Cyclosporine: An Emerging Therapeutic Agent for Paediatric Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis

Sir,

Stevens–Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are severe, though rare, cutaneous reactions that occur following exposure to medicines. They are characterised by extensive blisters and erosions of the mucocutaneous surfaces.[1] Both conditions differ from each other on the basis of the body surface area involvement, pure SJS (<10%) from pure TEN (>30%). When the cutaneous involvement is 10-30% of body surface area, it is called SJS/TEN overlap. Complications and death typically arise from these infections; hence, the use of corticosteroids is controversial in their management.[1] SJS and TEN in children are rare, with 5.3 and 0.4 cases per million children, respectively.[1] Nevertheless, paediatric SJS/TEN has high rates of complications, sequelae, and recurrences. Here, we present a paediatric patient with SJS/TEN overlap syndrome, who was successfully treated with cyclosporine.

A case of a 9-year boy presented with two-day history of generalised skin rash, sloughing skin at sites of friction, and minimal trauma. He also had severe oral mucosa involvement, with inability to take solids. The patient had abdominal pain about a week back, for which he was prescribed oral hyoscine butylbromide and omeprazole by a general practitioner. Subsequently, he had lesions, bloodshot eyes, and burning micturition. His rash started on the trunk and progressed to involve the whole body and oral mucosa. However, He had not taken any other medications in the past three months.

On examination, the patient appeared ill and was of lean build, with a blood pressure of 110/60 mm Hg, pulse rate of 98 beats/minute, respiratory rate of 19 breaths/minute, and temperature of 101°F. Cutaneous examination showed diffused dusky erythematous patches and plaques with erosions and vesicular and targetoid lesions scattered on the face, trunk, and limbs (Figure 1A, B). The body surface area involvement was 30% and Nikolsky's sign was positive. There were erosions, crusting and swelling of the lips, with purulent discharge and restricted mouth opening.

A diagnosis of SJS/TEN, probably due to hyoscine butyl bromide or omeprazole, was made. The patient's C-reactive protein (CRP) was 178.20 mg/dl. Complete blood count revealed total leucocyte count (TLC) of $21.9 \times 10^3/mm^3$ with 84% neutrophils. Biochemistry profiles were within normal range. His SCORTEN score was 1 at the time of admission. The patient's parents did not give consent for a skin biopsy. Pus culture from the purulent lesions yielded growth of *Staphylococcus aureus*. Blood, urine, nasopharyngeal, and conjunctival cultures did not reveal any pathogens. His chest imaging was clear.

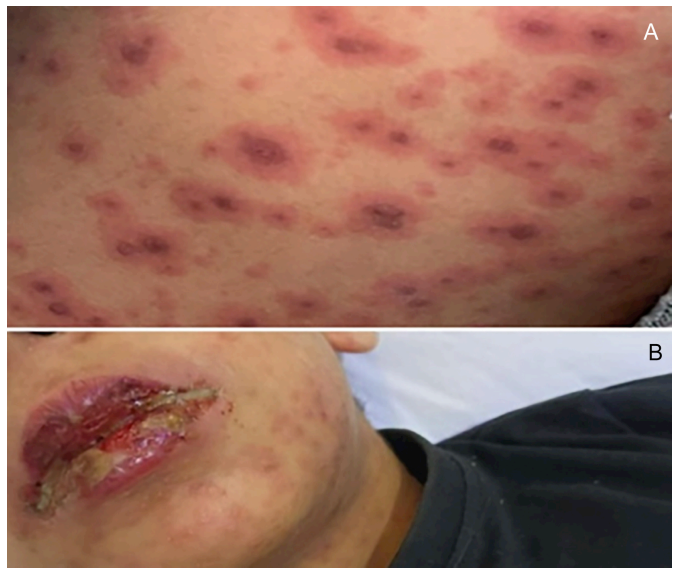

Figure 1: (A) Erythematous plaques with central dusky discoloration and necrosis surrounded by a zone of pallor (B) Erosions, haemorrhagic crusting with purulent discharge over lips and angles of mouth.

He was managed conservatively, along with daily wound dressing. Multidisciplinary approach was taken into consideration, including dermatology, paediatrics, urology, ophthalmology, and otorhino laryngology departments. In view of the pus culture yielding *Staphylococcus aureus* sensitive to co-amoxiclav, raised TLC and CRP, and following the confirmation of the absence of hypersensitivity, co-amoxiclav therapy was commenced, with artificial tears and steroid eye drops. Oral cyclosporine was started at a dose of 3 mg/kg body weight/day in two divided doses. Once the emergence of new lesions stopped and older ones showed signs of healing, cyclosporine was decreased to 2 mg/kg body weight/day. And after the complete resolution of lesions, *i.e.* after 3 weeks, it was stopped altogether. His blood pressure and renal function tests remained normal, without having any side effects.

Currently, there are no specific guidelines for the treatment of paediatric SJS/TEN. Removal of offending agent with supportive care, including nutritional support, fluid and electrolyte balance, and wound care, is the mainstay of management. Insufficient evidence exists regarding the effectiveness of immunomodulatory agents in paediatric SJS/TEN. The role of systemic corticosteroids and intravenous immunoglobulins remains controversial. Cyclosporine is an immunosuppressant that inhibits calcineurin, reducing inflammatory cytokine production. It also displays anti-apoptotic properties. There are only scant case series published regarding the use of cyclosporine in children. St. John *et al*. have documented three paediatric cases that were successfully managed with cyclosporine monotherapy at a dose of 3 mg/kg/day divided twice daily for 3 weeks. Rapid healing of the mucocutaneous lesion

was observed ultimately resulting in a shorter hospital stay.[2] Singh *et al*. published their study on SJS/TEN, including one child with SJS who was effectively managed with cyclosporine at a dose of 3 mg/kg/day for two to three weeks.[3] A similar study by Balai *et al*. reported two paediatric cases managed with a higher dose of cyclosporine, *i.e*., 5 mg/kg body weight, untill complete re-epithelialisation was achieved—approximately two weeks.[4]

To conclude, this case adds to the growing body of evidence in medical literature supporting the use of cyclosporine monotherapy in paediatric SJS/TEN. Short-term use of cyclosporine may be considered a viable therapeutic option with a reasonable efficacy and safety profile.

COMPETING INTEREST:
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