



Case report

Primary varicella infection associated with Steven-Johnson syndrome

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Abstract

Steven-Johnson Syndrome (Erythema Multiforme Major) is a severe occasionally fatal variant of Erythema Multiforme which is abrupt in onset accompanied by fever, malaise, headache and erosions of conjunctiva, mouth and genitalia with skin lesions in the form of erythematous macules, papules and target lesions involving less than 10% of body surface area.

Varicella is caused by varicella zoster virus. It is a primary infection with a viraemic stage after which the virus persists in the sensory nerve ganglia cells, reactivation of which in the later life results in herpes zoster. Varicella is transmitted by droplet infection. Patients are usually infectious 2 days prior to 5 days after the onset of rash. Varicella confers lasting immunity and second attacks are uncommon in immunocompetent individuals. Immunoglobulin (Ig), IgG, IgM, IgA antibodies appear in about 1 week after the onset and the peak levels occur during the second and third week thereafter the titred gradually fall. Immunoglobulins have incomplete protective effect, CMI is more important against the infection and if the primary infection occurs when CMI is impaired as in organ transplant patients it may be fatal. We report a rare association of primary varicella with Steven Johnsons Syndrome successfully treated with a combination of systemic steroids and Acyclovir.

Key words: Steven-Johnson Syndrome, Varicella

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Steven-Johnson Syndrome (Erythema Multiforme Major EM) is a severe variety of Erythema Multiforme associated with high morbidity. It can be occasionally fatal. List of etiologic factors include medications, connective tissue disorders, immunization, malignancies but infectious agents are also considered to be a major cause of EM. The most commonly associated infections are Herpes simplex virus (HSV), *Mycoplasma pneumoniae*, vaccinia, or varicella zoster virus (VZV); immunizations. To the best of our knowledge, few cases of VZV infection are associated with Steven-Johnson Syndrome.

Case report

A 17 year old female patient reported with history of fever associated with skin rash and erosions of the oral cavity, eyes and lips of 6 days duration.

Onset was sudden, the patient had fever and skin rash associated with malaise, cough and prostration which was followed after 4 days by burning of the eyes, erosions in oral cavity, burning micturition and bullous lesions on the body. The patient did not take any medication after the onset of fever.

On physical examination, multiple discrete polymorphic lesions consisting of papules, vesicles

and pustules were present all over the body along with target lesions (Fig 1 & 2). Few bullae were noticed on the legs and trunk. The lips were covered with haemorrhagic crust, the oral cavity had erosions and tongue and the buccal mucosa had evidence of thrush (Fig 3 & 4).



Fig 1. Multiple discrete polymorphic lesions all over the body



Fig 2. Lesions consisting of papules, vesicles and pustules

Erosions were also seen over the eyelids and conjunctiva bilaterally.



Fig 3. Erosions were seen on tongue and buccal mucosa



Fig 4. Lips covered with haemorrhagic crust

Examination of the vagina revealed multiple erosions. Routine investigations revealed a Complete blood picture showing leucocytosis, urine examination, Liver function tests, renal function tests were within normal limits. Tzanck smear taken from an intact vesicle revealed multinucleated giant cells known as Tzanck cells and a biopsy was taken from the skin lesions for histopathological examination. Patient was started on IV Acyclovir in the dose of 10 mg/kg body weight 8th hourly along with Prednisolone 40mg/day in divided doses.

It was combined with IV fluids, injectable Augmentin, oral fluconazole, antihistaminics and other supportive treatment. Fever came down after 48 hours and cough subsided in 4 days. The skin lesions subsided within 8-10 days but erosions of

oral cavity and eyes receded in about 2 weeks. Injectable Acyclovir was stopped after 5 days whereas the antibiotics were continued for another 2 weeks. The dose of steroid was tapered after 7 days. The patient was discharged with advice on oral hygiene and topical application of antibiotics.

Discussion

Steven-Johnson Syndrome is defined as severe erythema multiforme like eruption of the skin associated with lesions of oral, genital and anal mucosa along with eye involvement associated with haemorrhagic crusting of lips. The disease is immunologically mediated involving the skin and mucosae with varying grades of severity.

It is often induced by drugs but viral infections are known triggers of this disease. Varicella zoster virus has been reported rarely as an etiological agent. It often begins with flu like symptoms followed by painful, red or purplish rash that spreads and blisters. An idiosyncratic delayed hypersensitivity reaction has been implicated in the pathophysiology. Antigen presentation and production of TNF alpha by local tissue dendriocytes results in recruitment of T lymphocytes and their imcreased proliferation which in turn enhances the cytc of other immune cells, activated CD8+ I₃₉ , cytes induce epidermal cell apoptosis via several mechanisms including release of granzyme B and perforin. Perforin is a pore making monomeric granule released from NK cells and cytotoxic T lymphocytes.

Apoptosis of keratinocytes can also take place via direct interaction between the cell death receptor Fas and its ligand and IFN gamma which induces Fas expression by keratinocytes.

Researchers have found increased level of soluble Fas ligand in patients' serum with Steven-Johnson Syndrome and Toxic Epidermal Necrolysis.

Keratinocyte death causes separation of epidermis from dermis. The apoptotic cells provoke recruitment of more chemokines which perpetuate the inflammatory process leading to extensive skin necrosis. Diagnosis is based on clinical features, Tzanck smear and confirmed by histopathology.

The pathogenesis of Erythema Multiforme with herpes virus association is consistent with a delayed hypersensitivity reaction. The disease begins with the transport of the viral DNA fragments by circulating peripheral blood mononuclear CD34+ cells (Langerhans cell precursors) to keratinocytes which leads to recruitment of herpes virus specific CD4+ TH cells. The inflammatory cascade is initiated by IFN gamma, which is released from CD4+ cells in response to viral antigens and immune mediated epidermal damage begins subsequently¹.

Steven-Johnson Syndrome occurring as a consequence of varicella zoster infection has been reported² and should be considered if bullae develop in addition to typical polymorphic rash of chickenpox³. Treatment with systemic steroids and Acyclovir is necessary⁴.

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Conflict of interest: None

References

1. Choy AC, Yarnold PR, Brown JE et al. Virus induced erythema multiforme and Steven-Johnson Syndrome. *Allergy Proc* 1995; 16: 157-161.
2. Viral infections JC Sterling Rook's Textbook of Dermatology. 7th Edition. Pg. 25.
3. Prais D, Grisuru- Soen G, Barzilai A, Amir J. Varicella zoster viral infections with Erythema Multiforme in children Infections 2001 29; 37-39.
4. Kokuba H, Imafuku S, Huang S, Aurelian L, Burnett JW. Erythema multiforme lesions are associated with expression of a herpes simplex virus gene and qualitative alterations in the HSV-specific T-cell response. *Br. J Dermatol* 1998; 138:952-964.