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CASE REPORT | PATHOLOGY

Liposarcoma Masquerading as Immunoglobulin G4–Related Disease

Prateek S. Harne, MD[1], Ujjwal Soni, MBBS[2], Ans Albustamy, MD[3], Arturo Suplee Rivera, MD[4], and Asif Zamir, MD, FACG[3]

[1]*University of Texas Health Science Center, Houston, TX*
[2]*University College of Medical Sciences, New Delhi, India*
[3]*Doctors Hospital at Renaissance, Edinburg, TX*
[4]*Baylor Scott & White, Dallas, TX*

ABSTRACT

This case report highlights the challenge of differentiating between immunoglobulin G4 (IgG4)-related disease (IGRD) and liposarcoma, which have similar symptoms and serological markers. A 40-year-old woman presented with right upper-quadrant pain and a retroperitoneal mass. Initial biopsy indicated increased IgG4-positive cells, leading to an IGRD diagnosis. However, the mass grew, despite prednisone treatment, prompting a repeat biopsy that revealed well-differentiated liposarcoma. Liposarcoma should be considered in patients with retroperitoneal masses and elevated IgG4 levels. Surgical resection is the primary treatment, emphasizing the need for early identification and close monitoring. Confirming IGRD or ruling out other diagnoses through histopathologic analysis is vital.

KEYWORDS: liposarcoma; IgG4; sarcoma; autoimmune

INTRODUCTION

Immunoglobulin G4 (IgG4)-related disease (IGRD) is characterized by lymphoplasmacytic tissue infiltration by IgG4-positive plasma cells and small lymphocytes and is known to involve multiple organs, sometimes simultaneously.[1] Retroperitoneal involvement is common with IGRD, often presenting as mass-like lesions and fibrosing disease such as retroperitoneal fibrosis[2] and sclerosing mesenteritis.[3]

Diagnosing IGRD is primarily based on the presence of appropriate clinical features and characteristic histopathological findings.[4] The serum IgG4 levels are widely used as a diagnostic tool for IGRD; however, they remain less specific because of elevation with other medical conditions such as allergic, infectious, and inflammatory etiologies. In addition, patients with confirmed IGRD on biopsy may not exhibit elevated levels of IgG4.[5]

Liposarcomas are uncommon cancerous tumors that originate from fat cells and are classified as a subtype of soft-tissue sarcoma based on their histological characteristics. Retroperitoneal liposarcoma (RPL) occurs in approximately 1 of every 2.5 million people, and it is the second most frequent location for liposarcoma after the lower limb.[6] The most common clinical feature of RPL is abdominal discomfort.[7] These tumors usually manifest at an advanced stage and have a poor prognosis. The unusual sites of occurrence and the rarity of the tumor can make the diagnosis challenging and delay the treatment.[8]

Although there is no established association, very few cases have been reported in the literature about strong IgG4 positivity and sarcomas.[3,9] Investigation usually warrants biopsy because imaging studies and serologies cannot differentiate between IGRDs and sarcomas. We highlight a case of a young patient who presented with typical features of IGRD and was found to have an aggressive RPL.

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Correspondence: Prateek S. Harne, MD (prateekharne17@gmail.com).

CASE REPORT

A 40-year-old woman presented with right upper-quadrant pain for 3 months. The patient was hemodynamically stable with a physical examination demonstrating fullness and tenderness in the right upper quadrant. Computed tomography (CT) of the abdomen revealed a heterogenous, macrolobulated mass of size 12.9 × 11.8 × 8.7 cm located in the retroperitoneal space inferior to the lower hepatic border and in the hepatorenal recess (Figure 1). CT-guided biopsy of the mass revealed increased IgG4-positive cells identified by immunohistochemical studies; however, FISH MDM2 amplification studies were inconclusive. The patient's serum IgG4 levels were also elevated at 205 mg/dL, and a possible diagnosis of IGRD was made according to the 2020 revised comprehensive diagnostic (RCD) criteria for IGRD.[10] The patient was started on prednisone taper therapy. At her 2-month follow-up, the patient's serum IgG4 levels had decreased, but physical examination demonstrated a firmer and larger mass. A decision to repeat a CT-guided biopsy was made. MDM2 amplification studies this time revealed an overexpression of MDM2 gene, strongly suggestive of a liposarcoma (Image B). She underwent liposarcoma resection, lymph node dissection, and right nephrectomy (adherent to the mass). Histopathologic analysis revealed a final diagnosis of stage I well-differentiated liposarcoma. The patient now follows up for surveillance of her liposarcoma.

DISCUSSION

IgG4-related disease is a rare autoimmune disorder characterized by elevated levels of IgG4, inflammation, and fibrosis in various organs, whereas liposarcomas are cancerous tumors that originate from fat cells.[1,6]

Although elevated IgG4 levels are a hallmark of IGRD, they are not specific to the disease and can also occur in allergic, infectious, and autoimmune conditions.[11] Therefore, it is important to confirm the diagnosis of IGRD or exclude other potential diagnoses through histopathologic analysis of affected tissues.

This aligns with the 2020 revised comprehensive diagnostic criteria for IGRD comprised 3 critical domains namely clinical and radiological features indicating organ involvement, elevated serum IgG4 levels exceeding 135 mg/dL, and a pathological diagnosis with atleast 2 among dense plasma cell and lymphocyte infiltration with fibrosis, a ratio of IgG4-positive plasma cells to IgG-positive cells surpassing 40%, the presence of over 10 IgG4-positive plasma cells per high-powered field, or characteristic tissue fibrosis, particularly storiform fibrosis, or obliterative phlebitis. Patients meeting all 3 RCD criteria receive a definitive IGRD diagnosis, whereas those satisfying criteria 1 and 3 are categorized as probable IGRD cases. For cases such as ours, where criteria 1 and 2 are met, a diagnosis of possible IGRD is considered.[10]

A sensation of a mass and abdominal discomfort is reported as the most common presenting symptoms of RPL as in our case.[7,12] A case report similar to ours by Nizar and Toubi, highlighted a patient with abdominal discomfort, found to have a retroperitoneal mass with a biopsy strongly positive for IgG4-related fibrosis. Glucocorticoids, methotrexate, and rituximab were used with no significant improvement. Ultimately, the mass was excised surgically, and a histopathological diagnosis of liposarcoma was established like our case.[13]

This case report highlights the challenges in differentiating between IGRD and liposarcoma, which can have similar initial presentations such as retroperitoneal masses and overlapping serological markers, including elevated levels of IgG4. A repeat biopsy should be considered if the initial diagnosis is doubtful or if the patient does not respond well to corticosteroid therapy, which is the first-line treatment for IGRD whereas the

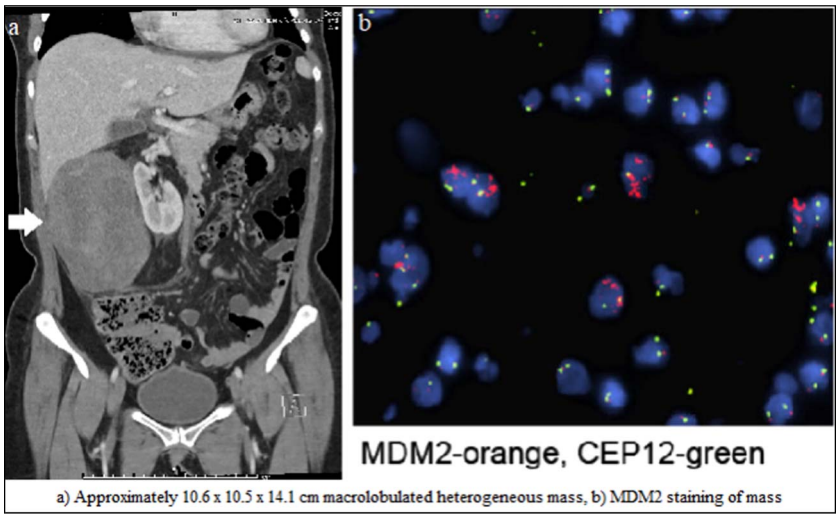

Figure 1. (A) Approximately 10.6 × 10.5 × 14.1 cm macrolobulated heterogeneous mass (arrow). (B) MDM2 staining of mass.

first-line therapy for RPL remains surgical excision, whenever possible. Although elevated IgG4 levels are a hallmark of IGRD, they are not specific to the disease and can also occur in infections, malignancies, and autoimmune conditions. On the other hand, the amplification of the MDM2 gene is characteristic for liposarcomas.[14] Therefore, it is crucial to confirm the diagnosis of IGRD, especially when its definite criteria is lacking, or exclude other potential diagnoses through FISH, immunohistochemistry, and histopathologic analysis of affected tissues.

DISCLOSURES

Author contributions: All authors contributed to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; were involved in drafting the work or revising it critically for important intellectual content; gave final approval of the version to be submitted; and are in agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. PS Harne is the article guarantor and accepts full responsibility for the conduct of the study.

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REFERENCES

1. Stone JH, Zen Y, Deshpande V. Mechanisms of disease: IgG4-related disease. *N Engl J Med*. 2012;366(6):539–51.
2. Vaglio A, Salvarani C, Buzio C. Retroperitoneal fibrosis. *Lancet*. 2006; 367(9506):241–51.
3. Abe A, Manabe T, Takizawa N, et al. IgG4-related sclerosing mesenteritis causing bowel obstruction: A case report. *Surg Case Rep*. 2016;2(1):120.
4. Vasaitis L. IgG4-related disease: A relatively new concept for clinicians. *Eur J Intern Med*. 2016;27:1–9.
5. Carruthers MN, Khosroshahi A, Augustin T, Deshpande V, Stone JH. The diagnostic utility of serum IgG4 concentrations in IgG4-related disease. *Ann Rheum Dis*. 2015;74(1):14–8.
6. Wethmar DrEI. Retroperitoneal liposarcoma: A case report and review of literature. *Glob J Med Res*. 2021;21(F3):1–7.
7. Guzmán Martínez-Valls PL, Ferrero Doria R, López Alba J, et al. Retroperitoneal liposarcoma. Apropos of 3 cases. *Arch Esp Urol*. 1997;50(5):529–31.
8. Vijay A, Ram L. Retroperitoneal liposarcoma: A comprehensive review. *Am J Clin Oncol*. 2015;38(2):213–9.
9. Bledsoe JR, Della-Torre E, Rovati L, Deshpande V. IgG4-related disease: Review of the histopathologic features, differential diagnosis, and therapeutic approach. *APMIS*. 2018;126(6):459–76.
10. Umehara H, Okazaki K, Kawa S, et al. The 2020 revised comprehensive diagnostic (RCD) criteria for IgG4-RD. *Mod Rheumatol*. 2021;31(3):529–33.
11. Ebbo M, Grados A, Bernit E, et al. Pathologies associated with serum IgG4 elevation. *Int J Rheumatol*. 2012;2012:602809.
12. Fernández-Ruiz M, Rodríguez-Gil Y, Guerra-Vales JM, Manrique-Municio A, Moreno-González E, Colina-Ruizdelgado F. Primary retroperitoneal liposarcoma: Clinical and histological analysis of ten cases. *Gastroenterol Hepatol*. 2010;33(5):370–6.
13. Nizar AH, Toubi E. IgG4-related disease: Case report and literature review. *Autoimmun Highlights*. 2015;6(1–2):7–15.
14. Lokka S, Scheel AH, Dango S, et al. Challenging dedifferentiated liposarcoma identified by MDM2-amplification, a report of two cases. *BMC Clin Pathol*. 2014;14(1):36.