical diagnosis was Stevens Johnson Syndrome as the lesion noticed in eyes & genitals. Differential diagnosis thought were pemphigus vulgaris & stomatitis medicamentosa. We had subjected the patient to only the hematologic investigation as the lesion being acute; the patient was under severe discomfort. Her complete blood picture revealed hemoglobin 11g/dl, raised ESR - 50 mm/1st hour & total leucocyte count was 12000 cells/mm³, platelet count was 208 X 10⁹/L.

We treated her under a expert guidance of dermatologist with systemic steroids, Inj. Prednisolone 10 mg qid for 7 days, which was gradually tapered to 10 mg tid for 7 days, 10 mg bid for 5 days, then Tab Prednisolone 10 mg once daily for 5 days respectively, Benzhydramine hydrochloride 0.15% oral rinse for oral ulcers. Gention violet application for lip lesions was advocated. Clotrimazole cream 1% for vaginal lesion & Ofloxacin eye drops 0.3% for eye lesion. Liquid & soft diet was advised. All the lesions healed within 1 & ½ month; there was absence of burning micturation & lacrimation.

**DISCUSSION**

Stevens-Johnson syndrome is a severe, episodic mucocutaneous intolerance reaction described by Hebra in 1866 and Albert Mason Stevens and Frank Chambliss Johnson in 1922. Erythema multiforme (EM), Stevens-Johnson syndrome and Toxic epidermal necrolysis (TEN) are part of a clinical spectrum. TEN is the most severe form of drug-induced skin reaction and is defined as epidermal detachment of >30% of body surface area. SJS presents with epidermal detachment of <10% of body surface area, whereas involvement of 10%-30% of body surface is defined as SJS/TEN overlap.

The first large study to assess the risk of developing SJS or TEN distinguished between drugs usually used for short-term periods and drugs used for months or years.

The highest risk in the first group was documented for trimethoprim-sulfomethoxazole and other sulfonamide antibiotics, followed by chlorimezone, cephalosporins, quinolones and aminopenicillins. In the long-term-use group, the increased risk was confined largely to the first 2 months of treatment. The drugs showing highest risk in second group was carbamazepine, followed by oxcarbam nonsteroidal anti-inflammatory, corticosteroids, phenytoin, allopurinol, Phenobarbital and valproic acid. Other factors associated with SJS/TEN are infectious diseases such as those caused by human immunodeficiency virus, herpesvirus or Mycoplasma pneumoniae, and hepatitis A virus and noninfectious conditions including radiotherapy, lupus erythematosus, and collagen vascular disease. (HLA)-B12, HLA-B*5801, HLA-B*1502 are involved with increased risk of developing SJS/TEN.

Specific drug hypersensitivity leads to major histocompatibility class I restricted drug presentation and is followed by an expansion of cytotoxic T-lymphocytes, leading to an infiltration of skin lesions with cytotoxic T-lymphocytes and natural killer cells. Granulysin probably is the key mediator for disseminated keratinocyte death in SJS/TEN. Granulysin levels in the sera of patients with SJS/TEN are much higher than in patients with ordinary drug induced skin reactions or healthy controls. Furthermore granulysin levels correlate with clinical severity. The mechanism is not IgE mediated, a desensitization of the triggering drug is not an option.

Drug-induced SJS typically presents with fever and influenza-like symptoms after the application of the suspected drug. One to 3 days later, signs begin in the mucous membranes, including eyes, mouth, nose, and genitalia in up to 90% of cases. Skin lesions manifest as generalized macules with purpuric centers. The macules progress to large conflating blisters with subsequent epidermal detachment, yet never show involvement of the hair. In the following 3 to 5 days, separation of the epidermis progresses and leads to large denuded areas. The large wound area leads to extreme pain, massive loss of fluid and protein, bleeding, evaporative heat loss with subsequent hypothermia, and infection.

Histopathology shows separation of the epidermis at the dermal-epidermal junction of the skin, extracutaneous epithelium, and mucous membranes. Clinically, this can be detected by a positive Nikolsky sign, which describes detachment of the full-thickness epidermis when light lateral pressure is applied with the examining finger.

Gastrointestinal involvement frequently occurs in the mouth and esophagus but also in the small bowl and colon.
Involvement of the gastrointestinal tract may lead to stenosis or strictures and consecutive long-term complications with dysphagia and ileus-like symptoms. Pulmonary edema and progressive respiratory failure develop within the first days and large ulcerations and epithelial necrosis of the bronchial epithelium occur. Vulvovaginal involvement may also lead to vaginal stenosis or strictures. Extensive scarring due to overgrowth with conjunctival epithelium, membranous or pseudomembranous conjunctivitis, ankyloblepharon, or symblepharon with additional complications like entropion or lagophthalmos leads to a severe dry eye syndrome or loss of vision.

Other organ manifestations occur rarely. Involvement of the kidneys with glomerulonephritis, tubulonecrosis, and pancreatitis, as well as involvement of the liver including hepatocellular necrosis or cholestasis, has been reported. The mortality of SJS is estimated to be 1%-3%. In contrast, mortality rates for TEN are between 30% and 50%. Early diagnosis with the prompt recognition and withdrawal of all potential causative drugs is essential for a favorable outcome. Corticosteroids have for years been the mainstay therapy for SJS in most cases, as in our case. Fluid balance and aseptic care of wounds is also important. Lid-globe adhesions should be cautiously removed with a glass rod twice daily to avoid occlusion of the fornices, taking care not to strip pseudomembranes, which may lead to bleeding and increased conjunctival scarring. Complications such as thromboembolism and disseminated intravascular coagulation and damage to vital organs such as the kidney deteriorate the prognosis. In our case, no such complications have been reported in a 2-year follow-up period.

CONCLUSION

In conclusion, we would like to state that patients started with any common drug regimen may a potential risk of developing SJS. The oral erythema and ulcerations are usually the initial presenting complaint which the patient may ignore. There are documented reports in the literature where an early diagnosis of SJS could be made due to the presence of oral lesions. Symptomatic management of the oral lesions is necessary in order to enable the patient to have oral feeds to maintain nutritional balance. Increased clinical vigilance is required to identify hypersensitivity reactions like rash, vesiculobulles lesions, and/or other clinical symptoms such as fever, nausea, and abdominal pain. Early diagnosis helps the clinician to elude secondary infection and subsequent complications. The offending drug should be discontinued and never be rechallenged.

REFERENCES


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