

# Immunoglobulin A Nephropathy and Prurigo Nodularis Predating the Diagnosis of Hodgkin Lymphoma: A Case Report

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**Keywords** Immunoglobulin A  
(IgA) nephropathy; Proteinuria;  
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Lymphoma

## Abstract

**Background:** The association between Hodgkin lymphoma and IgA nephropathy is rarely reported.

**Case presentation:** A 20-year-old Saudi female patient presented with picture of immunoglobulin A nephropathy and prurigo nodularis. The patient was treated with oral steroid for 6 months; however, by the end of the course, she developed fever, night sweet, and weight loss. Work up was positive for Hodgkin lymphoma involving mediastinal lymph nodes, which was treated with chemotherapy and radiation. Both prurigo nodularis and IgA nephropathy are in complete remission 4 years after cure of lymphoma.

**Conclusion:** The temporality in presentation and sustained renal remission following lymphoma treatment, may suggest a causal association. Therefore, considering underlying lymphoma in patients with IgA nephropathy may be suggested.

**Keywords:** Immunoglobulin A (IgA) nephropathy; Proteinuria; Prurigonodularis; Hodgkin lymphoma; Lymphoma

**Core tip:** The association of IgA nephropathy with Hodgkin's lymphoma is very rare. In this case report, the temporality and persistent complete remission of proteinuria after lymphoma cure suggest a causal link.

## Introduction

Immunoglobulin A (IgA) nephropathy is a glomerular disease, first described by Berger and Hinglais in 1968 [1]. It is the most common cause of primary glomerulonephritis throughout most developed countries [2-4]. It is highly variable in its clinical and pathological presentation. Clinical features range from asymptomatic urine abnormalities to Rapidly Progressive Glomerulonephritis (RPGN). Pathologically, a number of glomerular lesions may be observed, but mesangial proliferation with prominent IgA deposition is seen in almost all biopsies. Although IgA nephropathy follows somehow benign course in most patients, long-term follow-up data demonstrated progression to End-Stage Renal Disease (ESRD) in some cases [3]. Therefore proper recognition and consideration of treatment are crucial.

Hodgkin's Lymphoma (HL) was first described by Thomas Hodgkin in 1832. Among the nodal lymphomas, HL is characterized by its onset in young age, and the presence of CD30+/CD15+ Reed-Sternberg cells [4]. The association of HL with glomerular disorders is mostly reported with minimal change disease. Its association with IgA nephropathy is rare. In fact, the rare cases of IgA nephropathy associated with lymphoma are described more with non-Hodgkin lymphoma and skin T cell lymphoma rather than HL [2,5]. Only a few cases of IgA nephropathy-HL association are reported in children and adults with variable manifestations ranging from mild proteinuria to RPGN [6-8]. The presence of prurigo nodularis as skin lesions commonly affecting the extensor surfaces of lower extremities, in patients with Hodgkin lymphoma is considered a non-specific finding, and has been reported variably.

Although IgA nephropathy had been reported in association with several skin lesions; up to our knowledge, this is the first case reporting the presence of IgA nephropathy with prurigo nodularis, predating the diagnosis of Hodgkin lymphoma.

## Case Presentation

### Patient information and clinical findings

A 20-year-old female who was well until 7 months prior to her presentation, developed sudden frank haematuria, skin rash in both lower limbs. She was empirically started on oral prednisolone

60 mg daily in a peripheral hospital and she felt improvement. Five months later she developed generalized fatigue, weakness and symptoms of upper respiratory tract infection with mild bloody discharge from the right ear and persistent haematuria. She denied receiving any medications prior to the onset of her symptoms. Her family history was not contributory for any skin or kidney disorders. She is single, college student and non-smoker.

On Examination; she looks pale and weak. Blood pressure was 146/88 mmHg. HEENT examination revealed congested right ear with bloody discharge, and normal left ear, with a mildly congested throat. The chest is clear. She has mild tenderness over both flanks on abdominal examination. Lower limb examination revealed bilateral macular rash with keratotic papules and some excoriated lesions on the extensor surfaces of the ankles and legs. No peripheral edema.

**Diagnostic assessment**

Laboratory investigations upon presentation are given in Table 1. A Kidney Biopsy was performed and revealed global proliferative changes with prominent capillary loop thickening involving 18 out of 25 glomeruli, and an active crescent in one glomerulus. On immunofluorescence, there were mesangial deposits of IgA and C3, with no deposition of IgG, IgM, and C1q. Electron microscopy demonstrated mesangial deposits. No global glomerular sclerosis and no significant interstitial fibrosis or tubular atrophy. Findings were consistent with IgA nephropathy (Figure 1). Biopsy findings from the skin lesions were consistent with Prurigo Nodularis.

**Therapeutic interventions, follow-up, and outcomes**

Upon her admission to the hospital, she was prescribed Fluticasone ointment for the skin lesions and was diagnosed to have otitis media which was treated with Ofloxacin. Lisinopril was started, and after the results of kidney biopsy, prednisolone 60 mg daily along with mycophenolate mofetil 500 mg every 12 hours (with a plan of dose escalation) was initiated.

5 months later, she had a dramatic improvement, no ear symptoms, her skin lesions were better, serum creatinine went down to 48 umol/L, the 24 hours urine protein was 282 mg and the random glucose was 5.8 mmol/L. The patient stopped Lisinopril on her own. Prednisolone was tapered off by completing 6 months course.

2 months later, she presented to the clinic for follow-up, and she was found to have a fever, night sweating, and weight loss. Her serum creatinine was 54 umol/L. Mycophenolate mofetil was stopped. Workup revealed mediastinal lymphadenopathy and further work up

by oncology including lymph node biopsy confirmed the diagnosis of Hodgkin lymphoma stage IIB. The course of treatment included 6 cycles of ABVD (Adriamycin, bleomycin, vincristine, decarbonize). Her symptoms resolved but with residual mediastinal mass for which she was subjected to 15 sessions of radiation therapy.

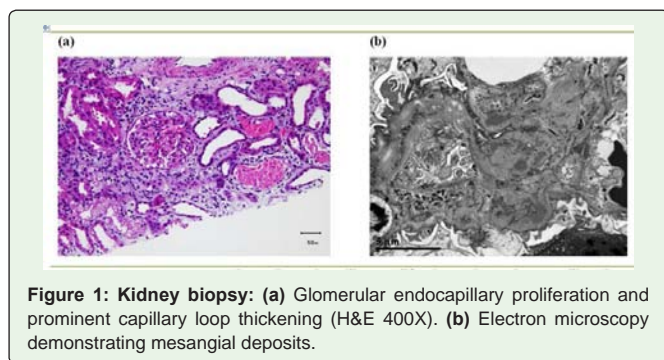
In her most recent visit to nephrology clinic, four years after the diagnosis of IgA nephropathy, she continued to be in complete remission with a serum creatinine of 62 umol/L, normal urine protein: Creatinine ratio, serum albumin of 46 and hemoglobin of 14.8. The skin lesion disappeared. She currently takes no medications and is in complete remission of both lymphoma and IgA nephropathy.

**Discussion**

We describe a young girl diagnosed with HL involving primarily the mediastinal lymph nodes in association with IgA nephropathy and prurigo nodularis. The presentation of IgA nephropathy was of gross hematuria, subnephrotic proteinuria, and mild elevation of serum creatinine. The onset of hematuria, proteinuria and prurigo nodularis was one year before the typical symptoms and diagnosis of HL.

**Table 1:** Laboratory investigation results.

Laboratory variable	Level
Na <sup>+</sup>	138 mmol/L
Cl <sup>-</sup>	102 mmol/L
K <sup>+</sup>	3.9 mmol/L
HCo <sub>3</sub> <sup>-</sup>	22 mmol/L
Glucose	4.3 mmol/L
Urea	6.2 mmol/L
Creatinine	92 umol/L
Serum Albumin	3.5 g/L
Urinary Protein	1725 mg/24 Hours
CRP	116.1
ANA	Negative
Anti-DNA	Negative
C-ANCA	Negative
P-ANCA	Negative
C3 and C4	Normal
WBC	10.5 per mm <sup>3</sup>
Hemoglobin	9.4 g/dl
MCV	82.3 fL
MCH	28.2 pg
PLT	369 per mm <sup>3</sup>
AST	369 U/L
LDH	303 U/L
Ferritin	478 ug/L
Iron	6.1 umol/L
Transferrin	478 ug/L
Direct antibody test	Positive



There are some limitations to the approach in diagnosis and treatment of this case. The patient presented several months to a peripheral hospital where the level of proteinuria and course of treatment including dosages was not available to us. There was a delay in the biopsy. We have treated her after the biopsy with steroid and mycophenolate mofetil. Although this is not the standard first-line treatment, we have considered this course after discussion with the patient and based on the fact that she was showing clinical relapse with hematuria and proteinuria despite a minimum of 6-month course of steroid treatment. In addition mycophenolate mofetil was chosen to act as steroid-sparing agent as she was reluctant to repeat the course of steroid treatment. The diagnosis of HL at the time of her presentation was not sought. A chest X-ray was not requested before treatment for IgA nephropathy as she had no chest symptoms. Another point is the presence of anemia with positive direct antibody test which can be a hint toward other hematological diagnoses. The patient was referred to a hematologist, however as her hemoglobin had responded very well to treatment of IgA nephropathy, no additional active work up or intervention was offered. Hence, she could have had evidence of HL earlier than the time she was diagnosed.

Our case adds to the current literature supporting HL-IgA nephropathy association and presents a unique association of IgA nephropathy with prurigo nodularis predating the typical symptoms and diagnosis of HL. Based on a literature search, the association of IgA nephropathy with HL is rare with only a few cases reported [6-8]. Renal disease may precede, coincide or develop after diagnosis of HL. In our case, all three diagnoses, IgA nephropathy, HL and prurigo nodularis, were based on biopsies. Successful treatment of lymphoma in our patient resulted in resolution of the renal disease with sustained remission for more four years. This provides another possible proof supporting a causal association.

Most cases of IgA nephropathy are clinically limited to the kidneys [3,9-11], but it may be associated with other conditions. Some associations are well established, others are anecdotal observations that should be interpreted with caution since associations may be coincidental rather than causal. Conditions associated with a high frequency of glomerular IgA deposition include cirrhosis, celiac disease, and HIV infection. A less frequent association is described with other diseases including dermatitis herpetiformis, ankylosing spondylitis, small cell lung cancer, lymphoma (particularly non-Hodgkin lymphoma and T-cell lymphomas, including mycosis fungoides), disseminated tuberculosis, bronchiolitis obliterans, and inflammatory bowel disease [9,12,13]. Other skin lesions that were reported in association with IgA nephropathy include Henoch-Schönlein purpura [14], Sjogren's syndrome [15], Lupus vulgaris with tubercular lymphadenitis [16], and acquired reactive perforating collagenosis [17].

The presence of IgA and Complement 3 (C3) in the glomerular mesangium of patients with IgA nephropathy suggests deposition of circulating immune complexes resulting in activation of the complement cascade [11]. Therefore an immune mechanism is considered in the pathogenesis with deposition of immune complexes that include galactose-deficient IgA1 auto-antigens [18]. Therefore, it is possible that systemic or environmental triggers of immunologic abnormalities may induce IgA nephropathy.

The development of glomerular proteinuria in patients with HL, suggests a possible role for immunological abnormalities in the pathogenesis. It is well known that autoimmune disorders have been linked to lymphomas [19]. In the past, it is suggested that nephropathy in HL may be related to abnormalities of T-lymphocyte and Natural killer cells [20,21]. Therefore, supporting a biological plausibility underlying a causal pathway.

Lastly, prurigo nodularis is characterized by a presence of pruritic nodules on the extensor surfaces of the lower extremities, first described in middle-aged women in 1909 [22]. Since that time cases affecting children and men have also been reported [23]. Its etiology remains unknown; however, a variety of systemic conditions have been described to be associated with prurigo nodularis including HL [24,25]. No previous cases reporting an association between IgA nephropathy and prurigonodularis. In our patient, the presence of prurigo nodularis may be linked to HL rather than IgA nephropathy. However, the presence of prurigo nodularis may represent an additional alarming indication to work up patients with IgA nephropathy for underlying HL.

## Conclusion

Although the association between HL and IgA nephropathy is rare, the temporal presentation, as well as treatment response with sustained remission of IgA nephropathy after successful treatment of lymphoma in our case, provides possible support for a causal association. Until more reports are described, a possible association between IgA nephropathy and HL should be kept in mind. The presence of prurigo nodularis along with IgA nephropathy should provide additional hint supporting a search for underlying HL.

## Informed Consent Statement

This article is a Case Report and does not require approval from Institutional Review Board, however, data are presented anonymously and informed consent to publish the case report including the clinical data is obtained with a signature from the patient.

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