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A case of IgG4-related renal pseudotumor in a child with history of Wilms tumor

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Introduction

IgG4-related disease (IgG4-RD) is a novel immune-mediated systemic disease characterized by lymphoplasmacytic infiltration and fibrosis of tissues.[1] While the pathophysiology has yet to be elucidated, malignancy has been shown to be associated with future development of IgG4-RD.[2] IgG4 pseudotumors fall within the scope of IgG4-RD, most commonly presenting as orbital, pancreatic, pulmonary, hepatic, or thyroid masses, although involvement of other organs has been described.[3] Originally described in 2003, there is a paucity of literature regarding IgG4-RD in the pediatric population. There have been 3 reported cases of renal IgG4-RD in children, with all cases having multiorgan involvement.[3] Herein, we describe the first case of an isolated renal IgG4 pseudotumor in an 11-year-old boy with a history of previously treated Wilms tumor (WT).

Case presentation

An 11-year-old asymptomatic male presented to clinic with a right upper pole renal mass, found on surveillance imaging in follow up for WT. At age 4 he was treated for stage III WT of the left kidney with nephrectomy, chemotherapy (actinomycin, vincristine, doxorubicin), and flank radiation. He had no concerning findings on surveillance imaging between initial treatment and age 11 years. Surveillance ultrasound followed by computed tomography scan showed a right upper pole 2.3 cm mass concerning for malignancy (Fig. 1). Given his history of solitary kidney and potential local upstaging with biopsy given concern for metachronous WT, the patient underwent right partial nephrectomy with regional lymph node dissection.

A right subcostal incision from midline to mid-axillary line was made. Vascular control was achieved with manual clamping of the renal parenchyma; neither the renal artery or vein was clamped during excision. The mass was excised sharply. The collecting system was entered intentionally to achieve a grossly negative margin. There were no areas of rupture or spill noted. The specimen was then taken fresh to pathology while left retroperitoneal lymph node sampling was performed.

Gross inspection demonstrated a well circumscribed but unencapsulated, tan-yellow, solid, lobulated lesion adjacent to the pelvocalyceal surface measuring 3 cm. Microscopic examination revealed an abundant mononuclear infiltrate consisting of predominantly plasma cells within the interstitium of the cortex and medulla (Fig. 2). Scattered lymphoid follicles were present. The glomeruli entrapped at the interface of the lesion and normal cortex show mild thickening of the basement membranes and segmental and global sclerosis, while the remaining glomeruli were unremarkable. The background stroma showed only focal well-developed fine fibrosis, most prominent at the margins. The margins were negative for tumor. CD138 staining showed diffuse membranous staining of abundant plasma cells, many of which also stained for IgG. Focal areas also showed strong cytoplasmic IgG4 staining (> 30 per high power field, Fig. 3) and an IgG4/IgG ratio of 34%, highly suggestive of an IgG4 pseudotumor.[4] There was no evidence of WT or microorganisms. Due to the pathologic findings, serum IgG4 levels were drawn 16 days after surgery and were within the normal range at 65.4 mg/dl (reference range: 1.0–121.9 mg/dL). The patient continues to be managed for stage III chronic kidney disease (eGFR 58 mL/min/1.73m^2) as a result of his two renal mass resections. Fortunately, he remains without disease recurrence **5 years post resection**.

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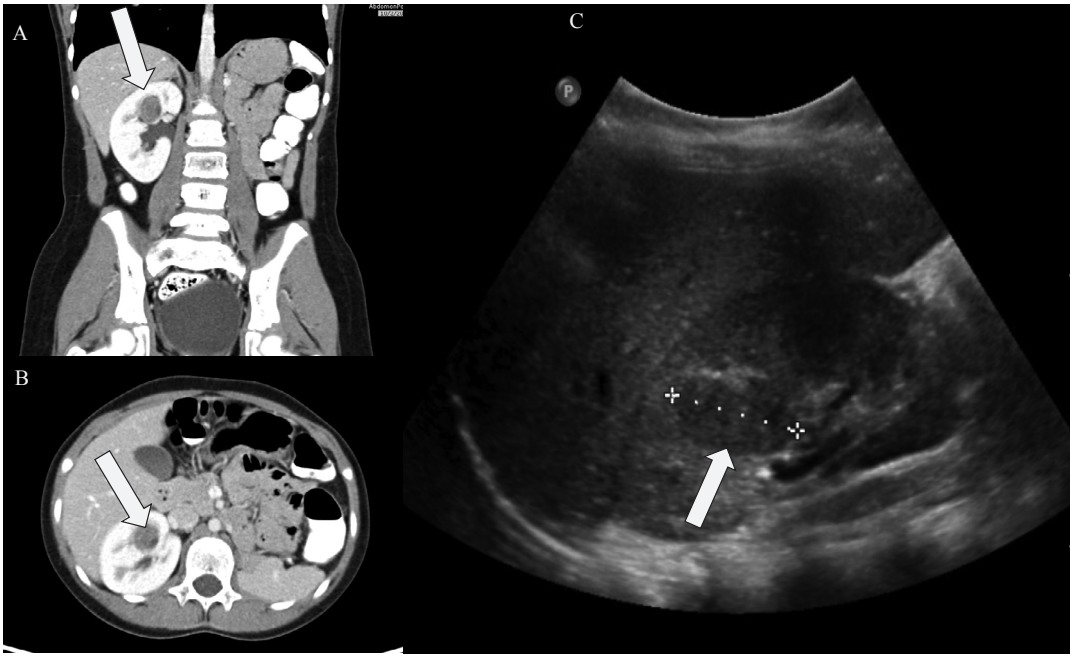

Fig. 1. Concerning right upper pole mass (yellow arrows) on CT scan (a and b) and ultrasound (c).

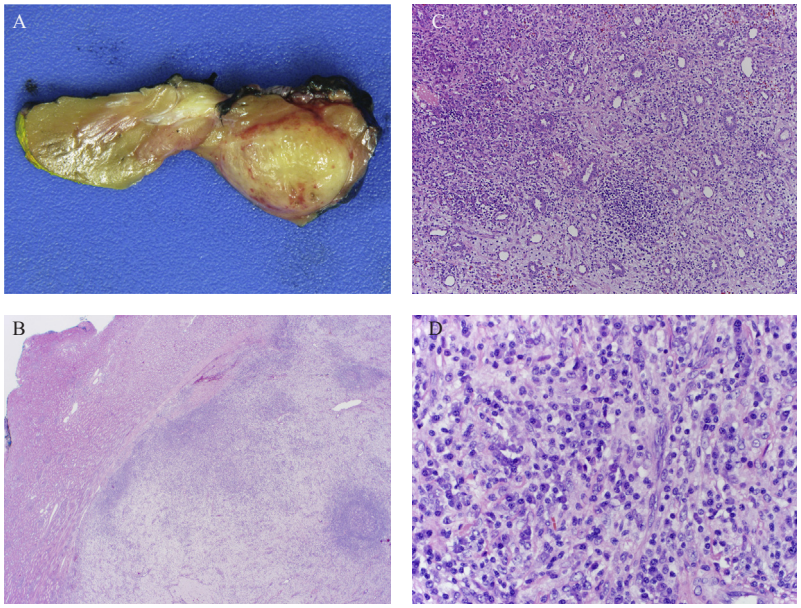

Fig. 2. a) Gross image demonstrating the well-circumscribed, unencapsulated mass. Microscopic examination of H&E staining of b) The well-circumscribed mass (x20), c) Tubulointerstitial inflammation (x100), and d) An abundance of plasma cells (x400).

Discussion

IgG4-RD was first reported in 2003 linked to autoimmune pancreatitis and usually seen in men over 50 years of age. Since then, many diseases have been reclassified as IgG4-RD, including sclerosing sialadenitis, Riedel thyroiditis, as well as certain variants of Hashimoto thyroiditis and retroperitoneal fibrosis.[1] Renal involvement of IgG4-RD usually presents as a tubulointerstitial nephritis, with pseudotumors being exceedingly rare. In the largest review of IgG4-RD in children, median age of presentation was 13 years, with the most common organs affected being the eyes (44%) and pancreas (12%). Renal involvement occurred in 3 cases, always in conjunction with other organ manifestations and never as a solitary finding. While IgG4-RD can lead to organ dysfunction if left untreated,[1] Prednisone showed a favorable clinical response in 83% of the cases.[3]

Stone et al. recently described a relationship between history of malignancy and subsequent development of IgG4-RD. Their study found that a history of malignancy was 3 times more likely in IgG4-RD patients than that of case-control subjects. Furthermore, IgG4-RD was diagnosed an average of 8.8 years after malignancy.[2]

While several proposals have been made to create diagnostic criteria for IgG4-RD, disagreement remains. According to the criteria proposed by Umehara et al., our case meets the criteria of probable IgG4-RD based on radiologic and histologic findings.[4] Serum IgG4 was normal 16 days post-operatively, though no pre-operative level was obtained. Without the pre-operative serum IgG4, a definitive diagnosis of IgG4-RD, supported by serum IgG4 cutoff level > 135 mg/dL remains in question. It is worth noting that the serum half-life of IgG4 is 21 days, so

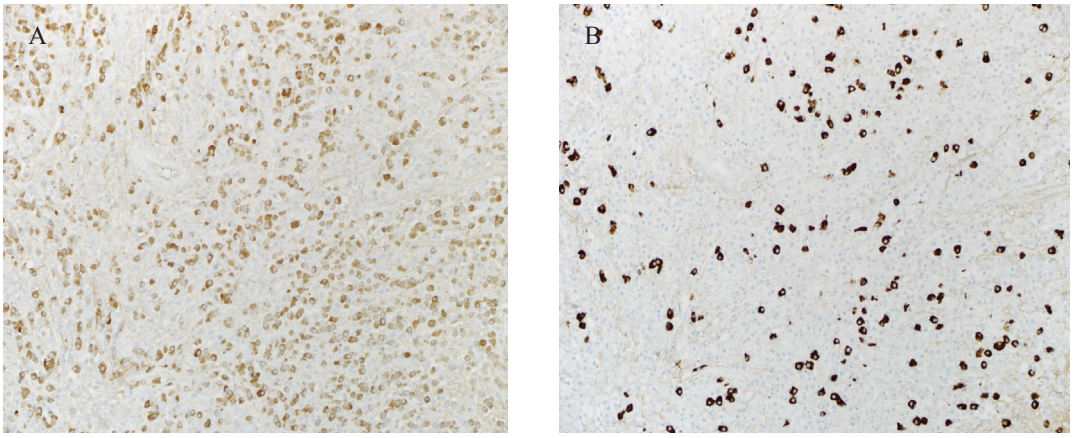

Fig. 3. a) IgG immunostaining highlighting abundant plasma cells (x400), b) IgG4 immunostaining positive in greater than 30 plasma cells per high power field (x400).

it is possible our patient would have had an elevated IgG4 before resection. **While, there are data that IgG4 levels are lower in single organ involvement than in systemic disease, it remains unknown what effect resection has on IgG4 levels in single-organ manifestation**.[5] While storiform fibrosis and obliterative phlebitis are major histopathological features of the disease, they are not always seen in organ-specific disease such as lymph nodes, lung, and kidneys, and the guidelines suggesting these as diagnostic requirements are not intended to replace organ-specific diagnostic criteria.[6]

In our case, the history of WT complicated the initial diagnosis and treatment plan. As mentioned, surveillance imaging revealed a suspicious lesion, which may have represented either benign or malignant etiologies. Biopsy was determined to carry a prohibitive risk due to the possibility of upstaging disease if ultimate diagnosis was a WT. It is possible the history of WT contributed to the development of an IgG4 pseudotumor in this patient. Steroid treatment may have proved efficacious in this instance.

Conclusion

IgG4-RD is a recently defined condition that may present with a pseudotumor mimicking malignancy and is commonly misdiagnosed. History of malignancy may portend future IgG4-RD development. We present a case of isolated renal IgG4-related pseudotumor in a pediatric patient with a history of WT. This case highlights the need for additional investigation into IgG4-RD in the pediatric population with history of malignancy to avoid over resection.

Conflicts of interest

None of the authors of this manuscript have any financial or personal relationships to disclose that could inappropriately influence or bias our work.

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Declarations of interest

None.

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