CASE REPORT

Successful management of generalized bullous pemphigoid with rheumatoid arthritis using combination IVIG and low dose steroid in COVID 19 era

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ABSTRACT

The management of autoimmune disorders is as it is a challenging task. To top it, COVID 19 has imposed further restrictions in the already limited treatment options at our disposal. Here, we report successful management of a patient with rheumatoid arthritis and bullous pemphigoid with IVIG and low dose steroid.

KEY WORDS: Bullous pemphigoid, rheumatoid arthritis, IVIG in COVID-19, COVID-19 pandemic

INTRODUCTION

Both bullous pemphigoid (BP) and rheumatoid arthritis (RA) are autoimmune disorders and thus their manifestation in a single patient is more than a mere coincidence. Immunosuppressives are mainstay of treatment of these autoimmune disorders. However, COVID 19 pandemic has raised a genuine concern regarding choice of immunosuppressives, their dose, duration and combinations to avoid iatrogenic immunosuppression. Here, we report a case with these dual disorders and the therapeutic challenges faced in the management.

CASE DESCRIPTION

A 60-years-old woman presented to us with widespread tense bullous eruption all over the body for 3 months. The bullae had clear as well as hemorrhagic fluid and were present on normal skin, without being preceded by urticated lesions. They were severely itchy. Involvement extended over both eyelids sans conjunctival or corneal involvement. While, oral mucosa had minimal involvement in form of erosions. But, the patient complained of pain on swallowing. Other mucosal surfaces were spared. There was no history of preceding drug intake, neurological involvement or symptoms suggestive of underlying malignancy.

The patient also had multiple joint contractures, predominantly involving small joints of hands (Fig. 1) and feet (Fig. 2) and both knees. On taking detailed history, it was found that the patient had received treatment with tablet hydroxychloroquine (HCQ), colchicine, supplemented with anti- inflammatory drugs for RA from 2012-2014. The medication was discontinued without medical advice. During the hospital stay, she developed swelling and pain in both her elbow joints and was diagnosed with RA flare.

On examination, multiple, discrete, round to oval, tense bullae of size ranging from 0.5 X 0.5

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cm to as large as 3x3 cm were present all over body, predominantly over limbs. These were accompanied by erosions, fresh as well as healing, with dyspigmentation at the sites of previous lesions. (Fig. 1 and 2) Bilateral pitting edema of lower limbs upto lower third of legs, was noted. Bedsores were present over ischial tuberosities on both sides. They were deep, round, ulcers of size approximately 2x2 cm, with clean base and hard floor. The edges showed no signs of healing. The surrounding area showed re-epithelizing erosions. (Fig. 3)

Oral mucosa showed irregular ulcers over hard palate, floor of mouth and retromolar trigone but no intact vesicle or bullae. Rest of the mucosal examination was WNL. Scalp, nails, palms, soles were normal.

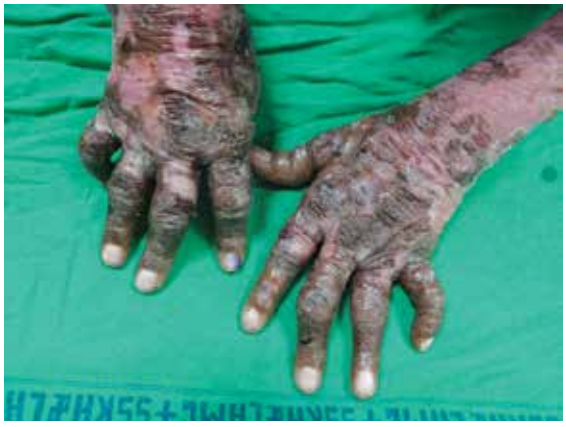

Fig. 1 Re-epithelizing erosions along with small joint deformities of hands

Fig. 2 Re-epithelising erosions and small joint deformities of feet

Fig. 3 Non-healing bed sores along with healing erosions

On investigations, the patient was found to have anaemia of chronic disease (hemoglobin 7.7 gm/dl) and hypoalbuminaemia (2.3 gm). Skin biopsy revealed subepidermal bulla with eosinophils. (Fig. 4) RA factor and anti CCP levels were highly elevated. X-rays of hands and feet showed diffuse osteoporosis, and that of spine with pelvis showed right sided hip dislocation and degenerative joint disease of left hip and spine. X-ray chest was normal.

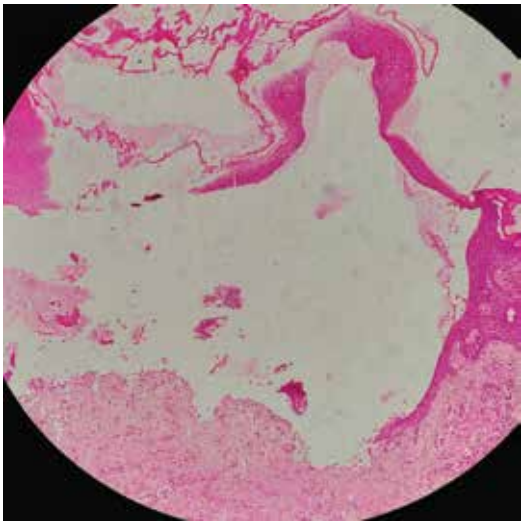

Fig. 4 Subepidermal bulla (hematoxylin and eosin, 40X)

Malignancy workup was done. CXR, CECT chest, USG abdomen-pelvis were WNL. Stool for occult blood was negative. CEA levels were normal. USG breast revealed fibroadenoma (BIRADS 3) which was subjected to FNAC. It showed benign ductal epithelial cells in a hemor-

rhagic background; no malignant cells in smear. Patient was started on tablet Doxycycline 100 mg BD and niacinamide 500 mg OD along with high protein diet and protein supplements. In view of her age and the ongoing pandemic, rituximab and moderate dose steroids were not favored. She was thus given low dose steroid (30 mg prednisolone), and IVIG (at 2gm/kg over 5 days) was started 7 days later when steroid failed to bring about response. The number of new blisters decreased significantly 2 days after IVIG was administered. Tab HCQ was given for her RA flare due to our inability to give methotrexate (anaemia of chronic disease and additional immunosuppression). Daily dressings were done for bedsores with improvement in the depth of ulcers.

DISCUSSION

While RA is chronic musculoskeletal disorder with presence of anti-citrulinated peptide autoantibodies and erosive joint involvement potential, BP is chronic blistering autoimmune disorder with autoantibodies against basement membrane. Presence of one autoimmune disorder can aid in the diagnosis of other.[1]

While multiple case reports of association of various autoimmune disorders with BP as well as with RA are available in literature, we came across only 1 similar case report of a patient with co-existing BP, RA and also vitiligo. At the time of presentation, this 81-years-old male patient had small joint deformities for 15 years and vitiliginous patches on hands, legs and trunk for 10 years and had started developing multiple tense bullae on erythematous base over scalp, face, trunk and extremities for 2 months. He was managed effectively using intravenous corticosteroids and tapering course of oral dexamethasone, followed by tetracycline and nicotinamide. The response to this immunosuppressive regimen in this patient was favorable.[2] Our patient too had pre-existing RA and developed generalized blistering few years later. Parenteral steroids in the dose of 0.5 mg/kg/day along with methotrexate/ mycophenolate mofetil (MMF)/azathioprine would have been the preferred treatment in our patient, but ongoing COVID pandemic and severe anaemia were limiting factors against both. We thus tried IVIG at the dose of 2g/kg divided over 5 days. Drastic improvement was seen. Similar to our case, a patient with BP with concomitant Mycobacterium avium-intracellulare complex (MAC) was successfully treated with IVIG, as steroids could not be administered with tuberculous focus.[3]

As for management of RA, methotrexate is recommended as 1st line management under EULAR recommendations. According to the guideline, methotrexate is to be combined with low dose glucocorticoids.[4] However, with existing severe hypoproteinaemia and fear of bone marrow suppression in this patient with severe anaemia, administering methotrexate was not feasible. Thus, other conventional synthetic disease modifying antirheumatic drug (csDMARD), HCQ 200 mg BD, was prescribed with success, also keeping in mind its use in patients of COVID-19.

The patient was followed up every 4 weeks. Steroids were tapered to physiologic dose of prednisolone and patient was readministered with an IVIG pulse (2 g/kg) with no new vesicles and bullae developing post-pulse.

Various factors that hindered management of the 2 autoimmune disorders in this patient with the conventional regimes, were the geriatric age

group, co-existing comorbidities of severe anaemia and hypoproteinaemia and controversial take on use of immunosuppressives in COVID-19 era. According to guidelines on use of immunosuppressives in Dermatology, by COVID Task Force of the Medical Dermatology Society and Society of Dermatology Hospitalists, published in Journal of American Academy of Dermatology, 2020, prednisolone >10 mg, methotrexate, azathioprine and MMF should be used with increased caution. While, antimalarials with their immunomodulatory properties, have not been associated with increased risk of infection.[5]

We thus hereby achieved successful treatment of BP in a patient with RA, with IVIG and HCQ. With no immunosuppressive and bone marrow suppressive potential, IVIG can be considered to be an effective therapeutic option available in our armamentarium against autoimmune disorders, especially in geriatric population where polypharmacy and treatment complicating comorbidities are rampant.

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