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CASE REPORT

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Toxic epidermal necrolysis in a 5-year-old boy - case report

Necrólise epidérmica tóxica em um relato de caso de um menino de 5 anos de idade

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ABSTRACT

Toxic epidermal necrolysis (TEN) and Stevens-Johnson syndrome (SJS) are considered a spectrum of acute life-threatening mucocutaneous reaction that differ only in severity, often induced by drugs. Varicella-zoster virus has been rarely reported as an etiological agent in TEN. Our case report highlights the association of varicella-zoster virus and TEN in a 5-year-old boy.

KEYWORDS

Life-threatening; Toxic epidermal necrolysis (TEN); Varicella-zoster virus.

RESUMO

Necrose epidérmica tóxica (NET) e síndrome de Stevens - Johnson (SSJ) são considerados um espectro de reação mucocutânea aguda com risco de vida , que diferem apenas em termos de gravidade, muitas vezes induzidos por drogas. Vírus varicela-zoster tem sido raramente relatada como agente etiológico em casos de NET. O nosso relato de caso destaca a associação do vírus varicela- zoster e TEN em um menino de 5 anos de idade.

PALAVRAS-CHAVE

Ameaça de vida; Necrose epidérmica tóxica (TEN); Varicela-zoster vírus.

INTRODUCTION

TEN is a serious systemic disorder with the potential for severe morbidity and even death. The term toxic epidermal necrolysis (TEN) was first used by the Scottish dermatologist Alan Lyell in 1956 to indicate a rare life-threatening mucocutaneous disorder characterized by extensive, and rapidly evolving, epidermal detachment, erythema and necrosis [1]. TEN is defined as detachment of skin (full thickness epidermis) involving more than 30% of the body surface area in affected individuals [2]. TEN is a life-threatening exfoliative skin re¬action that lies on a spectrum with Stevens-Johnson syndrome (SJS) [3]. SJS/TEN is considered to be a drug hypersensitivity reaction mediated by cytotoxic T cells [4]. Genetic predisposition has been reported in relation to specific human leucocyte antigen (HLA)-A, B or C alleles [5]. Recent genome-wide association studies identified ATP-binding cassette transporter and proteasome pathways as potentially being implicated in nondrug-specific SJS/ TEN [6]. Epidermal cell death results from necrosis and massive T-cell-mediated apoptosis via three described pathways: Fas–Fas ligand interaction, perforin–granzyme B and granulysin [7]. Elevated levels of TNF-alpha have been found in the blister fluid and keratinocytes of SJS/ TEN [8]. However, drug-specific cytotoxic cells are probably not the sole effector mechanism of epidermal necrolysis [9], as in our case which is induced by varicella-zoster virus.

Varicella-zoster virus, a type of herpes

virus, causes varicella (chicken pox) and after endogenous reactivation, herpes-zoster (shingles). Varicella which is recognized by a characteristic vesicular rash, arises mainly in young children, although older individuals can be affected. Serious complications including central nervous system involvement, pneumonia, secondary bacterial infection and even death are sometimes seen [10].

CASE REPORT

A 5-year-old boy reported in a debilitating condition having severe erosive vesiculobullous lesions all over the body since 2 days with high grade fever of 39.4°C. Extra-oral examination revealed epidermal detachment over the face, swollen lips with hemorrhagic crusting and mucopurulent discharge from both the eyes (Figure 1). Areas of epidermal detachment were also evident on chest, thigh and both upper and lower limbs. Patient's back showed epidermal necrosis, intact bullae, and denuded skin with exposed dermis (Figure 2). Palms and soles of the patient showed peeling of skin in sheets leaving glistening, eroded, erythematous dermis (Figure 3). Intra-oral examination revealed multiple, irregular shaped ulcerative lesions present on bilateral buccal mucosa covered by pseudomembrane with erythematous surrounding. On manipulation, bleeding was present. Similar lesions with irregular borders associated with flaccid bullae were present in the lower buccal vestibule in relation to molar region. Erosive lesions were seen involving posterior hard plate, soft palate, faucial pillars and extending to the oropharynx. Patient's parents gave history of chicken pox 4 days prior, following which the symptoms commenced in the form of rash over face and limbs. History of cold, cough, burning micturition, vomiting, abdominal pain, and gradual increase in fever was present, which subsided after medical intervention. Patient also had history of myoclonic epilepsy for which sodium valproate was prescribed for 4 months. All investigations including complete hemogram and blood biochemistry were within normal limits. Differential diagnosis of erythema multiforme, staphylococcal scalded

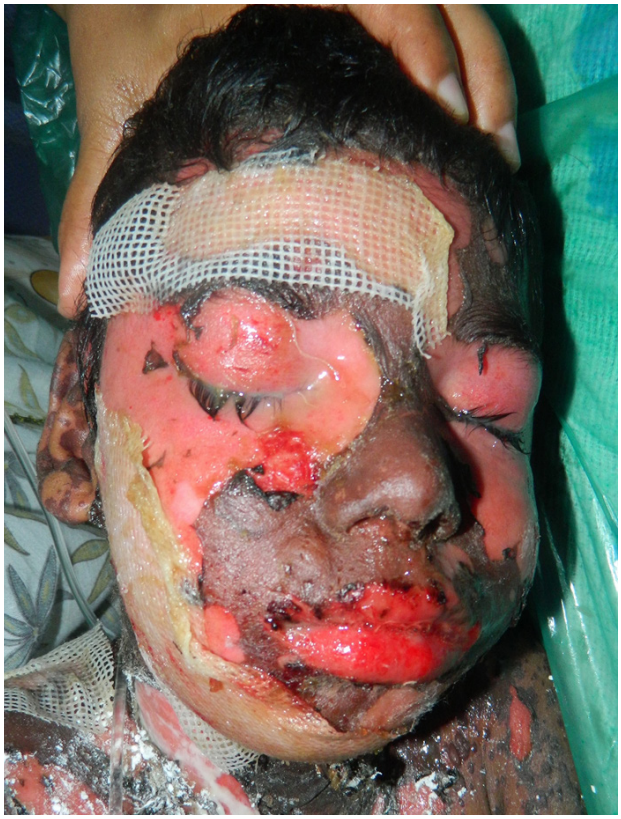

Figure 1 - Epidermal detachment over the face, swollen lips with hemorrhagic crusting and mucopurulent discharge from both the eyes.

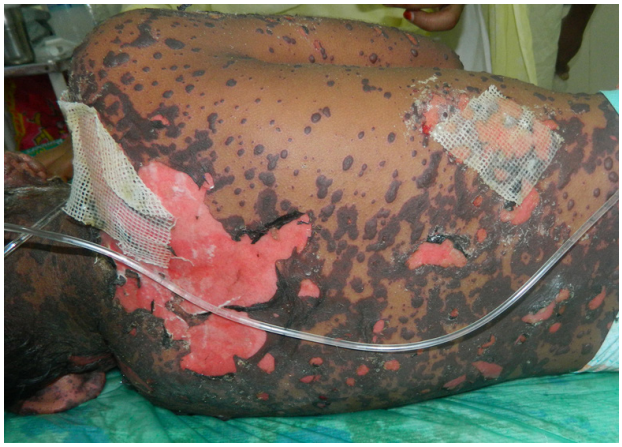

Figure 2 - Patient's back showed epidermal necrosis, intact bullae, and denuded skin with exposed dermis.

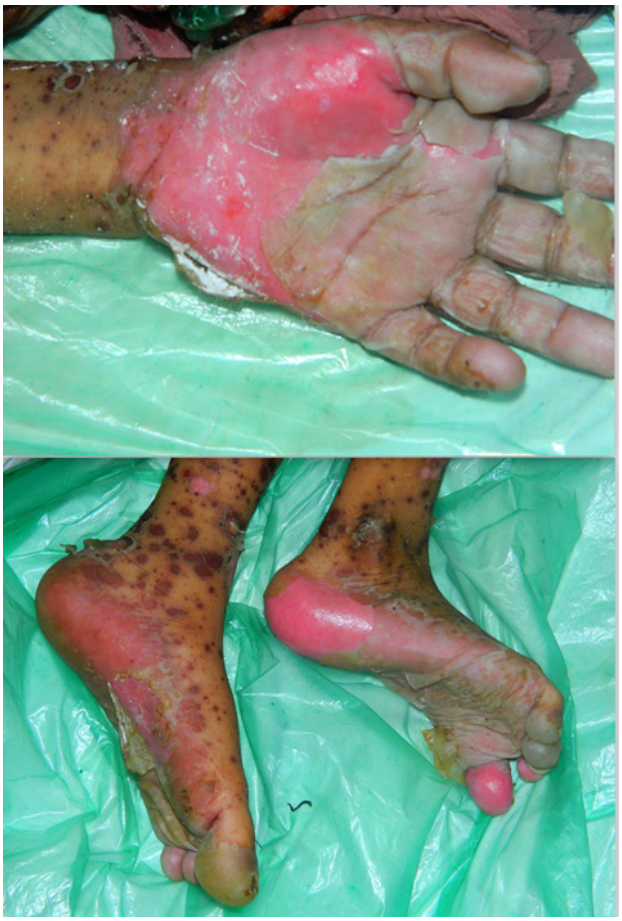

Figure 3 - Palms and soles of the patient showed peeling of skin in sheets leaving glistening, eroded, erythematous dermis.

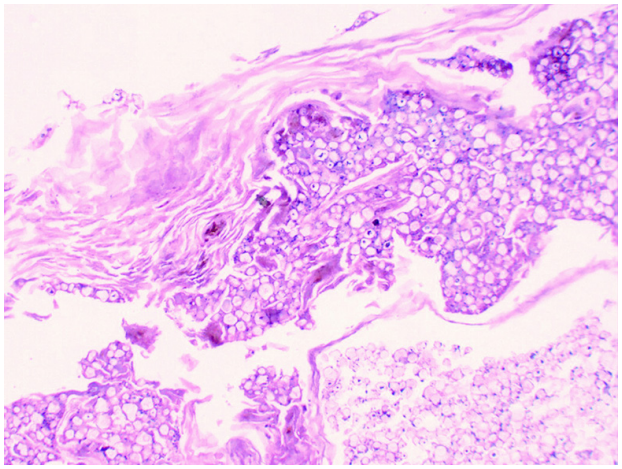

Figure 4 - Epithelial cells exhibiting vacuolar changes with basophilic appearance above and pale below the cleft.

skin syndrome, pemphigus vulgaris, and bullous pemphigoid were considered. Histopathological examination of skin biopsy showed surface keratin layer, epithelial cells exhibiting vacuolar changes with basophilic appearance above and pale below the cleft. Keratin like fiber was also seen in the center of the cleft, without significant inflammation (Figure 4).

Patient was administrated a tapered dose of intravenous injection of hydrocortisone, and intravenous injection of meropenem, intravenous immunoglobulin (IVIg), fluconazole, linezolid. Topical application of bactigreen and neosporin powder on exposed dermis was advised. Despite this treatment, the patient's condition gradually declined. Within a week of treatment the patient was unable to open his eyes due to keratitis, developed pneumonia, abscess formation in multiple organs, followed by a swelling over the abdomen which was attributed to secondary infection. Unfortunately within a month patient died because of secondary bacterial infection and multiple organ failure.

DISCUSSION

Currently, TEN and SJS are considered to be two ends of a spectrum of severe epidermolytic adverse cutaneous drug reactions, differing only by their extent of skin detachment. Drugs are assumed or identified as the main cause of SJS/TEN in most cases, but Mycoplasma pneumoniae and Herpes simplex virus infections are also the documented causes with unknown pathologenesis [11]. Varicella-zoster virus induced TEN leads to serious complications- including central nervous system involvement, pneumonia, secondary bacterial infection and death [10].

Bastuji-Garin S et al [2]. grouped TEN into five categories as follows: 1) bullous erythema multiforme, detachment below 10% of the body surface area plus localized "typical targets" or "raised atypical targets";

2) Stevens-Johnson syndrome, detachment below 10% of the body surface area plus widespread erythematous or purpuric macules or flat atypical targets; 3) overlap Stevens-Johnson syndrome-toxic epidermal necrolysis, detachment between 10% and 30% of the body surface area plus widespread purpuric macules or flat atypical targets; 4) toxic epidermal necrolysis with spots, detachment above 30% of the body surface area plus widespread purpuric macules or flat atypical targets; and 5) toxic epidermal necrolysis without spots, detachment above 10% of the body surface area with large epidermal sheets and without any purpuric macule or target. In our case the child had more than 30% of skin detachment based on which a diagnosis of TEN was made.

Cleavage of the epidermis from the dermal plane, results in impaired barrier function of the skin with inevitable bacterial colonization. Infection is generally considered to be the major factor associated with morbidity and mortality in TEN [12]. Wide skin detachment, leads to water, electrolytes and protein loss. TEN patients raise clinical challenges similar to burn patients [13]. Mortality rate associated with SJS is between 1% and 3%, and with TEN is 30% to 50% [14].

Bay A et al. [15], Bhattarai S et al. [16] also reported a cases of SJS/TEN induced by varicella infection. Lim VM et al. [17] in his study of SJS/TEN cases suggested overall mortality rate of 23.7% (18/76) while Hamilton GM et al. [18] found no mortality in his institutional retrospective review of SJS/TEN cases. Finkelstein Y et al. [19] in his study of 55 cases stated recurrence rate of 18% for SJS and 0% for TEN with a mortality rate of 2%. The SCORTEN scale is used for measuring severity-of-illness of TEN [20].

Although sepsis is currently accepted as the main cause of morbidity, much of the morbidity and subsequent threat to life is orchestrated by an exaggerated inflammatory response, with major outpouring of cytokines and destructive matrix metalloproteins [21]. Multiple organ dysfunction is a possible sequelae of TEN and is associated with poor prognosis, while total body surface area of involvement has not been shown to be related to poor prognosis [22].

TEN epitomizes the diagnostic chal¬lenges that can be presented to the dental surgeon and the need to be aware of this rare-but-serious disease. Early identification and discontinuation of the inciting drug are most important. Prompt transfer to a burn unit for aggressive skin care improves the chances of survival.

CONCLUSION

TEN is a clinical entity characterized by high grade fever, bullae formation and followed by mucocutaneous sloughing, which can be extensive and life-threatening. Patient with extensive TEN should be treated, by medical staff skilled in management of burns. When a patient with primary varicella infection presented, it should always be kept in mind that the progression of non-life-threatening varicella infection can develop in to a fatal condition as TEN/SJS, as evident in present case.

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