

A Case of Immunoglobulin A Nephropathy in a Patient with Kimura's Disease

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Kimura's disease is an angiolymphoid-proliferative disorder that manifests with benign subcutaneous swelling predominantly in the head and the neck. Kidney involvement, including proteinuria, occurs in 12-16% of patients with the disease, and 60-78% of such cases is nephrotic syndrome. Reported etiologies of nephrotic syndrome in Kimura's disease include membranous glomerulonephritis, mesangial proliferative glomerulonephritis, minimal-change disease, focal segmental glomerulosclerosis, diffuse proliferative glomerulonephritis and immunoglobulin A (IgA) nephropathy. There have been only two case reports of IgA nephropathy in Kimura's disease, in 1998. In this report, we present a third case of IgA nephropathy associated with Kimura's disease.

Key Words: Glomerulonephritis, Immunoglobulin A, Angiolymphoid hyperplasia with eosinophilia, Proteinuria

INTRODUCTION

Kimura's disease is a rare granulomatous disease of the dermis, subcutaneous tissue, and lymph nodes.¹ It presents as benign subcutaneous swelling, predominantly involving the head and neck. Microscopically, the subcutaneous swelling is characterized by newly developed lymphoid follicles, increased vascularity, and marked eosinophilic infiltration.² Additional characteristics include marked peripheral eosinophilia and elevated immunoglobulin E (IgE) levels.³ Kidney involvement occurs in 12-16% of patients with Kimura's disease, and 60-78% of kidney involvement is in the form of nephrotic syndrome.^{4,5} Although various types of glomerulonephritis,

such as membranous glomerulonephritis, mesangial proliferative glomerulonephritis, minimal-change disease, focal segmental glomerulosclerosis, and diffuse proliferative glomerulonephritis, have been reported to be associated with Kimura's disease,⁶ only 2 cases of Immunoglobulin A (IgA) nephropathy have been reported in Kimura's disease to date; thus, the association between these 2 diseases remains unclear.^{7,8} We report a third case of IgA nephropathy associated with Kimura's disease to provide further evidence of an association.

CASE

A 17-year-old, previously healthy Korean male noted 2 nodular, subcutaneous, painless masses, 1 in the region of his elbow and 1 in his right submandibular area. Peripheral eosinophilia or proteinuria was not observed. Excision of both masses was performed in July of 2003. Histopathology of the masses was consistent with Kimura's disease (Fig. 1). After surgical excision, the patient visited our clinic for recurrence of the right submandibular mass in March of 2005.

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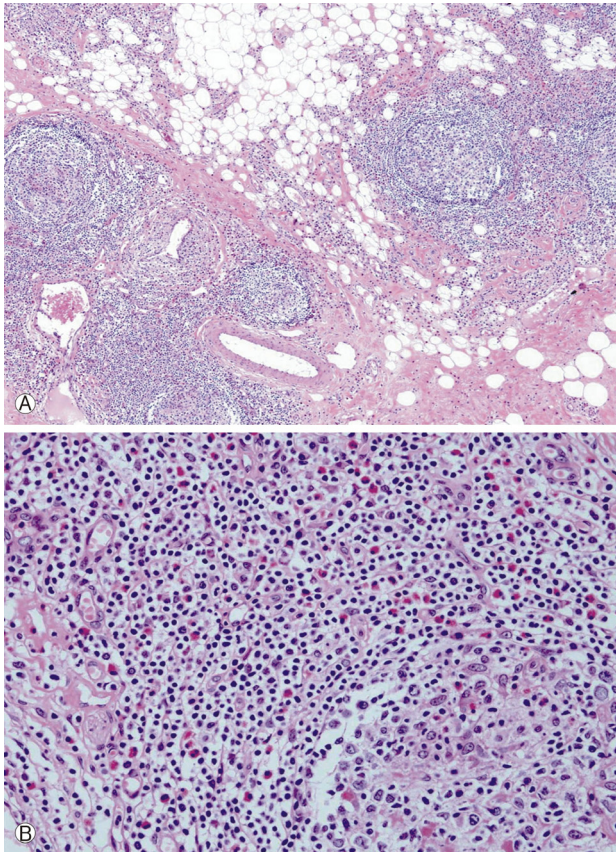


Fig. 1. Histopathology of the right submandibular mass. (A) Reactive lymphoid follicles with germinal centers are present (H&E stain, $\times 40$). (B) Eosinophils and lymphoid cells are infiltrated (H&E stain, $\times 200$).

Computed tomography (CT) scan showed residual localized subcutaneous infiltration in the right submandibular area and bilateral reactive neck lymphadenopathy. The patient refused to undergo biopsy, treatment with oral steroids, or secondary surgery. Nine years later, the patient returned to our clinic after proteinuria had been found during a routine health check at the local clinic in February of 2012. A complete blood count revealed a hemoglobin level of 18.4 g/dL, white blood cell count of 10,010/mL (neutrophil 69.2%, lymphocyte 23.5%, eosinophil 0.4%), and a platelet count of 221,000/mL. Serum creatinine and albumin were within normal limits (0.9 mg/dL and 4.0 g/dL, respectively). Urinalysis showed 3+ protein, and random urine protein/creatinine ratio was 1.97 g/g. Renal biopsy revealed mild inflammation and fibrosis. Immunohistochemistry and special stains were positive for IgA and C3 in the glomerulus. Final diagnosis suggested IgA nephropathy, subclass III (Fig. 2).

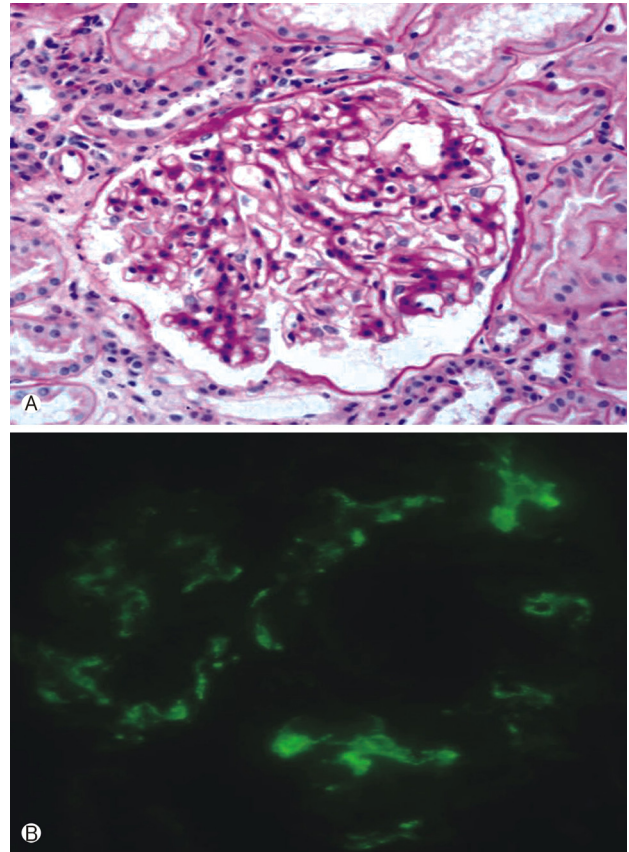


Fig. 2. Histopathology of the kidney biopsy. (A) There are mild mesangial matrix expansion and mild increase in cellularity without crescent or sclerosis (PAS stain, $\times 400$). (B) It shows dominant IgA staining in the mesangium by immunofluorescence.

Because the patient did not present with any mass-related symptoms and had a subnephrotic range of proteinuria, an aldosterone-receptor blocker (losartan 50 mg daily) was started in February of 2012. Currently, the level of proteinuria (random urine protein/creatinine ratio: 1.30 g/g) and serum creatinine (0.78 mg/dL) is being maintained without worsening with maintenance taking losartan 50 mg daily in May 2013.

DISCUSSION

Kimura's disease was first described by Kim and Szeto in 1937,⁹ followed by Kimura et al. in 1938.¹ Asian men are more susceptible to the disease than are men of other races.⁹ A benign painless swelling of the head and neck, with peripheral eosinophilia and an elevated serum IgE level, should raise the suspicion of Kimura's disease. Lymph node biopsy can confirm the diagnosis. In Kimura's disease, histopathology

shows deep involvement in tissues, well-formed germinal centers, marked eosinophilic infiltration, fibrosis around lymphoid follicles, and proliferation of blood vessels. Immunohistologic characteristics include lymphoid follicles (T cells surrounding B-cell germinal centers), many eosinophils with intact and degranulated granule proteins, mast cells with intact granule proteins (no degranulation), and neutrophils with intact granule proteins (no degranulation).² The differential diagnosis of Kimura's disease should include angiolymphoid hyperplasia with eosinophilia (AHLE). AHLE has no preference for gender or race, and lesions are smaller and more superficial compared to those in Kimura's disease.

Approximately 12-18% of patients with Kimura's disease have renal involvement, and 60-78% of them present with nephrotic syndrome.^{4,5} Renal biopsies from these patients show various forms of renal pathology, including membranous glomerulonephritis, mesangial proliferative glomerulonephritis, minimal-change disease, focal segmental glomerulosclerosis, and diffuse proliferative glomerulonephritis.

In Kimura's disease, there is no gold standard for treatment; surgery and corticosteroids are the most widely used treatments, followed by corticosteroids alone. Due to intermittent dependency on corticosteroid, immunoglobulin therapy was tried for the treatment of Kimura's disease as a steroid-sparing therapy.³ Recently, a study showed the efficacy of tacrolimus on Kimura's disease.¹⁰

The 2 previously reported patients with IgA nephropathy were treated with corticosteroids and showed significant decrease in proteinuria.^{7,8} However, in the Vietnamese patient, a full-blown nephrotic syndrome rapidly recurred after steroids were tapered.⁷ The proteinuria responded to increased dose of steroid. Our patient showed no eosinophilia and proteinuria at the time of the submandibular mass excision and relapse in 2005. Therefore, he was not treated with steroids or surgery. The proteinuria was found on Feb 2012, and the renal biopsy at that time revealed IgA nephropathy. Since then, the patient has shown no symptoms and has had minimal proteinuria; an aldosterone-receptor blocker (losartan 50 mg daily) was prescribed to minimize the proteinuria. Currently, proteinuria is being maintained without worsening.

Actually, IgA nephropathy is common glomerulonephritic disease in Korea. So, it is not surprising that IgA nephropathy

is combined with any disease. But there's rare case with IgA nephropathy in Kimura's disease. And it is not clear why the IgA nephropathy is combined with the Kimura's disease and what the pathologic reason is. So, we thought reporting this case is useful to urge to further study.

IgA nephropathy is a possible etiology for proteinuria in Kimura's disease. Considering the wide variety of nephropathies in Kimura's disease, management of the nephropathy should be carefully determined by its clinical and pathologic manifestations. Although it is safe to use steroids to control proteinuria in Kimura's disease, it may be possible to control milder cases with more conservative treatment strategies.

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