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LETTER TO THE EDITOR

Mixed-type Castleman Disease Can Mimic IgG4-Related Disease

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Immunoglobulin G4 (IgG4)-related disease is an autoimmune disease with increased serum IgG4 concentrations (≥135 mg/dL). Histopathologic examination shows marked plasmacyte infiltration with IgG4+/IgG+ plasma cells >40%.[1] Castleman disease is a rare lymphoproliferative disease presenting with lymphadenopathy, hepatosplenomegaly, hyperglobulinemia and anemia. It can be pathologically classified into three types: hyaline-vascular, plasma cell, and mixed.[2] Meanwhile, Castleman disease can also present elevated IgG4 level[3] and mimic IgG4-related disease. Here, we report a case of mixed type Castleman disease initially misdiagnosed as IgG4-related disease.

A 47-year-old man had fatigue for more than two years without palpable superficial lymph nodes or hepatosplenomegaly. Lab results showed anemia (Hemoglobin 7.1 mg/dL), polyclonal hyperglobulinemia (85.1 g/L, IgG 72.10 g/L, immunoglobulin A (IgA) 5,130.00 mg/L with negative blood immune fixation electrophoresis and urinary Bence-Jones protein) and elevated plasma IgG4 level (>3.56 g/L). Computed tomography showed enlarged lymph nodes in the retroperitoneum with obvious enhancement on contrast. The lesion was surrounded by blood vessels and had punctate calcifications (Figure 1, a, b). Puncture biopsy of a lymph node showed massive infiltration of mature plasma cells with CD38(+), CD138(+), Kappa(+), Lambda(+), IgG(+) and IgG4(+), with IgG4+/IgG+ plasma cells >40% (Figure 1c-e). The patient was diagnosed with IgG4-related disease and administered oral prednisone, but lymph node enlargement persisted. Laparoscopic

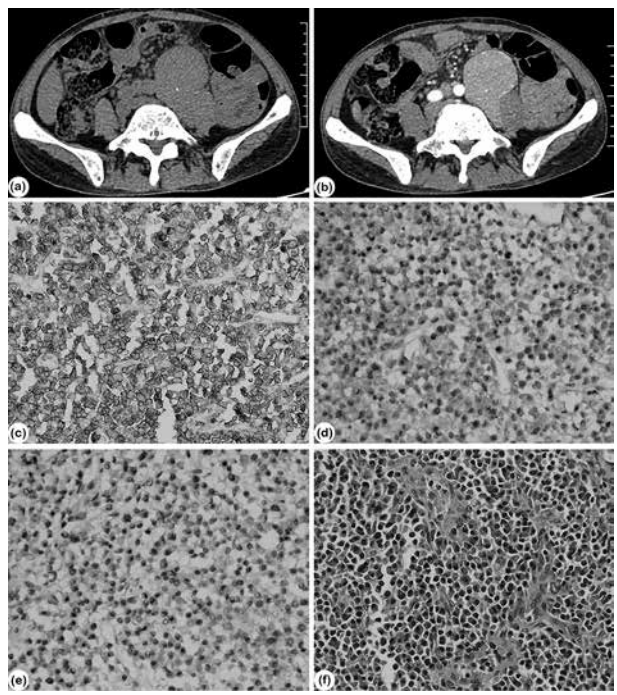

Figure 1. (a) Punctate calcification in the lymph nodes. **(b)** Blood vessels in the rim of the lesion and the computed tomography value increased. **(c)** Infiltration of CD38(+) plasma cells. **(d-e)** IgG4+/IgG+ plasma cells >40%. **(f)** Tubular thickened vascular walls (H-E×10×40). IgG: Immunoglobulin G.

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resection was then performed. Pathological examination showed an intact lymph node structure. Tubular thickened vascular walls were seen among numerous mature plasma cells, with IgG (+), IgG4 (+), and IgG4+/IgG+ plasma cells <40% (Figure 1f). The patient was finally diagnosed with Castleman disease, mixed type. Oral prednisone was tapered gradually within three months. The patient returned to our clinic with a normal immunoglobulin level and no enlarged lymph nodes two years later.

This patient had abdominal masses, elevated plasma IgG4 level, obvious plasmacyte infiltration with IgG4+/IgG+ plasma cells >40%; all of these met the diagnostic criteria for IgG4-related disease,[1] which was the initial diagnosis. However, computed tomography scan, pathology, and reaction to treatment led us to suspect the diagnosis. Lesions of Castleman disease with hyaline-vascular or mixed type are significantly enhanced in computed tomography scans due to profuse capillaries in the lesions or arteries around them; however, calcification is rare, about 5%.[4,5] Plasmacyte infiltration with IgG4+/IgG+ plasma cells >40% can be seen both in IgG4-related disease and Castleman disease. The resected lymph nodes showed massive infiltration by mature plasma cells and tubular vessels in the follicles, both signs of Castleman disease, mixed type.[2] At this time, IgG4+/IgG+ plasma cells <40% may be affected by the use of glucocorticoids. Most patients with IgG4-related disease respond well and swiftly to glucocorticoids, at least partially[1,6] while a complete resection of the lesion of unicentric Castleman disease can cure all patients, regardless of histologic subtype.[7] This patient recovered completely after total resection of the enlarged abdominal lymph nodes.

Elevated IgG4 levels are reported in numerous malignancies, such as melanoma, renal cell carcinoma, lymphoma, and Castleman disease.[3,8-10] Thus, even if a patient meets the diagnostic criteria for IgG4-related disease, we should suspect a malignant disease and monitor regularly. In particular, hematologic malignant tumors should be suspected if the lymph nodes are the only involved organ.

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