IJD Case Report

Systemic tacrolimus in the management of psoriasis associated with PLA2R antibody positive membranous nephropathy: a case report

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Psoriasis is a chronic inflammatory disorder, which affects the skin, nails, and joints. Psoriasis can be associated with systemic diseases such as diabetes mellitus, metabolic syndrome, renal diseases, and cardiovascular diseases.

Renal involvement among patients with psoriasis has been increasingly reported. These disorders include conditions such as IgA nephropathy, membranoproliferative glomerulonephritis, secondary renal amyloidosis, and C3 glomerulonephritis. The various clinical and laboratory features that need consideration to rule out underlying renal disease in such patients include hypertension, edema of bilateral lower limbs, microscopic hematuria, and proteinuria.

Herein, we present a case of a 49-year-old patient with chronic plaque psoriasis, who was diagnosed with nephrotic syndrome 8 years after the onset of psoriasis. Immunohistochemical analysis of the renal biopsy samples revealed membrane nephropathy with M-type phospholipase PLA 2R positivity.

Due to the concurrent presence of severe psoriasis lesions, oral corticosteroid was deferred, and the patient was treated with oral Tacrolimus 4 mg per day for membranous nephropathy, which resulted in significant improvement of cutaneous lesions.

Keywords: psoriasis, PLA 2R, nephropathy, tacrolimus

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INTRODUCTION

Psoriasis is a chronic inflammatory disorder with a genetic predisposition that can affect the skin, hair, nails, and joints. Patients with psoriasis are more likely to acquire comorbidities such as psoriatic arthritis, metabolic syndrome, coronary heart disease, cancer, chronic obstructive pulmonary disease, cardiovascular disease, inflammatory bowel disease, depression, renal disease, and osteoporosis [1]. Renal involvement in psoriasis has remained a controversial issue, with increased involvement being observed recently [2]. The various spectrum of glomerular and tubular diseases associated with psoriasis include IgA nephropathy, secondary renal amyloidosis, membranoproliferative glomerulonephritis, membranous glomerulopathy, C3 glomerulopathy, chronic kidney disease. These are more common in psoriatic patients than in the general population [3]. Membranous glomerulopathy is

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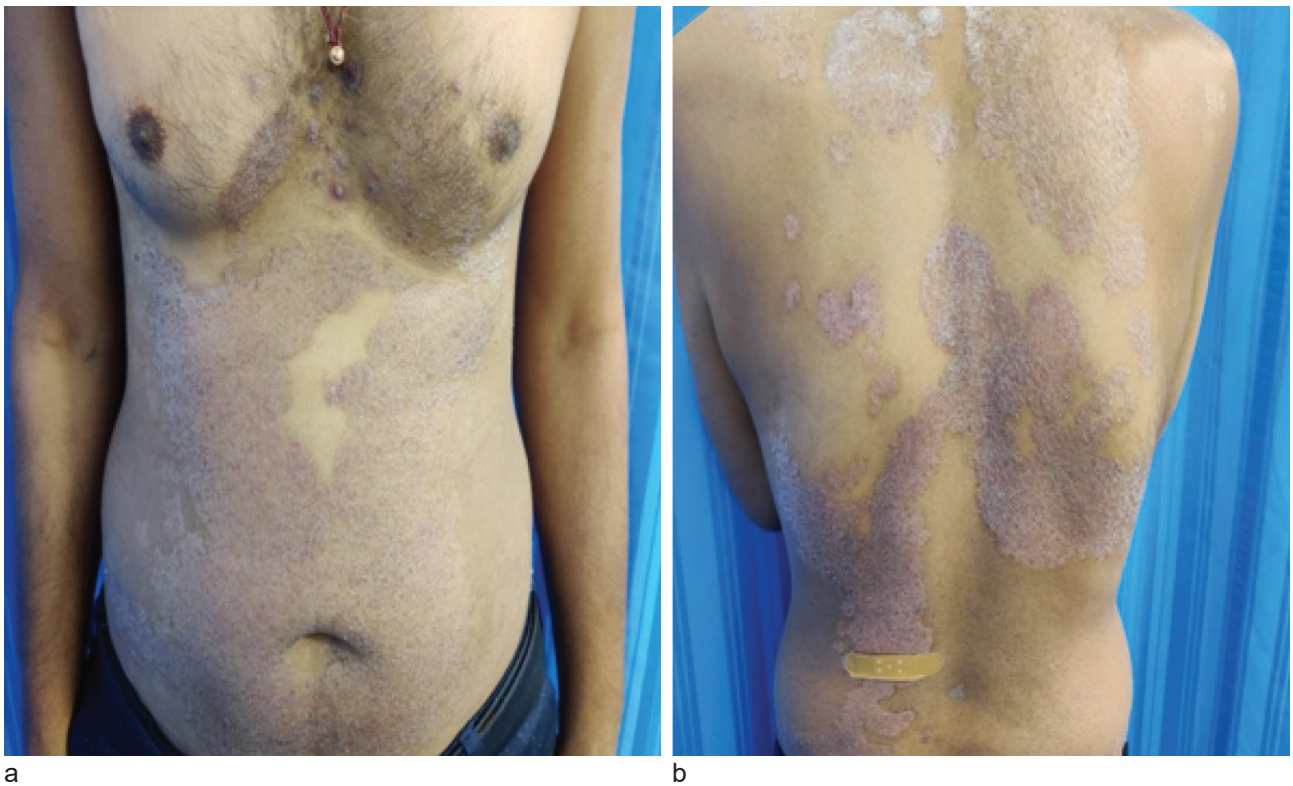
a common cause of nephrotic syndrome in adults and is characterized by sub-epithelial immune deposits in the glomerulus [4]. Circulating autoantibodies against podocytes transmembrane receptor (M type phospholipase A2 receptor -PLA2R) are associated with primary membranous nephropathy [5]. Herein, we report a case of chronic plaque psoriasis with concurrent anti-PLA2R antibodies, whose psoriatic skin lesions responded well to oral Tacrolimus.

CASE PRESENTATION

A 49-year-old man presented to the hospital with pedal edema of both legs for 10 days. The patient was diagnosed with chronic plaque psoriasis for 8 years and was on indigenous oral and topical medications. Dermatological examination revealed multiple, symmetrically distributed erythematous scaly plaques distributed over the nape of the neck, trunk, gluteal region, and lower limbs. The patient's Psoriasis Area and Severity Index (PASI) score was 42.8. Investigations revealed proteinuria (4+), 24-hour urine protein (7g/day), urine red blood cell count (10-15/high power field), Serum total cholesterol (456 mg/dL), and triglycerides (209 mg/dL). The ultrasound abdomen revealed bilateral grade 1 renal parenchymal changes.

On renal biopsy, the glomerulus showed global and segmental sclerosis with mild periglomerular fibrosis, with thickened glomerular basement membranes with spikes and lucencies on silver staining. The arteries showed mild fibroelastosis, while the arterioles showed medial hyperplasia. A direct immunofluorescence study reported that glomeruli showed peripheral granular deposits of IgG (2+) and C3 (2+), with no staining for IgA, IgM, C1q, kappa, and lambda light chains. The immunohistochemistry study revealed M-type phospholipase A2 receptor (PLA 2R) positivity. A final diagnosis of Psoriasis with PLA2R-positive membranous glomerulopathy was made. The presence of normal complement levels (C3) and negative antinuclear antibody, rheumatoid factor (RF), and hepatitis B and C serology ruled out other secondary causes of membranous glomerulopathy.

He was prescribed Tacrolimus 2 mg twice daily, Torsemide 10 mg once daily, and Diltiazem 30 mg once daily. As the patient had extensive skin disease, oral corticosteroids were deferred due to the risk of developing erythrodermic and pustular psoriasis.



a b

Figure 1. Before starting systemic tacrolimus therapy (a and b).

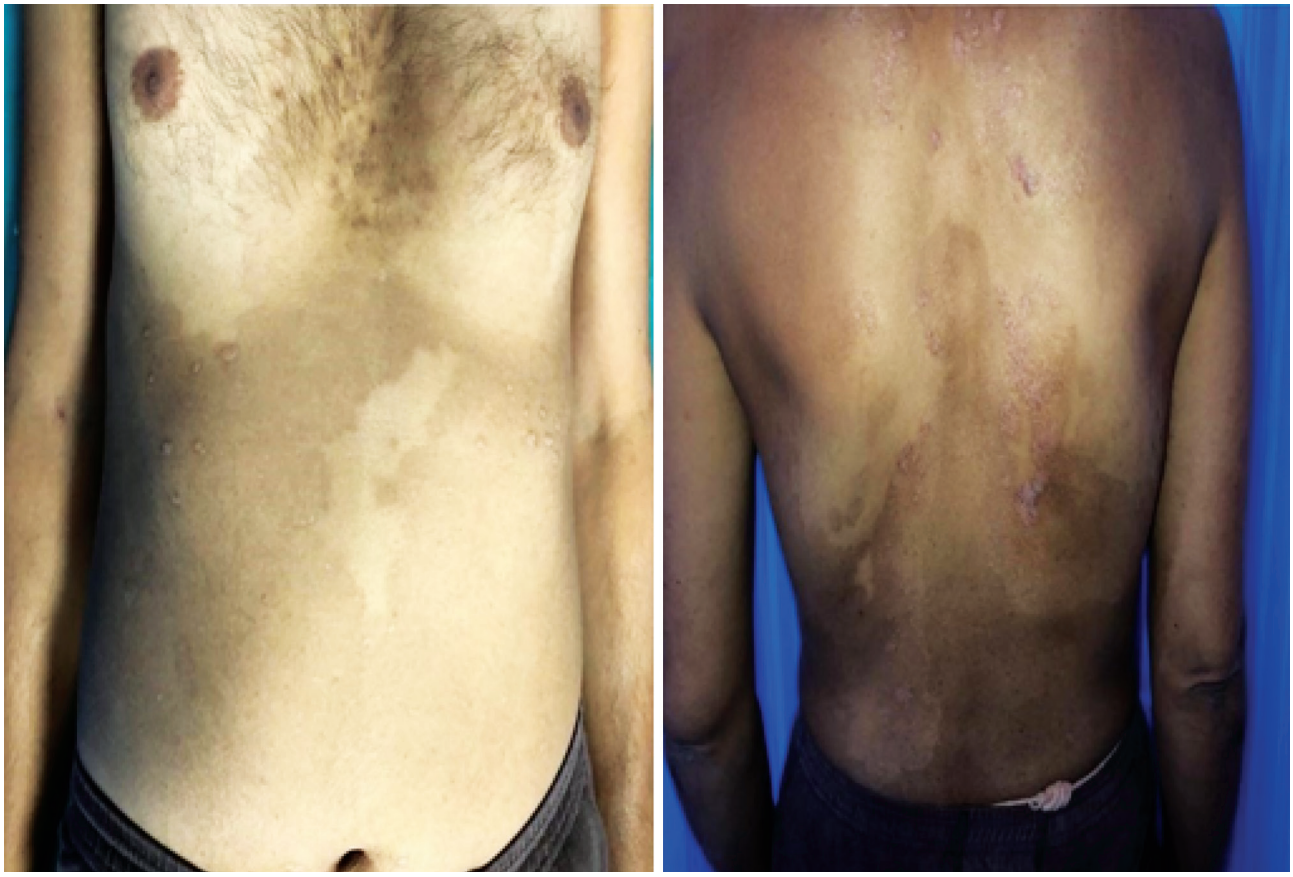


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Figure 2. At the second month of follow-up (a and b).

He was treated with emollients for skin lesions. After 2 months of follow-up, the patient showed improvements in psoriasis lesions with a reduction of PASI score to 3.7 (Figures 1 and 2), as well as a reduction in urinary red blood cell (1-2/high power field) with persistent proteinuria (3+) after 6 months of follow-up. During therapy, no side effects were noted, and creatinine levels remained normal during the patient's monthly follow-up.

DISCUSSION

Psoriasis is an inflammatory disorder affecting the skin, joints, and nails. In recent years, there has been an increase in the reporting of renal involvement among patients with psoriasis, with IgA nephropathy being the most common finding in renal biopsy specimens [6].

Membranous glomerulopathy is a prevalent cause of nephrotic syndrome in adults, and early recognition is critical because up to 40% of these patients may develop end-stage renal disease within 5-15 years.

Antibodies detected against PLA2R, a transmembrane glycoprotein expressed on glomerular podocytes, can serve as a probable marker for categorizing idiopathic versus secondary membranous glomerular nephropathy [7].

Beck Jr LH *et al.* identified PLA2R as a major target antigen for idiopathic membranous glomerulopathy [5].

Tacrolimus is a macrolide calcineurin inhibitor, produced by *Streptomyces tsukubaensis*, which suppresses T-cell activation.

Nikolaidis *et al.* treated seven cases of severe plaque psoriasis with 0.3 mg/Kg/day of Tacrolimus for 4 weeks and noted complete remission of lesions [8].

Arora *et al.* employed systemic steroids together with oral Tacrolimus to treat moderately severe psoriasis (PASI score 10 to 18), with clinically significant improvement in dermatological lesions and a partial response of renal disease [7].

Mittal *et al.* conducted an open pilot label study on 30 adult patients with severe and recalcitrant psoriasis and found that 0.1 mg/Kg/day in divided doses of

Tacrolimus was more effective and safer for treating severe plaque psoriasis. Diarrhea and abdominal pain were the most common side effects reported by patients during the 12-week study period. The majority of the side effects observed during the study period were self-limiting and easily controllable [9].

The present patient had severe psoriasis, evidenced by PASI 42.8. We deferred managing the patient with systemic steroids since it would predispose him to develop more severe forms of psoriasis, such as pustular and erythrodermic variants, once the therapy was discontinued. As a result, we administered oral Tacrolimus 2 mg twice daily along with emollients for the skin lesions. The studied patient did not experience any inadvertent side effects while on Tacrolimus. The PASI was reduced to 3.7 during the second month of follow-up, and creatinine levels remained normal during subsequent monthly follow-ups of the patient. However, renal disease responded only partially, which was evidenced by a reduction in urinary red blood cell count (1-2/high power field) with persistent proteinuria (3+) at the 6-month follow-up.

CONCLUSION

Psoriasis is a chronic, multisystemic, inflammatory disease, that can be associated with renal disease. Diligent screening and investigation of renal disease by routine urine analysis for proteinuria is necessary for patients with chronic plaque psoriasis. Dermatologists may use positive anti-PLA2R antibody positivity to predict the clinical course, response to treatment, and relapse rate in direct proportion to their titers, not only for membranous glomerular nephropathy but also for the associated psoriasis [7].

This reported case highlighted the efficacy, safety, and steroid-free usage of oral Tacrolimus therapy in managing patients with severe chronic plaque psoriasis and PLA2R-positive membrane nephropathy.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient gave his permission for his photos and other clinical information to be published in the journal. The patient acknowledged that his name and initials will not be published, and due efforts will be made to hide his identity; however, anonymity cannot be guaranteed.

Authors contributions

All authors contributed equally to this study. Dr Ananya B Reddy wrote the paper. Dr Malcolm Pinto was mentor/ guide. Dr Santhosh Pai is the nephrologist who managed the renal comorbidity. Dr Manjunath M Shenoy and Dr Spandana P Hegde revised the manuscript and supervised it. All authors read and approved the final manuscript.

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