Levamisole in Childhood Pemphigus Vulgaris

Sir,

Management of childhood pemphigus vulgaris is difficult and warrants concerns for side effects of immunosuppressive therapy. As long-term use of potent corticosteroids can cause systemic side effects, choice of nonsteroidal immunosuppressive agent is very important to maintain long-term remission. We report a case of extensive childhood pemphigus vulgaris, who was successfully treated with long-term levamisole therapy along with low dose steroid and did not relapse.

A 12-year-old boy, diagnosed a case of pemphigus vulgaris from a government hospital, presented to us with multiple, erythematous erosions over face, chest, abdomen, back, bilateral upper limbs, lower limbs, groins, and buttocks with purulent discharge and crusting over few erosions [Figure 1]. Nikolsky sign was positive, indicating the active state of disease. A few well-defined erythematous erosions with crusting were present over the scalp. Oral examination revealed multiple erosions over lower lip and bilateral buccal mucosa and fissured tongue.

Five months back, the patient developed itchy fluid filled lesions over scalp which progressed to involved his face, trunk, and extremities. He went to a government hospital, where he was diagnosed as a case of pemphigus vulgaris and treated with oral prednisolone and dapsone. He showed improvement after treatment for a month, but relapsed, 1 month before he presented to us.

At our hospital, he was treated with intravenous dexamethasone and antibiotics, to which he responded but relapsed after 1 month. He was then started on levamisole, in a dose of 1.5 mg/kg/day: 50 mg once daily, along with oral prednisolone 30 mg. The patient responded drastically and his lesions resolved within a month. Oral prednisolone was tapered gradually (by 5 mg every 15 days) to a maintenance dose of 5 mg, every alternate day within 3 months. He has maintained remission since then.

He continued his maintenance therapy of tab prednisolone 5 mg, alternate day and tablet levamisole 50 mg A/D for the next 18 months and then again tapered to oral prednisolone 5 mg, once a week and tab levamisole 50 mg A/D, which is being continued. No adverse effects were seen [Figure 2].

Levamisole is an antihelminthic drug with immunomodulatory properties. It enhances innate immune responses and modulates cortisol levels during stress.[1] Further studies revealed that it stimulated T-helper 1 immunity by increasing serum levels of interferon-γ, interleukin (IL)-5 and tumor necrosis factor-α cytokines, IgG, IgM and total blood cell counts and upregulated the mRNA expression levels of IL-2, IL-4, and IL-5. At the cellular level, in the spleen, it increased immunoreactivity of CD4 and CD8.[2] However, the exact mechanism of action of levamisole in autoimmune inflammatory diseases remains unknown. In a study of patients with chronic oral ulcers, both levamisole 150 mg/day and prednisolone 15 mg/day for 3 consecutive days in a week was given.[3] The patients showed significant improvement; oral lesions resolving within 4–8 weeks and maintained remission. Oral ulcers due to lichen planus remained in remission for 6 months while remission

Figure 1: Extensive erosions over body.

Figure 2: Posttreatment: No active skin lesion.
lasted for 3 years in mucosal pemphigoid and pemphigus vulgaris. In combination with steroids, levamisole reduced the dose of steroids required for remission in patients of pemphigus vulgaris.[4]

Levamisole has been used in pediatric population in steroid-dependent nephrotic syndrome which is an antibody-mediated autoimmune disease like pemphigus vulgaris, in a dose of 2.5 mg/kg (daily or alternate day) and it helped in reducing relapse, maintaining remission and lowering the dose of steroids; daily dosing being more effective than alternate day low dose prednisolone.[5,6] No side effects associated with levamisole were reported in these patients. Levamisole is a relatively safer drug with minimal adverse effects. It includes rash, fever, nausea, abdominal cramps, taste alteration, alopecia, arthralgia, a flu-like syndrome and rarely, agranulocytosis, necrosis syndrome.[7] Based on proven safety of levamisole in children and its efficacy in antibody-mediated nephrotic syndrome in children, we decided to use levamisole in our patient.

Thus, we report a successful use of levamisole in severe and recalcitrant pemphigus vulgaris in a child with no side effects. We suggest that it can be used as an excellent steroid sparing alternative, especially in children where there are concerns of side effects due to other immunosuppressive drugs.

Declaration of patient consent
The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

Apurva Aditi, Sushil Pande, Millind Borkar
Department of Dermatology, Lata Mangeshkar Hospital, NKP Salve Institute of Medical Sciences, Nagpur, Maharashtra, India

Address for correspondence:
Dr. Apurva Aditi
Department of Dermatology, Lata Mangeshkar Hospital, NKP Salve Institute of Medical Sciences, Nagpur - 440 019, Maharashtra, India.
E-mail: apurva.mini@gmail.com

REFERENCES
1. Pahor-Filho E, Castillo AS, Pereira NL, Pilarski F, Urbinati EC. Levamisole enhances the innate immune response and prevents increased cortisol levels in stressed pacu (Piaractus mesopotamicus). Fish Shellfish Immunol 2017;65:96-102.
2. Mohamed EH, Baiomy AA, Ibrahim ZS, Soliman MM. Modulatory effects of levamisole and garlic oil on the immune response of Wistar rats: Biochemical, immunohistochemical, molecular and immunological study. Mol Med Rep 2016;14:2755-63.
3. Lu SY, Chen WJ, Eng HL. Response to levamisole and low-dose prednisolone in 41 patients with chronic oral ulcers: A 3-year open clinical trial and follow-up study. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1998;86:438-45.
4. Lozada F, Silverman S, Cram D. Pemphigus vulgaris. A study of six cases treated with levamisole and prednisone. Oral Surg Oral Med Oral Pathol 1982;54:161-5.
5. Donia AF, Ammar HM, El-Agroudy Ael-B, Moustafa Fel-H, Sobh MA. Long-term results of two unconventional agents in steroid-dependent nephrotic children. Pediatr Nephrol 2005;20:1420-5.
6. Elnas AT, Tabel Y, Elnas ON. Short-and long-term efficacy of levamisole in children with steroid-sensitive nephrotic syndrome. Int Urol Nephrol 2013;45:1047-55.
7. Gupta LK, Balai M, Khare AK, Singh A, Mittal A. Levamisole-induced drug fever. Indian J Drugs Dermatol 2016;2:111-2.

This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.