CLINICAL IMAGE

Kimura disease and immunoglobulin G4–related disease: a possible overlap in a patient with severe systemic symptoms

Grzegorz Biedroń[1*], Joanna Kosałka[1*], Jolanta Gąsior[1], Mamert Milewski[1], Krystyna Gałązka[2], Jacek Musiał[1]

1 Department of Internal Medicine, Jagiellonian University Medical College, Kraków, Poland
2 Department of Pathology, Jagiellonian University Medical College, Kraków, Poland

A 30-year-old white man diagnosed with immunoglobulin G4–related disease (IgG4-RD) was admitted to the Department of Clinical Immunology with clinical and laboratory symptoms of hypoalbuminemia. IgG4-RD was diagnosed a year earlier based on clinical symptoms (sinusitis, blepharitis with ptosis of the left upper eyelid, cervical lymphadenopathy, and gingivitis), elevated serum IgG4 levels (335 mg/dl; reference range, 8.0–140.0 mg/dl), and lymph node histopathology (IgG4/IgG plasma cells >80%; FIGURE 1A). He was treated with dexamethasone (maximum dose, 8 mg/d) for 1 month, with excellent clinical and laboratory response.

Eleven months later, the patient was admitted to the Department of Surgery with acute abdominal pain. Computed tomography angiography revealed disseminated arterial emboli involving the superior mesenteric artery, both deep femoral arteries, and the left popliteal artery. He underwent successful embolectomy of the superior mesenteric artery and left popliteal artery, with rapid clinical improvement. However, he developed significant hypoalbuminemia.

On admission to our department, laboratory tests revealed nephrotic syndrome with daily proteinuria of 7.33 g, elevated levels of serum troponin I (1234 ng/l; reference range <19.0 ng/l) and immunoglobulin E (IgE) (7890 IU/ml; reference range, 0.0–100.0 IU/ml), and peripheral blood eosinophilia ($3.58 \times 10^3/mm^3$; reference range, $0.04–0.54 \times 10^3/mm^3$). Kidney biopsy showed membranous glomerulonephritis with substantial eosinophil infiltrates but without plasmocytic infiltration (FIGURE 1B). On electrocardiography, deep negative T waves in precordial leads with periodic wide QRS complexes were observed, suggesting ischemic cardiac damage, most probably due to disseminated thrombi inside the coronary arteries. Doppler ultrasound of the lower limbs

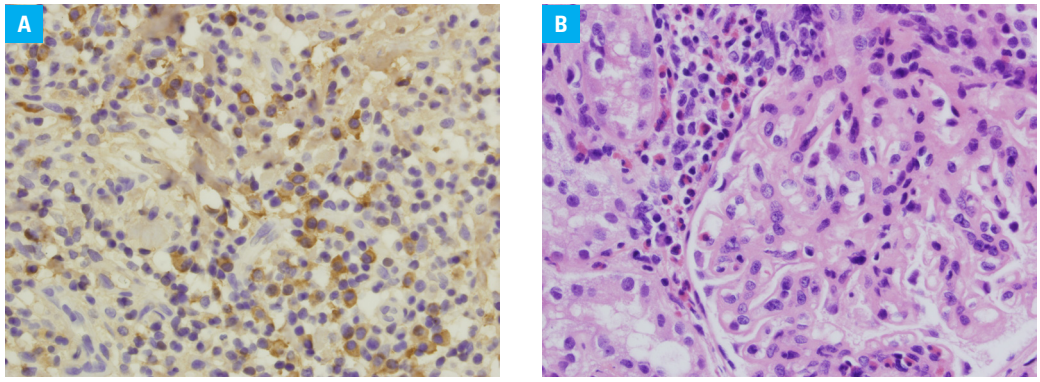

FIGURE 1 **A** – numerous immunoglobulin G4–positive plasma cells in the lymph node. Immunohistochemical staining for immunoglobulin G4; magnification × 40. **B** – kidney biopsy specimen; at the glomerulus with higher cellularity and prominent basement membranes, a focus of inflammatory infiltrate is visible, rich in eosinophils, with scattered plasma cells. Hematoxylin and eosin staining; magnification × 60.

Correspondence to:
Grzegorz Biedroń, MD, Department of Internal Medicine, Jagiellonian University Medical College, ul. Skawińska 8, 31-066 Kraków, Poland, phone: +48 12 430 52 66, email: gbiedron@op.pl
Received: October 15, 2018.
Revision accepted: November 30, 2018.
Published online: December 13, 2018.
Conflict of interest: none declared.
Pol Arch Intern Med. 2019; 129 (2): 125-126
doi:10.20452/pamw.4424

* GB and JK contributed equally to this work.

demonstrated disseminated thrombi in the arteries and veins of both calves. Evaluation of the previous laboratory results and pathological examinations revealed persistent peripheral blood eosinophilia accompanied by elevated serum IgE levels. Atopic diseases and parasitic infestation were excluded. Kimura disease (KD) was suspected. The patient was treated with methylprednisolone (60 mg/d with dose reduction) and mycophenolate mofetil (3.0 g/d), in addition to angiotensin-converting enzyme inhibitors, statins, diuretics, and antithrombotic therapy (initially low-molecular-weight heparin, later switched to warfarin with an international normalized ratio of 2.0 to 3.0). Due to persistent proteinuria (6 g/24 h), mycophenolate mofetil was replaced by cyclosporine, resulting in a prompt decrease in daily proteinuria to 0.48 g/24 h and normalization of eosinophil count. The treatment was continued for 8 months, and the disease course was uneventful.

KD is a rare chronic inflammatory disease of unknown origin.[1] It often affects the soft tissues of the head, neck, and extremities and is associated with eosinophilia and elevated serum IgE concentrations.[1,2] Only a few cases of nephrotic syndrome, endocarditis, and so-called thrombotic storm (disseminated thrombi in numerous arterial and venous beds) were reported.[2]

IgG4-RD is a systemic fibroinflammatory condition characterized by elevated serum levels of IgG4 and infiltration of IgG4-expressing plasma cells with fibrosis of the involved organs.[1] It can affect the pancreas, bile ducts, orbits, salivary gland, and kidneys.[1] Eosinophilia, elevated serum IgE concentrations, and eosinophilic infiltrates of the tissues were described in IgG4-RD.[3] The most common renal manifestation is tubulointerstitial nephritis; however, cases of membranous glomerulonephritis have also been reported.[4] This case shows the overlapping features of KD and IgG4-RD along with difficulties in an unequivocal distinction between both entities.[1,5]

REFERENCES

1 Li J, Ge X, Ma J, et al. Kimura's disease of the lacrimal gland mimicking IgG4-related orbital disease. BMC Ophthalmol. 2014; 14: 1-4.

2 Sakaguchi Y, Nakajima T, Kawamoto A, et al. A case of eosinophilic myocarditis complicated by Kimura's disease (eosinophilic hyperplastic lymphogranuloma) and erythroderma. Jpn Circ J. 1999; 63: 141-144.

3 Della Torre E, Mattoo H, Mahajan VS, et al. Prevalence of atopy, eosinophilia, and IgE elevation in IgG4-related disease. Allergy. 2014; 69: 269-272.

4 Alexander MP, Larsen CP, Gibson IW, et al. Membranous glomerulonephritis is a manifestation of IgG4-related disease. Kidney Int. 2013; 83: 455-462.

5 Liu L, Chen Y, Fang Z, et al. Kimura's disease or IgG4-related disease? A case-based review. Clin Rheumatol. 2015; 34: 385-389.