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Use of Intravenous Immunoglobulin in Children with Stevens-Johnson Syndrome: Case Report

Amar Taksande

*Professor, Department of Pediatrics, Jawaharlal Nehrul Medical College, Sawangi Meghe, Wardha, Maharashtra - 442102.

Abstract

Stevens-Johnson syndrome (SJS) is the most severe cutaneous reactions affecting skin and mucosal surfaces in pediatrics. Supportive therapy is the standard of care for SJS. The use of systemic corticosteroids has been controversial. Human intravenous immunoglobulin has been using in a number of autoimmune and cell-mediated blistering disorders of the skin. We report a successful used of intravenous immunoglobulin in a child affected with SJS.

Keyword: Stevens-Johnson syndrome; Immunoglobulin; Skin lesion.

Introduction

Stevens-Johnson syndrome (SJS) is a severe reactive condition affecting skin and mucosal surfaces. It was first described in 1922 by Stevens and Johnson as a febrile illness with stomatitis, purulent conjunctivitis, and skin lesions.[1] SJS is defined as extensive skin involvement, vesiculobullous erythema multiforme of the skin accompanied by erosions of at least two mucosal surfaces. Supportive therapy like monitoring of fluid and electrolyte status, nutritional support, wound care, and control of pain and infection is the standard care for SJS. The use of systemic corticosteroids remains controversial. Use of intravenous immunoglobulin (IVIG) in pediatric patients with SJS is rare.[2] We report a case of SJS in whom IVIG was given successfully.

Case Report

A five-year-old boy was admitted following complaints of vesiculobullous lesion all over body since six days. The lesion first appeared on the hand and then progressed all over the body. Fever was present prior to lesion and the patient had taken ayurvedic medication from a local practitioner. Prescription of medication was not brought by relatives. He appeared toxic and in severe distress. Blood pressure was 90/60mmHg, pulse rate 110/ min. and regular, and temperature 1020F. The oral lesions were so painful that the patient could not swallow his own saliva. He had conjunctival congestion with discharged. The tongue was coated along with ulceration, which involves the buccal mucosa, hemorrhagic crusts of the lips and superficial erosions of the tongue and hard palate. Vesicle and large bullae were present on his chest, abdomen and back [Figure 1, Figure 2]. As the vesicles spread, they coalesced into larger bullae and sloughed off. Other systemic

Corresponding Author: **Dr. Amar M. Taksande,** Department Of Pediatrics, Jawaharlal Nehru Medical College, Sawangi Meghe, Wardha, Maharashtra - 442004. E- mail: amar.taksande@gmail.com

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Figure 1: Child Showing Mucopurulent Eye Discharge, Facial Edema, Conjunctival Injection, Erosions, and Crusting of Lips

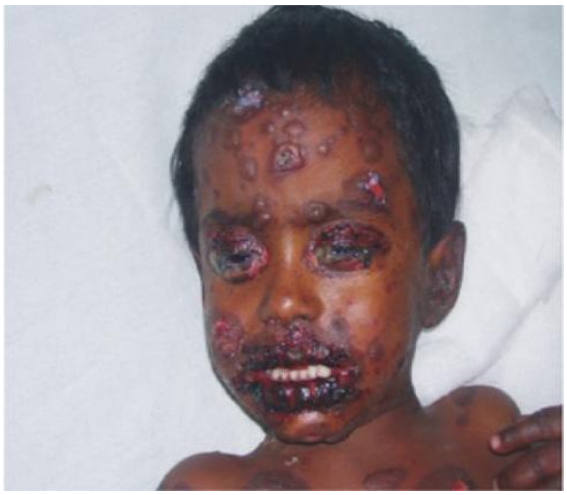
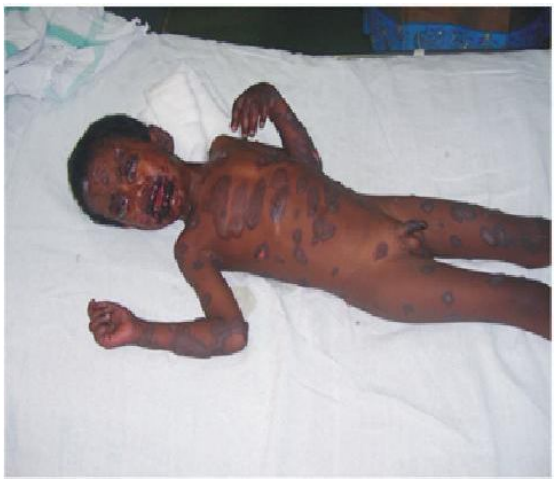


Figure 2: Child Showing Discrete Erythematous Patches, Vesicle, and Vesiculobullous Eruption on the Chest, Abdomen and Extremities



examination was normal.

Complete blood cell revealed anemia (Hb: 8gm/dl), normal platelet count and TLC: 11,000/cumm, DLC: N62%L36%E2%. Urea and electrolyte were normal. Chest x-ray film was normal. Blood and urine culture were sterile. Skin biopsy was consistent with features of SJS. Symptomatic treatment was started which included analgesic, lidocaine viscous oral solution, diphenhydramine hydrochloride and intravenous fluids. The skin lesions were treated twice daily with a mixture of urea and triamcinolone in a lotion base. Ophthalmologic evaluation showed bilateral conjunctivitis which was treated with artificial tears and polymyxin B sulfate ointment combined with neomycin sulfate. Because of septicemic and toxic look, injectable cefotaxime was given. Intravenous immunoglobulin was administered at a dose of 400 mg/kg/day for five days (total dose 2 gm/kg). After five days of therapy, the skin and mucous membrane lesion improved dramatically and child started accepting orally. The patient was discharged on 15th day after admission. On follow-up after three months, he was well with no recurrence of lesions.

Discussion

SJS is a rare condition, with a reported incidence of 1-6/million person/year. It is an immune complex mediated hypersensitivity disorder that may be caused by viral infections like herpes simplex virus, Coxsackie virus, echovirus, adenovirus, mycoplasma, allergic reaction to drugs like sulfonamide, penicillin, quinolone, cephalosporin, anticonvulsant agents, nonsteroidal antiinflammatory drugs, malignancies or idiopathic factors.[3] No definitive causative factor was found in our case. The prodromal symptoms are fever, malaise, sore throat, and myalgias[1] followed by conjunctivitis and bullae on the skin and mucosal membranes of the mouth, nares, pharynx, esophagus, urethra, vulvovaginal and anal regions. SJS commonly affects multiple organs, and developed complication like esophageal strictures,[4] ocular,[5] pulmonary or renal.[6] Skin biopsy is the definitive diagnostic study which demonstrate subepidermal bullae, epidermal cell necrosis and infiltration of perivascular areas by lymphocytes.

No specific drug treatment exists for SJS. Intensive multidisciplinary supportive management like increasing caloric intake, preventing sepsis, correcting electrolyte disturbance, discontinuation of the causative drug are the cornerstones of management. The choice of antibiotic depends on the associated infection.[7] Some author reported

controversial use of corticosteroids in the treatment of SJS because of increased mortality in the reported cases.[8,9] Many studies showed beneficial effects of using steroid agents in children. Crion S *et al*[10] concluded that the treatment with systemic steroids is useful in the management of toxic epidermal necrolysis. The immunosuppressive and anti-inflammatory properties of corticosteroids are not totally understood, but it could decrease the severity of the disease and prevent the development of serious complications if they were administered early in the course of the illness.[11] Corticosteroids negatively affect the inflammatory response by maintaining vascular integrity, promoting synthesis of lipocortins, and decreasing the expression of leukocyte adhesion molecules. It is also known to down-regulate cytokine gene expression, which results in inhibition of several immune functions as immune modulation.[12] Other authors also reported that systemic corticosteroids provoke prolonged wound healing, increased risk of infection, masking of early signs of sepsis, severe gastrointestinal bleeding and increased mortality. Previous two retrospective studies revealed that there was no difference in mortality rates or infectious complications in patients who received steroids before or after referral.[13,14] The role of steroids is controversial and better avoided when infectious etiology is suspected[15] because of these reason we did not give steroid therapy in the child.

In SJS, the activate keratinocyte production of an CD95 (fas) ligand (apoptotic ligand) leads to epidermal detachment and binding of this ligand to a CD95 (fas) apoptotic receptor located on the keratinocyte cell surface lead to programmed cell death. In Intravenous Immunoglobulin (IVIG), antibodies present which blocked Fas-mediated keratinocyte death *in vitro* and had the capacity to block the apoptotic ligand from binding to the receptor. Thus it helps in preventing keratinocyte apoptosis and subsequent epidermal detachment. IVIG also has anti-infectious properties and restores protein and fluid which limit the extent of fluid loss that occurs through the denuded skin in severe cutaneous drug reactions children.[2,16] Because of all this advantage, we had given the trial of IVIG in the SJS. In our case, IVIG was given along with antibiotics, which responded very well without the use of corticosteroids. Viard L *et al* reported 100% survival after treated with IVIG in patients with moderate severity of toxic epidermal necrolysis.[17] Recovery from SJS may require two to three months, depending on the number of organs affected and the severity of disease.

Conclusion

SJS is a potentially fatal multiorgan disease with multiple etiological factors. Intravenous immunoglobulin is a useful and safe therapy for children with severe cutaneous drug reactions in SJS.

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