CASE REPORT
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A Case of Insidious Onset of Kimura Disease-associated Immunoglobulin A Nephropathy without Eosinophil Infiltration in the Renal Tissue

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ABSTRACT

Kimura disease (KD), also known as eosinophilic lymphogranuloma, is a rare chronic inflammatory or allergic disease. It can present with immune-related diseases such as nephrotic syndrome, asthma, and ankylosing spondylitis. In this study, we report a case of KD combined with immunoglobulin A nephropathy that first presented as a mass in the inguinal region, followed by recurrent renal involvement. Previous reports suggested that renal involvement caused by KD was due to direct infiltration of eosinophils; however, in this case, no eosinophil infiltration was found in the renal tissue after renal biopsy. This observation reminds us to approach the case from an immune-related molecular perspective to investigate the exact cause of renal damage due to KD.

Keywords: Immunoglobulin A nephropathy; Infiltration of eosinophils; Kimura disease; Renal involvement

INTRODUCTION

Kimura disease (KD), also known as eosinophilic lymphogranuloma, is a rare chronic inflammatory or allergic disease that was first described by Kimm and Szeto in 1937.[1] The Japanese scholar Kimura studied the disease in more detail in 1948,[2] and it became known as Kimura's disease.[1] KD is prevalent in Asians, with a male-to-female ratio of 4:1.[3] Its slow progression is accompanied by elevated peripheral blood eosinophil counts and serum immunoglobulin (Ig) E levels. Simple KD without other organ damage often presents as painless subcutaneous masses on the head and neck but may also appear in the axillae, inguinal region, abdomen, chest wall, and peripheral limbs, but it is very rare.[4] In this case, because of the insidious onset and atypical location of the mass, no eosinophil infiltration was found in the renal tissue after renal biopsy, which caused great difficulties for the clinician in the diagnosis and choice of subsequent treatment modalities. Here, we

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report a case of KD combined with immunoglobulinA nephropathy.

In June 2019, the patient presented to the Department of Nephrology of the Fourth People's Hospital of Zigong for an examination that revealed microscopic hematuria, and he was diagnosed with hematuria and proteinuria.

The patient visited the Department of Nephrology at the Affiliated Hospital of Southwest Medical University in October 2019 with worsening proteinuria and hematuria. He was previously in excellent health, with no diabetes, hypertension, or hepatitis history. Laboratory evaluations indicated albuminuria +++ (normal range, negative), and albuminuria at 24 h was 3.5 g. The erythrocyte count in urine was 22/HP (normal range: 0–2/HP). Urine phase-contrast microscopy showed predominantly aberrant red blood cells, indicating glomerular hematuria.

Renal function revealed a serum creatinine concentration of 156 μmol/L (normal range: 52–101 μmol/L) and a urea concentration of 3.68 mmol/L (normal range: 2.7–7.0 mmol/L). The results were negative for antineutrophil cytoplasmic antibody, anti-streptolysin O, and antinuclear antibody. After obtaining informed consent from the patient, a renal biopsy was performed. Pathological results showed that glomerular stromal and mesangial cells were diffusely proliferating, and a small number of erythrophilic protein deposits were observed in the mesangial region. Granular and vacuolar degenerations were observed in the renal tubular epithelium. Protein casts could be seen in some cystic, dilated renal tubules. No eosinophil infiltration was observed in the renal interstitium. These findings were consistent with those of mesangial hyperplastic IgA nephropathy (Figure 1). The patient received methylprednisolone(Shandong Lukang pharmaceutical Co, No.88, Deyuan Road, Hi-tech Zone, Jining City, Shangdong Province, China) pulse therapy for 3 days, followed by oral methylprednisolone combined with cyclophosphamide(Tianjin Jinshi Pharmaceutical Co, No.6, Xinghua Jiuzhi Road, Xiqing Economic Development Area, Tianjin, China). He was discharged in remission after 2 weeks and was maintained on methylprednisolone after discharge.

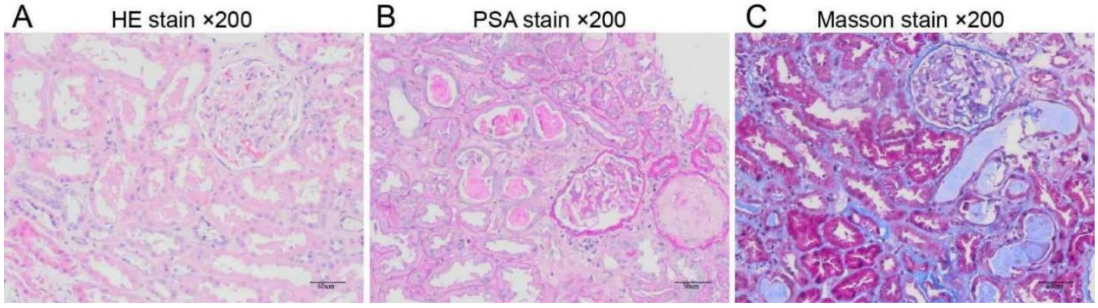

Figure 1. Renal tissue biopsy. (A and B) hematoxylin-eosin (HE) and periodic acid-schiff (PAS) stains showed no eosinophil infiltration in the renal interstitium, and diffuse proliferation of glomerular stroma and mesangial cells. (C) Masson stain showed a small number of immune complexes deposited in the mesangial region.

On 10 January 2021, the patient visited the General Surgery Department of the Affiliated Hospital of Southwestern Medical University with the chief complaint of a mass in the right inguinal region for 3 years and a significantly enlarged mass in the past 2 months. Blood pressure and temperature on admission were 140/86 mmHg and 37.8°C, respectively. Physical examination revealed a painless, mobile soft tissue mass of approximately 21.5 x 16 x 8 cm^3 in size in the right inguinal region, with normal overlying skin. Laboratory tests showed serum creatinine of 122 μmol/L (normal range: 52–101 μmol/L), albuminuria +++ (normal range, negative), and albuminuria at 24 hours of 3.8 g. The erythrocyte count in the urine was 25/HP (normal range: 0–2/HP). The erythrocyte sedimentation rate was 23.00 mm/h (normal range: 0–15 mm/h). A full blood count revealed a normal white blood cell count of 9.94×10^9/L (normal range: 4.1–11 x10^9/L), an increasing eosinophilia count of 4.13x10^9/L (normal range: 0.00–0.68x10^9/L), and an increasing percentage of eosinophils (41.5%; normal range: 0–9%). Serum IgE levels were elevated at 1200.00 IU/mL (normal range: 0–100 IU/mL). Ultrasonography indicated a hypoechoic mass (predominantly fatty echogenicity) with multiple enlarged lymph nodes in the right inguinal region (Figure 2). Computed tomography examination of the inguinal

region showed solid nodules and masses in the right inguinal region, combined with subcutaneous fascial swelling and a small amount of effusion (Figure 2).

In summary, we made a clinical diagnosis of Kimura's disease-associated immunoglobulinA nephropathy by combining body mass, elevated eosinophil counts and IgE levels, and manifestations of renal involvement. On 15 January 2021, we decided to surgically remove the patient's inguinal region mass for biopsy under general anesthesia to clarify the diagnosis. Intraoperatively, a huge mass was seen in the right inguinal region, measuring about 22 x 16 x 8 cm^3, with an unclear boundary between the mass and the surrounding tissues, involving the deep fascia, without invading the muscular layer, and with a rich blood supply (Figure 3). Histopathology indicated hyperplasia of lymphatic follicles in the lymph nodes and abundant eosinophil and lymphocyte infiltration, with localized eosinophilic abscess formation (Figure 3). Therefore, KD was diagnosed by a pathologist. Postoperatively, the patients received oral cyclophosphamide (50 mg/day) and methylprednisolone (40 mg/day). After 4 weeks, the serum creatinine level decreased to normal, and urine protein was negative. We then continued treatment with methylprednisolone and a tapered dose until it was discontinued. Regular follow-up at 18 months after discharge showed no signs of recurrence.

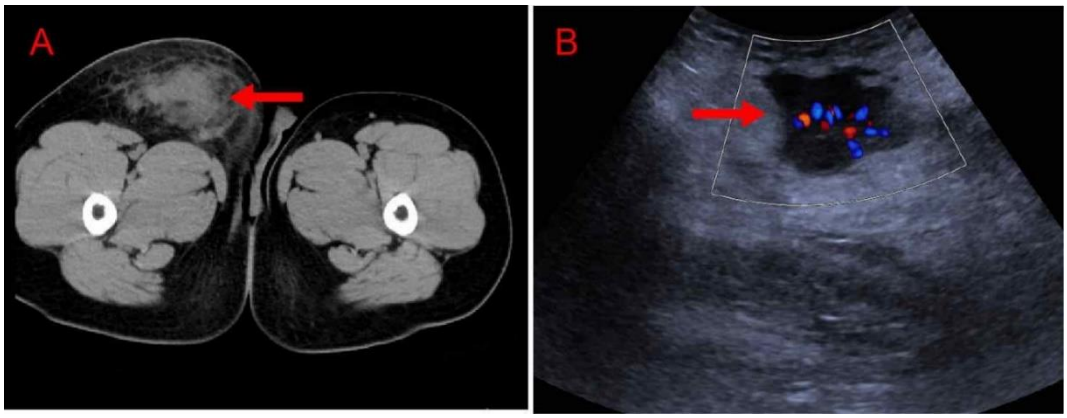

Figure 2. The preoperative computed tomography image (A) and ultrasound image (B) of KD. The inguinal region mass is marked by a red arrow.

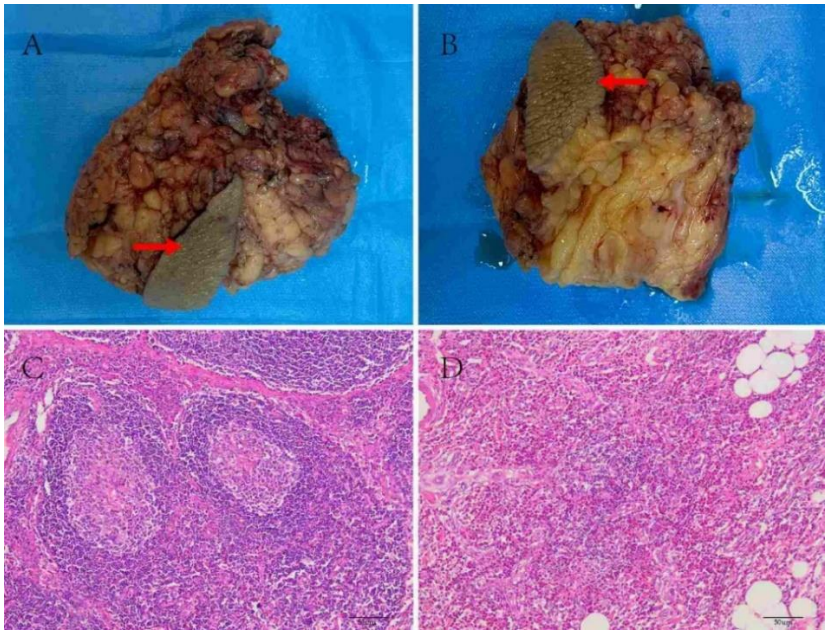

Figure 3. (A and B) Postoperative gross specimens. The excised skin is marked by a red arrow. (C) Hyperplasia of lymphatic follicles in the lymph nodes. (D) Abundant eosinophil and lymphocyte infiltration with localized eosinophilic abscess formation.

DISCUSSION

Currently, scholars usually consider KD as a benign lesion that can be associated with immune-related diseases such as nephrotic syndrome, asthma, and ankylosing spondylitis.[5,6] The incidence of kidney involvement due to KD has been reported to range from 12% to 60%. In comparison, 10% to 12% of patients present with nephrotic syndrome,[7] and kidney biopsies often show minimal change disease, membranous nephropathy, and mesangioproliferative glomerulonephritis. However, cases of KD-associated IgA nephropathy have rarely been reported.

Here, we report a case of insidious onset of KD-associated immunoglobulinA nephropathy without eosinophil infiltration in the renal tissue with good treatment outcomes after surgery, combined with corticosteroids and immunosuppressive agents. This case has provided tremendous inspiration for our clinical work:

First, KD is a rare disease and lacks specificity in its clinical presentation, making it prone to missed diagnoses and misdiagnosis. There are no uniform criteria for diagnosing KD combined with renal damage, which relies mainly on the characteristic clinical manifestations of KD and renal involvement. In short, the clinical diagnosis of KD combined with renal disease should be considered when patients present with superficial masses, elevated peripheral blood eosinophil counts, IgE levels, hematuria, and proteinuria.

Second, the etiology of KD and its pathogenesis causing renal involvement are still unclear and may be related to viral infections or toxins that induce IgE-mediated type I hypersensitivity reactions or alter T-cell immune regulation, leading to lymphokine release.[8] The most common pathological feature of KD-associated nephropathy is eosinophilic infiltration of the renal tissue. Interestingly, no eosinophil infiltration was observed in the renal tissue after renal biopsy in this case, which suggests that the renal damage caused by KD may not be due to direct infiltration of eosinophils but is related to the involvement of other immune factors (e.g., tumor necrosis factor and interferon).[9,10] This finding coincides with the fact that complications due to KD are often immune system diseases. This finding reminds us to cut into the case from the perspective of immune-related molecules and further investigate the exact cause of kidney involvement due to KD, which can be instructive for its treatment.

Third, the preferred treatment modality for KD has not been standardized, and its main treatment options include surgical resection, radiation therapy, surgery combined with radiotherapy, or drug therapy such as glucocorticoids and immunosuppressive agents. Some studies have also mentioned that surgical resection is the first-choice treatment for patients with a single lesion, a complete capsule, and a large, well-defined mass.[11] Surgery often does not allow complete and thorough excision for patients with multiple lesions, incomplete capsules, and poorly defined masses. It is, therefore, more likely to recur after surgery, with a recurrence rate of up to 25%.[12] So surgical excision needs to be combined with local low-dose radiotherapy or drug therapy as the preferred treatment.[13,14] In our case, because the patient had a large mass and recurrent renal damage, we considered a combination of glucocorticoids and immunosuppressive agents after surgical excision of the primary lesion as the most effective treatment, and there was no sign of recurrence during regular long-term follow-up.

STATEMENT OF ETHICS

Clinical information is published with the informed consent of the patient and family members.

FUNDING

No funding was received for this study.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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