



## Toxic epidermal necrolysis associated with acute measles infection

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### Abstract

Stevens Johnson syndrome (SJS) and Toxic Epidermal Necrolysis (TEN), is an infrequent but severe form of a hypersensitivity reaction that has been associated with a wide range of triggers. Several cases of SJS/TEN have been attributed to infections. This the first case report, to explore the clinical course, diagnosis and management of a case of TEN in a 13-year-old boy with acute measles infection.

### Keywords

Toxic epidermal necrolysis (TEN), Stevens Johnson syndrome (SJS), Measles

### Introduction

Stevens Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN), is an infrequent but severe form of a hypersensitivity reaction associated with high morbidity and mortality [1].

Initially described by A.M. Steven and F.C Johnson in 1922, SJS is characterized by sudden onset of erosion of mucus membranes predominantly oral mucosa and conjunctiva, with blistering of the skin and epidermal detachment which involves less than 10% of the Body Surface Area (BSA). SJS/TEN overlap involves 10% to 30% of the BSA and TEN involves more than 30% of the BSA. SJS/TEN range from two to seven cases per million people per year with a mortality of 30% globally, in South Africa there is a paucity of data on the incidence and prevalence of SJS/TEN [2-3].

Multiple causative agents have been described in the aetiology of SJS. Over one hundred drugs have been associated with SJS including analgesics, anti-epileptics and antibiotics. Infectious aetiologies include viral infections, bacterial and fungal infections. Rare causes include herbal medications, food, contrast medium, external chemical exposure and vaccinations We describe a case of a 13-year-old boy presenting with TEN overlap associated with an acute measles infection.

### Case Report

A 13-year-old male presented to the emergency department with a two-day history of, multiple painful lesions in the mouth and

throat, generalized weakness, malaise and purulent discharge from the eyes. Three weeks prior, the patient had been admitted following a grand mal seizure. Contrast CT Brain indicated leptomeningeal enhancement was present. Subsequent lumbar puncture was acellular, with respective TB, fungal and bacterial cultures negative. Serology for Neurocysticercosis, Toxoplasmosis and Human Immunodeficiency virus (HIV) were also negative, and the patient was subsequently discharged on sodium valproate 400mg twice daily. On examination, he was febrile (38.5°C), tachycardic (124 bpm), with a normal respiratory rate of (12 bpm), with an oxygen saturation of 97% on room air and a random glucose of 5.6mmol/l. The patient was alert, awake and responsive; the cardiovascular, respiratory, neurological, and gastrointestinal examinations were unremarkable. On examination of the skin, multiple vesicular lesions were present on the oral mucosa with overt swelling of the lips and sloughing of the skin. Numerous bullae and vesicles (approximately 20% of BSA) were present on the trunk. Targeted lesions were present on the palmar surfaces of the hands. Extensive involvement of the genitals was present, with sloughing of the skin. Bilateral suppurative conjunctivitis and tonsillitis was present. Dermatology, ophthalmology, dietetics and urology were urgently consulted. The differential diagnosis as this stage was SJS/TEN overlap secondary to sodium valproate, severe atypical presentation of measles and severe herpes simplex virus. The patient was subsequently managed as SJS/TEN overlap with a SCORTEN score of 2. Investigations included: baseline bloods, blood cultures, procalcitonin, pus swab of the oral lesions and purulent conjunctivitis, chest x-ray, urine MCS. Measles, Herpes Simplex Virus (HSV), Varicella Zoster Virus (VZV), HIV and Cytomegalovirus (CMV) serology were also performed.

Management included supportive care with empiric Ceftriaxime, Hydrocortisone, Perfalgan, fluids matched to input/output to prevent acute kidney injury, Vitamin A, Acyclovir and Clexane. Specific management included Chloromax ointment, Melloderm and Bactraban dressings. The Sodium Valproate was stopped on presentation. However, the extent of skin and mucosal involvement continued to worsen over the next two days extending to 35% of the body surface area. The patient was reclassified as TEN.

### Results of the Investigations Included

A normal urea, electrolytes and renal function, calcium, magnesium and phosphate were normal. Inflammatory markers were raised namely the WCC – 8.30 x 10<sup>9</sup>, CRP - 54 mg/l and the procalcitonin - 0.06 ug/l. The rest of the FBC was unremarkable. The initial blood cultures were negative; the superficial nasopharyngeal and oropharyngeal swabs yielded no growth. Most notably in the serology report, Measles IgM and IgG were positive, indicative of recent or current Measles infection. The patient was IgG positive, IgM negative for HSV 1 and VZV indicating previous infection. He was both IgG and IgM negative for HSV 2. Serology for HIV, CMV and Rubella were negative. The patient was managed by a multidisciplinary team including, dermatology, ophthalmology, urology and dietetics. The patient responded well to treatment. He fortunately did not develop a secondary infection. He made a full recovery and was subsequently discharged from the hospital after three weeks.

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## Discussion

There are numerous case reports documenting both SJS and TEN due to a wide range of aetiologies, the most common of which is adverse drug reactions. This particular case could be attributed to Sodium Valproate, as the patient had recently been started on the drug.

However; TEN has been known to occur secondary to viral infections. The positive Measles IgM raises the possibility that, this particular case may have been secondary to measles infection. Infections have been described as the aetiology of TEN in a number of cases.

Mycoplasma pneumonia is the most often infectious agent associated with TEN, with 7% of atypical community acquired pneumonias complicated by SJS/TEN overlap [4]. Infectious agents implicated in TEN include a number of viruses, namely: adenovirus, Epstein Barr virus, HSV, influenza, measles and VZV. Bacterial causes include pseudomonas aeruginosa, legionella, yersinia enterocoli and tuberculosis. syphilis and deep fungal infections have also been implicated. HSV 1 and CMV were described as the causative agents in immunosuppressed patients. Historically SJS/TEN overlap has been rarely reported after vaccinations. Four isolated cases have been described in the literature, occurring in childhood after measles, mumps and rubella vaccinations [5]. The patient in question had received all childhood vaccinations as per the government schedule. A record of his vaccination history was documented in his Road to Health card. However, there was no temporal relationship between the vaccination history and onset of symptoms in this particular patient.

In this particular case, the aetiology is most likely secondary to measles infection, which as yet, has not been described in the literature. Measles, an RNA virus of the paroxymoviridae family, is highly infectious. The disease process involves a primary viremia: the virus replicates at the site of inoculation and the reticuloendothelial cells, followed by secondary viremia, with the virus replicating in the skin, conjunctiva and mucus membranes. The measles skin manifestations are mainly due a hypersensitivity reaction. In this patient the initial presentation of seizures can be postulated to be a neurological complication of measles namely, acute measles encephalitis which is associated with seizures [6].

The presence of both acute measles infection and newly initiated sodium valproate in this patient raise the possibility that both played a role in the development of TEN. Several studies have shown that sodium valproate can induce viral replication. This stimulatory effect of sodium valproate was shown in studies involving CMV, poliovirus type 1, coxsackie B virus, HIV and measles. Researchers in these studies proposed that sodium valproate may worsen a patient's condition in viral infections. However, most of these studies were done in vitro and further studies are needed to ascertain the clinical significance of these effects.

There are no previous case reports documenting SJS/TEN due to measles virus. Though the case reports documenting SJS/TEN due to other viral infections do support this conclusion. However, in this case sodium valproate cannot be ruled out as the causative agent or as a contributing factor. SJS/TEN is a serious and often fatal condition and so all possible aetiologies should be considered and more research is required regarding this pathology.

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