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CASE REPORT

Psoriatic Nephropathy—Does an Entity Exist?

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Psoriasis is an immune-mediated chronic inflammatory disorder of the skin. Association with kidney disease has been debated for a long time. Secondary renal amyloidosis in psoriatic arthropathy and drug-induced renal lesions secondary to methotrexate or cyclosporine are accepted accompaniments of psoriasis. IgA nephropathy is also known to occur in psoriatics. We report three interesting cases of renal involvement in long-standing established psoriasis on topical therapy alone. The patients presented with hypertension, significant proteinuria, hypoalbuminemia, and dyslipidemia. Kidney biopsies revealed ''mesangioproliferative glomerulonephritis with IgA nephropathy,'' ''focal proliferative glomerulonephritis,'' and ''membranous glomerulonephropathy.'' The former two had marked active urinary sediment. Patients improved on prednisolone and angiotensin-converting enzyme inhibitors. Contrary to the belief that renal involvement in psoriasis is coincidental, we propose that kidney disease may be a common accompaniment of psoriasis, which may be labeled as ''psoriatic nephropathy'' or ''psoriatic kidney disease.'' The exact mechanism of this entity is yet to be elucidated.

Keywords psoriasis, nephropathy, IgA nephropathy, amyloidosis, hypertension, glomerulonephritis

INTRODUCTION

Psoriasis is a common chronic inflammatory disorder of the skin; however, it is a fascinating entity, besides being a therapeutic challenge for the dermatologist and the general physician alike. Apart from the skin, affliction of the joints in psoriasis is well established, but kidney involvement secondary to psoriasis is not yet universally agreed upon. We report here three cases of psoriasis vulgaris in patients who had associated renal involvement.

REPORT OF CASES

Case 1

A 23-year-old male diagnosed as a case of psoriasis vulgaris at the age of 12 years on intermittent topical steroids was detected to be hypertensive on routine follow-up. He was of average build, conscious and oriented, pulse was 90/min, regular, no radio femoral

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delay, blood pressure was 160/110 mm Hg, pitting pedal edema was present, and there were well-demarcated erythematous plaques with silvery scales on elbow, knees, and lower back. The rest of the general physical and systemic examination was noncontributory. Investigations revealed proteinuria with glomerular hematuria and mild to moderate active urinary sediment; hemoglobin (Hb) 12 g/dL, total leukocyte count of $9.8 \times 10^3/mm^3$ with polymorphs 80%, lymphocytes 20%; ESR 45 mm at the end of the first hour and normocytic normochromic blood picture. Blood sugar, liver function tests, and arterial blood gas analyses were normal. The salient investigations are indicated in Table 1. Urine volume over 24 hours was 1.13 L. Chest radiograph was normal, but echocardiography revealed concentric left ventricular hypertrophy. Abdominal sonography revealed normal-sized kidneys with increased cortical echogenicity with maintained cortico-medullary differentiation; suprarenal glands were normal. Doppler study of renal vasculature was normal. Kidney biopsy (Figures 1 and 2) showed features of ''mesangioproliferative glomerulonephritis associated with IgA nephropathy'' (total of eight glomeruli: two had global sclerosis, one had fibrous crescents, the rest showed mild increase in mesangial infiltration; patchy tubular atrophy, interstitial fibrosis, and chronic inflammation were evident; blood vessels were unremarkable; immunofluorescence showed mesangial deposits of IgA, IgM, and C3, and was negative for IgG).

The patient was started on prednisolone 1.5 mg/kg/day and ramipril 5 mg daily. Hypertension was controlled and proteinuria improved; however, patient was lost to follow-up after 2 months. He has resurfaced after 6 months of omitting treatment. He has a daily urine output of 2.5 L, 24 h proteinuria of 4.8 g, and normal blood urea and serum creatinine values. He has been restarted on prednisolone and ramipril in an attempt to induce a remission.

Case 2

A 65-year-old normotensive male presented with anasarca for 2 months, nausea, vomiting, oliguria for 1 month, and altered behavior of 2 days duration. Examination revealed conscious but drowsy elderly male with obvious flaps, facial and pedal swelling with ascites, and bibasilar crept. Note was also made of plaques over the scalp, forehead, extensor aspects of the hands, arms, elbows, and knees. Urinalysis revealed marked

Table 1
Blood and urine biochemistry and salient clinical characteristics of the cases

Characteristics	Case 1	Case 2	Case 3
Age	23 years	65 years	66 years
Duration of psoriasis	11 years	15 years	30 years
Significant anemia	Absent	Absent	Absent
Proteinuria (by dipstick)	3+	4+	4+
RBCs/HPF in urine	10–12	10–12	1–2
Dysmorphic RBCs	60%	40%	Nil
WBCs/HPF in urine	1–2	2–3	0–1
Casts in urine	RBC, hyaline, granular, cylindroid, and mixed casts	RBC and granular casts	Cylindroid casts
24 h proteinuria	3.4 g	3.9 g	4.2 g
Blood urea	58	120	28
Serum creatinine	185 μmol/L	352 μmol/L	70 μmol/L
Serum sodium	135 meq/L	136 meq/L	138 meq/L
Serum potassium	4.5 meq/L	6.0 meq/L	4.2 meq/L
CRP >6 ng/mL	Positive	Positive	Negative
ESR at end of first hour	45 mm	100 mm	98 mm
Total cholesterol	5.8 mmol/L	6 mmol/L	9.9 mmol/L
LDL-cholesterol	3.5 mmol/L	3.8 mmol/L	7.8 mmol/L
HDL-cholesterol	1.2 mmol/L	1.1 mmol/L	1 mmol/L
Serum triglycerides	1.8 mmol/L	2 mmol/L	2.4 mmol/L
Serum total proteins	45 g/L	45 g/L	48 g/L
Serum albumin	22 g/L	20 g/L	15 g/L

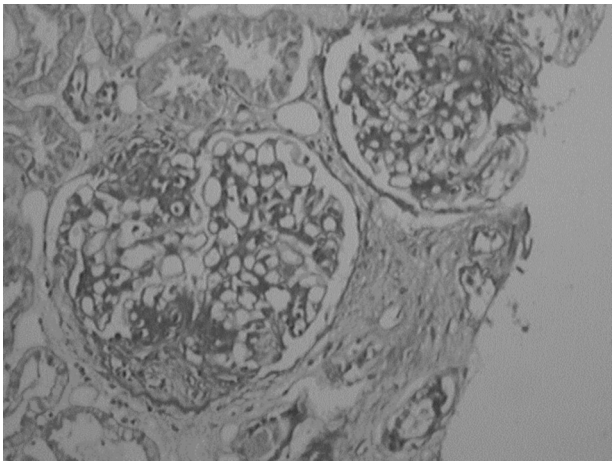

Figure 1. Kidney biopsy showing mesangioproliferative glomerulonephritis with mild increase in mesangial infiltration and patchy tubular atrophy. (Hematoxylin and Eosin, $\times 40$).

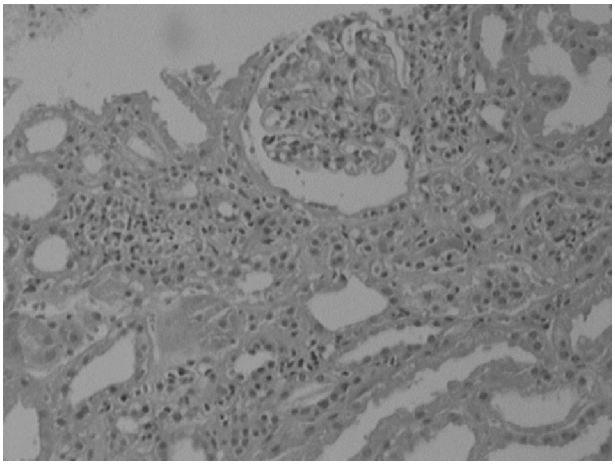

Figure 3. Glomerulus in the field shows focal mesangial proliferation with neutrophil infiltration and fibrin deposition. (Hematoxylin and Eosin, $\times 40$).

proteinuria with active urinary sediment and glomerular hematuria (Table 1). Abdominal sonography revealed ascites with normal-sized kidneys, increased echogenicity, and attenuated corticomedullary differentiation, with cortical thickness of 14–16 mm. Abdominal sonography done 2 months earlier was normal. Kidney biopsy (Figure 3) revealed ''focal proliferative glomerulonephritis'' (four glomeruli: two showed global sclerosis, one showed focal mesangial proliferation with neutrophil infiltration and fibrin deposition; no basement membrane thickening was evident; blood vessels showed moderate medial thickening; immunofluorescence showed focal mesangial deposits of C3, and was negative for IgA, IgG, and IgM).

The patient had to be intensively dialyzed in view of fluid overload and early uremic encephalopathy. His blood urea and serum creatinine stabilized at 90 mg/dL and 2 mg/dL, respectively, and hyperkalemia required potassium-binding resins.

Case 3

A 66-year-old psoriatic male was diagnosed hypertensive 10 years back when he developed anasarca. Investigations at that time (Table 1) suggested nephrotic

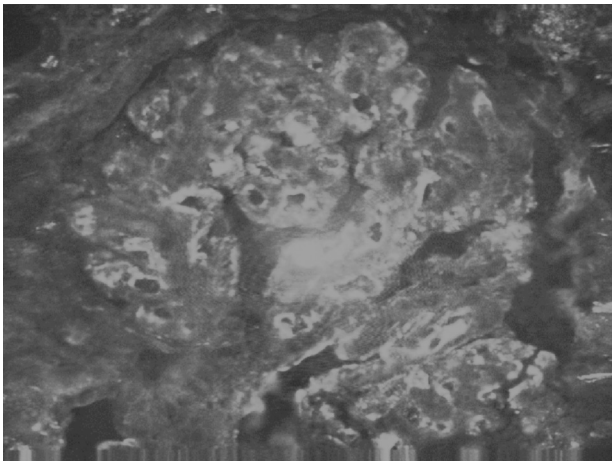

Figure 2. Immunofluorescent staining of kidney biopsy tissue showing mesangial deposits of IgA.

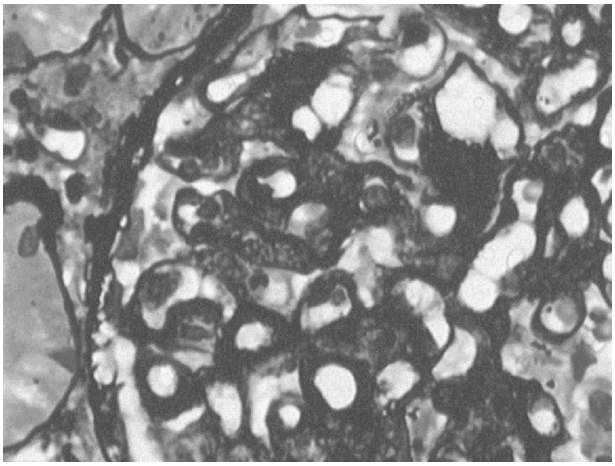

Figure 4. Membranous nephropathy showing thickened capillary walls, and numerous subepithelial ''spikes'' are present on the capillaries of the focused glomerulus. (Jones' silver stain, $\times 40$).

syndrome with normal kidneys on sonography. Patient had refused a kidney biopsy at that time and was empirically started on prednisolone 1.5 mg/kg/day and enalapril 10 mg daily. Albuminuria had decreased to 1.3 g/24 h at 3 months, and prednisolone was tapered to 10 mg daily; but unfortunately, patient was lost to follow-up and presented again a year back with anasarca and biochemical evidence of nephrotic syndrome, with a serum creatinine of 200 μmol/L. Patient was convinced to undergo kidney biopsy, which suggested ''membranous glomerulonephropathy'' with global and segmental sclerosis with coarse granular deposits of IgG, C3, and focal mesangial deposits of IgM (Figure 4). Patient was restarted on prednisolone and enalapril. His serum creatinine improved to 150 μmol/L, and albuminuria decreased.

Summary of Cases

In all three cases, antinuclear antibodies (ANA), rheumatoid factor, antistreptolysin O (ASO) antibodies, hepatitis B surface antigen, antibodies to hepatitis C virus and HIV-1 and -2, VDRL, and p-ANCA and c-ANCA were negative. Serum TSH and complement levels were normal. These patients did not have diabetes or clinical evidence of arthritis and did not have any other addiction, including smoking. No significant family history was evident. Skin biopsies done for all were consistent with the diagnosis of psoriasis.

DISCUSSION

Psoriasis is an immunomediated disease primarily affecting the skin and, at times, the joints. Renal involvement in psoriasis has been reported sporadically in the literature and has aroused keen interest. Definite well-planned studies have been conducted to identify the pathogenesis of kidney disease in psoriasis and to unravel any obvious predilection for renal involvement in psoriatic patients. Until recently, most reviews and papers had concluded that there is no higher prevalence of renal disease in psoriasis except for secondary renal amyloidosis in psoriatic arthropathy.[1,2] Only 20 cases of secondary amyloidosis complicating psoriasis have been reported in the literature.[1] However, there may be unknown mechanisms predisposing to a greater risk for renal disturbances.[1] In corroboration are reports of kidney biopsies that failed to demonstrate microvascular disturbances.[3–5] Evidence of systemic vascular involvement on histopathology is scarce in psoriatics as against the universal vascular involvement seen in psoriatic skin lesions.[2] To date, specific histological lesions associated with psoriasis have not been described.

Recent reviews[6,7] concluded that the only well-documented abnormality in renal tests in patients with psoriasis vulgaris is presence of microalbuminuria in some of them—42% in patients with most severe skin disease to 22% in all psoriatics, irrespective of severity of psoriasis. Average urinary albumin excretion in normotensive nondiabetic psoriatic patients is elevated, and it is hypothesized that subclinical glomerular dysfunction exists in some psoriatic patients who were never treated with systemic potentially nephrotoxic drugs.[6,7] In another study,[2] 24 h urinary β_2-microglobulin levels were reported to be higher in psoriatics, although the elevated values were still in the normal range. Another study[8] reported elevated urinary β_2-microglobulin levels in only two patients out of 42 studied. β_2-Microglobulinuria is regarded as a marker of renal tubular dysfunction, and both studies[2,8] concluded that tubular dysfunction is not altered in psoriasis vulgaris.

The other established renal disturbances in psoriatics are drug-induced, secondary to systemic therapy for psoriasis viz. with methotrexate, cyclosporine, and fumaric acid esters.[4,5]

IgA nephropathy exists in psoriasis;[7,9] about 10 such cases have been reported.[10] High serum IgA and circulating immune complexes containing IgA can be present,[7,11] and this could reflect general hyperfunction of the immune response as in other autoimmune diseases or may reflect an antibody response to a hypothetical infectious agent. In fact, 50% of psoriatics were reported to have elevated IgA levels.[12] Besides, a genetic predisposition to development of IgA nephropathy may also exist, HLA B-27 present in 25% of psoriatics may predispose to a structural defect in IgA leading to its deposition in mesangium.[10] One of our cases had IgA nephropathy. IgA nephropathy appears to be a distinct pattern in psoriatics with renal involvement. However, it cannot be considered as a hallmark lesion of ''psoriatic nephropathy,'' because secondary IgA nephropathy has been associated with celiac sprue; seronegative spondyloarthropathies; postinfectious arthritis; ulcerative colitis; regional enteritis; dermatitis herpetiformis; malignancies; mixed cryoglobulinemia; infections including tuberculosis, leprosy, and those caused by HIV, herpes simplex viruses 1 and 2; Epstein-Barr virus; cytomegalovirus; and idiopathic pulmonary hemosiderosis.

It is also interesting to note that psoriatics have higher prevalence of essential hypertension, cardiovascular disease, diabetes, and dyslipidemia.[11,13] Besides, they have a higher incidence of occlusive vascular disease.[14] High plasma endothelin-1 and plasma rennin activity are

believed to be the cause of hypertension and atherosclerosis in psoriasis.[15,16] Therefore, renovascular hypertension and nephroangiosclerosis should consequently be more prevalent in psoriatics, but no such report exists.[1]

The presentation of these three cases over a short span of 1 year prompted us to review renal involvement in psoriasis. None of the present cases had any chronic ailment except for long-standing psoriasis vulgaris and had not received cyclosporine/methotrexate or any other nephrotoxic medication. All had normal serum complement, ASO titers and were negative for HBV, HCV, HIV, and ANA. A secondary cause of nephropathy was thus not discernible, but psoriasis was common to all. Although the varied kidney biopsy presentations in these cases do not suggest a unified etiopathogenetic mechanism, they certainly point to the existence of mechanisms, still yet obscure, that predispose patients with psoriasis to renal disease. In fact, IgA nephropathy appears to be one of the distinct morphological patterns on kidney biopsy in psoriatics with overt renal involvement. Other morphological patterns in distinct subgroups of psoriatics include secondary amyloidosis in association with psoriatic arthropathy, and drug-induced renal lesions in patients on nephrotoxic medications. It is premature for us to push forward the existence of ''psoriatic nephropathy'' or ''psoriatic kidney disease'' solely on the basis of this article and the review therein, but we are more than justified in nurturing the thought that this entity is in conception, nearing the horizon, and the sunrise may not be far away. This paper would certainly prompt a more diligent screening and investigation of kidney disease in psoriasis by not only dermatologists and general practitioners but also nephrologists.

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