Abdominal Radiology (2019) 44:1230–1236
https://doi.org/10.1007/s00261-018-01885-1

SPECIAL SECTION: DISTINGUISHED PAPERS FROM JSAR

A case of immunoglobulin G4-related inflammatory pseudotumor mimicking renal cell carcinoma

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Published online: 3 January 2019

Abstract
In a 69-year-old woman with a history of Mikulicz's disease, a hypoechoic solitary renal mass was identified on routine ultrasound examination. Based on the findings of computed tomography (CT) and magnetic resonance imaging (MRI), renal cell carcinoma was a possible diagnosis. Subsequent partial nephrectomy revealed a mass characterized by an increased number of blood vessels, internal hemorrhage, and a thick fibrous capsule. Immunohistochemically, the mass comprised of tubulointerstitial nephritis with increased immunoglobulin (Ig)G4-positive plasma cells and fibrosis. Generally, diagnosis of IgG4-related kidney disease (IgG4-RKD) is not difficult when the kidney is involved together with other systemic involvements. However, diagnosis becomes harder when a solitary renal mass appears as a single-organ involvement. On precise review of our imaging findings, MRI signals were markedly affected by hemorrhage, so the mass showed hypointensity on both T1- and T2-weighted imaging, and the signal of in-phase images decreased. Dynamic MRI showed no apparent enhancement of the mass, while CT showed an apparent enhancement effect. Capsule formation was another key finding for IgG4-RKD and was recognized as a gradually enhancing boundary zone surrounding the mass on both CT and MRI. When a solitary renal mass is associated with hemorrhage and thick capsule formation, inflammatory pseudotumor should be considered as differential diagnosis.

Keywords IgG4-related disease · IgG4-RKD · Pseudotumor · Renal cell carcinoma

Introduction

Immunoglobulin (Ig)G4-related disease (IgG4-RD) is a systemic disease characterized by an elevated IgG4-positive plasma fibro-inflammatory condition [1]. Multiple organs can be involved, including the kidneys, and 35% of patients with autoimmune pancreatitis who underwent computed tomography (CT) or magnetic resonance imaging (MRI) reportedly show renal involvement [2]. Histopathologically, the key feature of IgG4-related kidney disease (IgG4-RKD)

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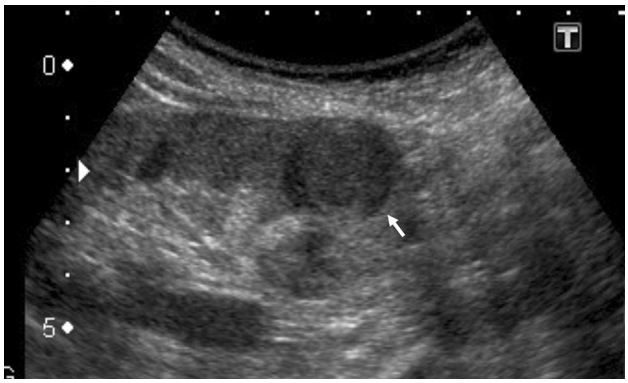

Fig. 1 Abdominal ultrasonography shows a hypoechoic mass in the right kidney. The mass is bounded by a hypoechoic band regarded as representing a capsule (arrow)

is tubulointerstitial nephritis with increased infiltration of IgG4-positive plasma cells to the renal interstitium with fibrosis [3]. Contrast-enhanced CT frequently shows multiple nodular lesions in both kidneys [4]. We present herein the case of a patient with a solitary renal mass that was difficult to distinguish from renal cell carcinoma.

Case report

A 69-year-old woman with swelling of the submandibular gland had been diagnosed as Mikulicz's disease 10 years earlier and had been well without symptoms by continuous immunotherapy. A hypoechoic renal mass was identified on routine ultrasonography (Fig. 1). At that time, laboratory tests showed mild impairment of renal function (creatinine, 0.77 mg/dL; estimated glomerular filtration rate, 56.8 mL/min/1.73 m^2), and an increased serum concentration of IgG4 (295 mg/L). Non-contrast-enhanced CT showed an ill-defined mass with a slightly high CT attenuation value of 55 Hounsfield units (HU) (Fig. 2a). After intravenous administration of iodide contrast media, the mass was enhanced up to 140 HU, slightly less than the attenuation of the renal cortex in the corticomedullary phase (Fig. 2b). The contrast enhancement effect continued until the excretory phase, and the CT attenuation value was 120 HU (Fig. 2c). The mass was surrounded by a low-density rim in the corticomedullary phase, and this rim was slightly enhanced in the excretory phase (Fig. 2b, c). On MRI, the mass showed hypointensity on both T1-weighted imaging (T1WI) and T2-weighted imaging (T2WI). Signal intensity of the mass on in-phase T1WI was decreased compared with that on out-of-phase imaging. Diffusion-weighted imaging (DWI) (b value = 1000) also showed hypointensity (Fig. 3). MRI dynamic study showed no apparent enhancement of the mass and the rim displayed pale enhancement (Fig. 4). On positron emission tomography (PET)-CT, the difference in ^{18}F-fluorodeoxyglucose uptake between the mass and surrounding renal parenchyma was unclear. Based on the imaging findings mentioned above, the most likely diagnosis was papillary renal cell carcinoma. Laparoscopic partial nephrectomy was subsequently performed. Macroscopically, the resected specimen showed a 16 × 14 × 10-mm mass with mixed brownish and yellowish surfaces (Fig. 5a). Histologically, bleeding and deposition of hemosiderin was conspicuous, and blood vessels were notably increased. Diffuse plasma cell infiltration was observed not only in the area bounded by thick fibrous capsule, but also in the surrounding renal tissue outside the capsule (Fig. 5b). Immunohistochemically, infiltration of IgG4-positive plasma cells was diffusely found both inside and outside of the mass, accounting for about 600 cells per high-power field (HPF) (Fig. 5c). More than 90% of plasma cells positive for IgG were positive for IgG4. More than 500 IgG4-positive plasma cells per HPF were also observed in the renal parenchyma outside of the mass. Based on these findings, the renal lesion was diagnosed as IgG4-related inflammatory pseudotumor.

Discussion

Generally, diagnosis of IgG4-RKD is not difficult when the kidney is involved along with lesions in multiple organs. Conversely, diagnosis becomes difficult when a solitary renal mass in a single organ is involved. Our case shows two additional pathological features that have not been mentioned in previous reports. The first is an increased number of blood vessels and intra-tumoral bleeding. There is a close relationship between inflammation and angiogenesis [5], and it is presumed that inflammation lasting for a long time could induce angiogenesis. New vessels are often vulnerable and may be easy to bleed [6]. Our case shows an intense enhancement effect on dynamic CT reflecting the pathological findings. According to the several reports of

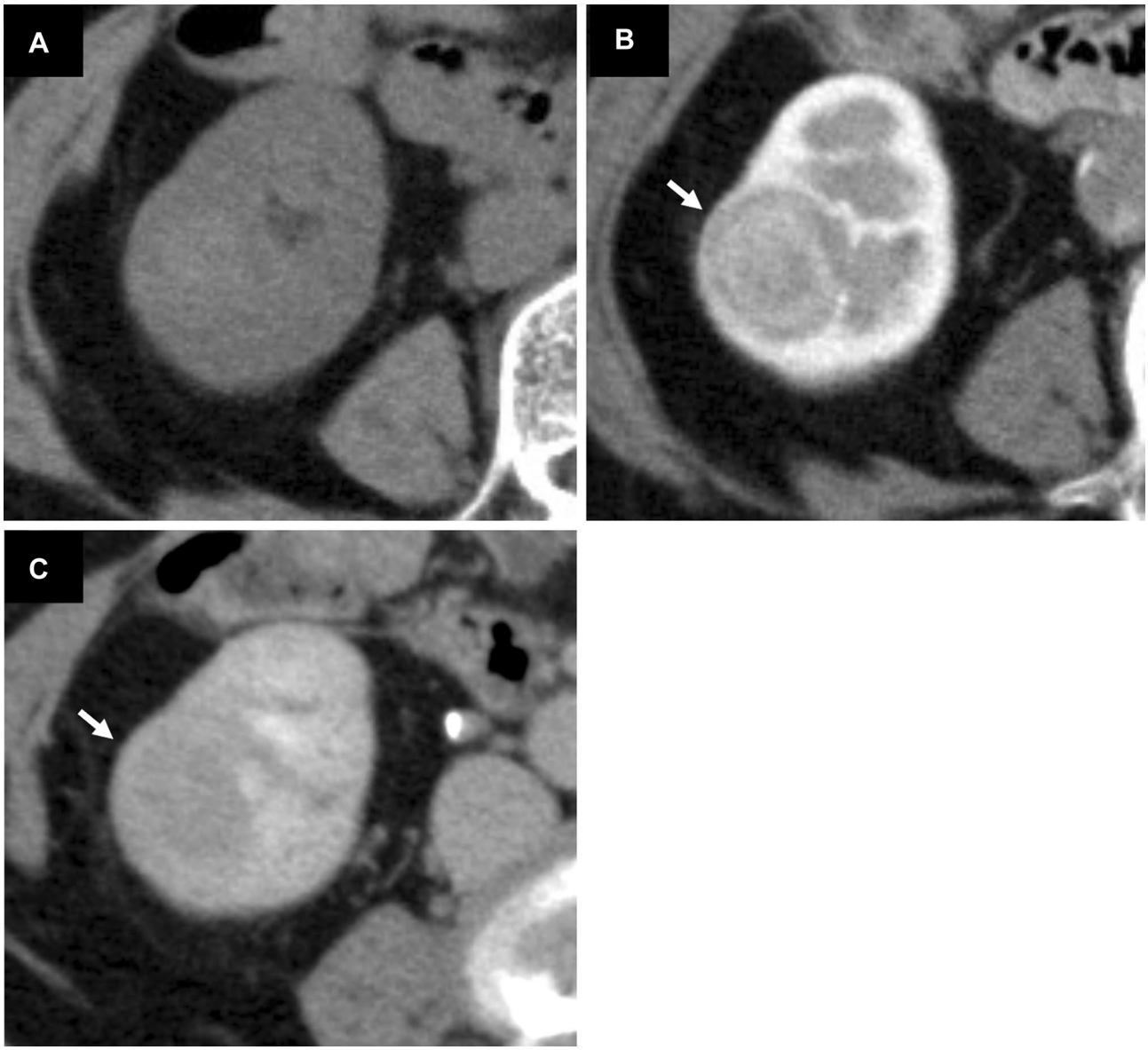

Fig. 2 Non-contrast-enhanced CT shows a mass with slightly higher density than surrounding renal parenchyma (**a**). The mass shows weak enhancement on contrast-enhanced CT in the corticomedullary phase (**b**). The contrast effect of the mass lasts throughout the excretory phase (**c**). The rim of the mass shows hypodensity in the corticomedullary phase (arrow in **b**) and equivocal enhancement in the excretory phase (arrow in **c**)

IgG4-related inflammatory pseudotumors of the kidney [4, 7, 8], hypervascular nature has not been well documented or not emphasized. In the presence of hemosiderin deposition we should pay attention to MRI signals, in which intense signal decrease occurs on T2WI, DWI (b value = 1000), and T1WI, and enhancement effect could be interfered. The second is the formation of a thick fibrous capsule. Fibrosis is the end of chronic inflammatory reactions [9], and long-term inflammation of the mass could accelerate the formation of a thick capsule. The capsule is well observed on macroscopic observation, as well as on ultrasonography and contrast-enhanced CT. When the fibrous band may be isointense to

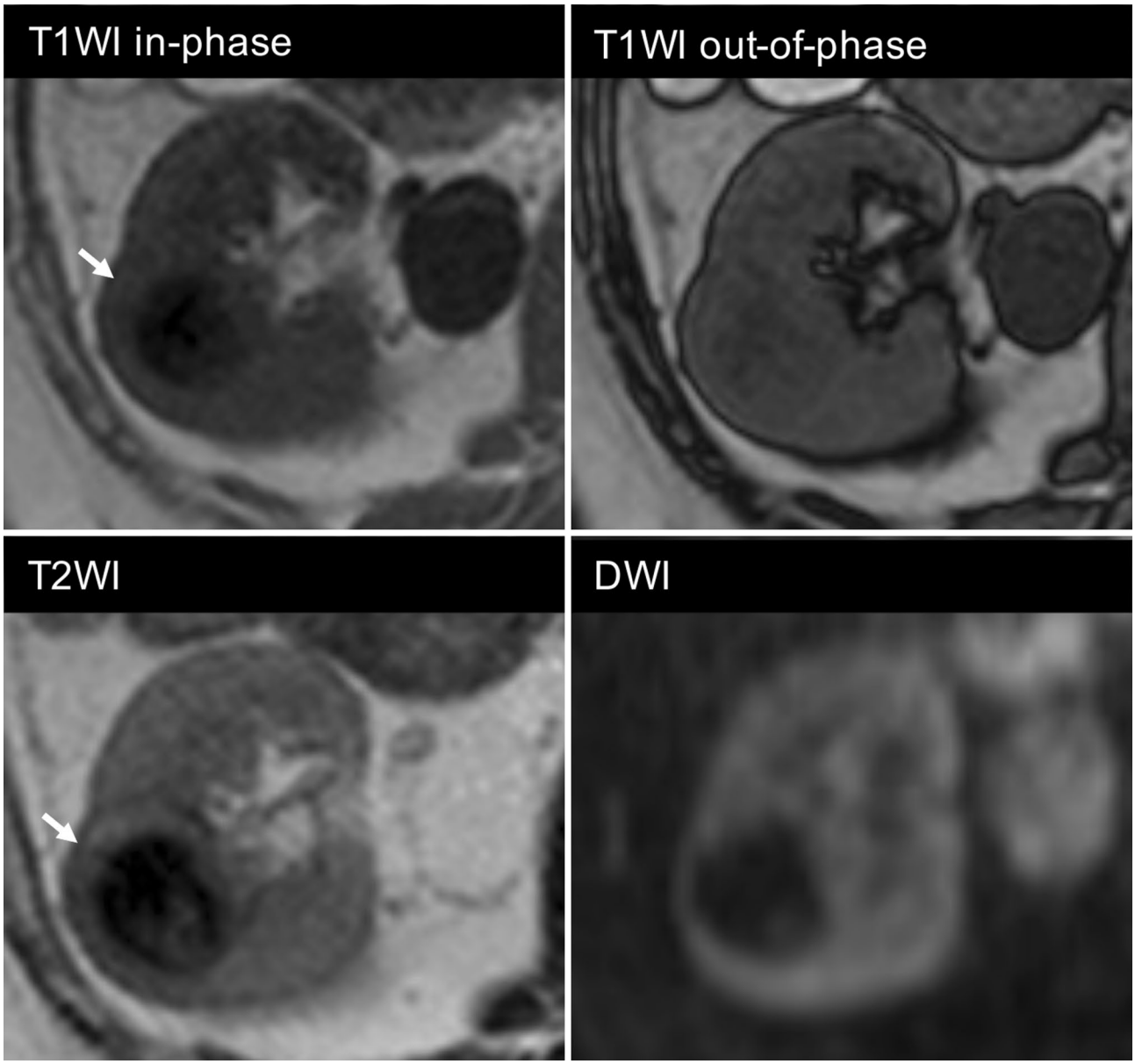

Fig. 3 On MRI, the mass shows hypointensity on both T1WI and T2WI. The signal from in-phase images is decreased. DWI (*b* value = 1000) also shows decreased intensity. The rim of the mass shows almost equal intensity with renal parenchyma on T1WI and T2WI (arrows)

the surrounding renal tissue on T1WI and T2WI, dynamic MRI should be carefully evaluated to distinguish enhancement differences in the boundary zone.

In our case, it is difficult to completely distinguish IgG4-RKD from papillary renal cell carcinoma. However, when a mildly enhanced renal mass is associated with hemorrhage and capsule formation, inflammatory pseudotumor like IgG4-RKD should be considered as differential diagnosis and percutaneous biopsy could be recommended to avoid unnecessary surgery.

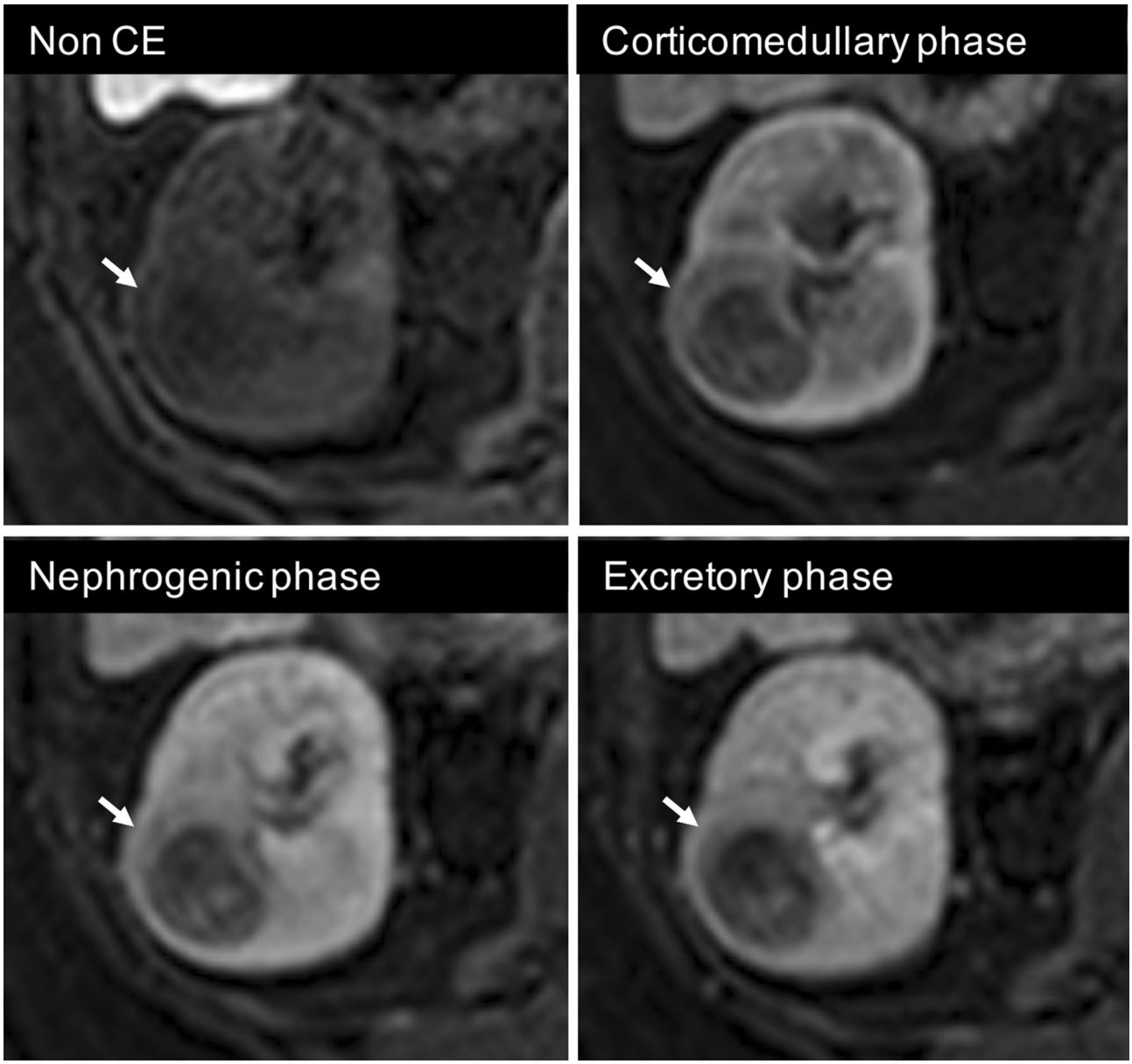

Fig. 4 On contrast-enhanced MRI, the mass is not enhanced except for small nodular parts, and the rim of the mass displays pale enhancement (arrows)

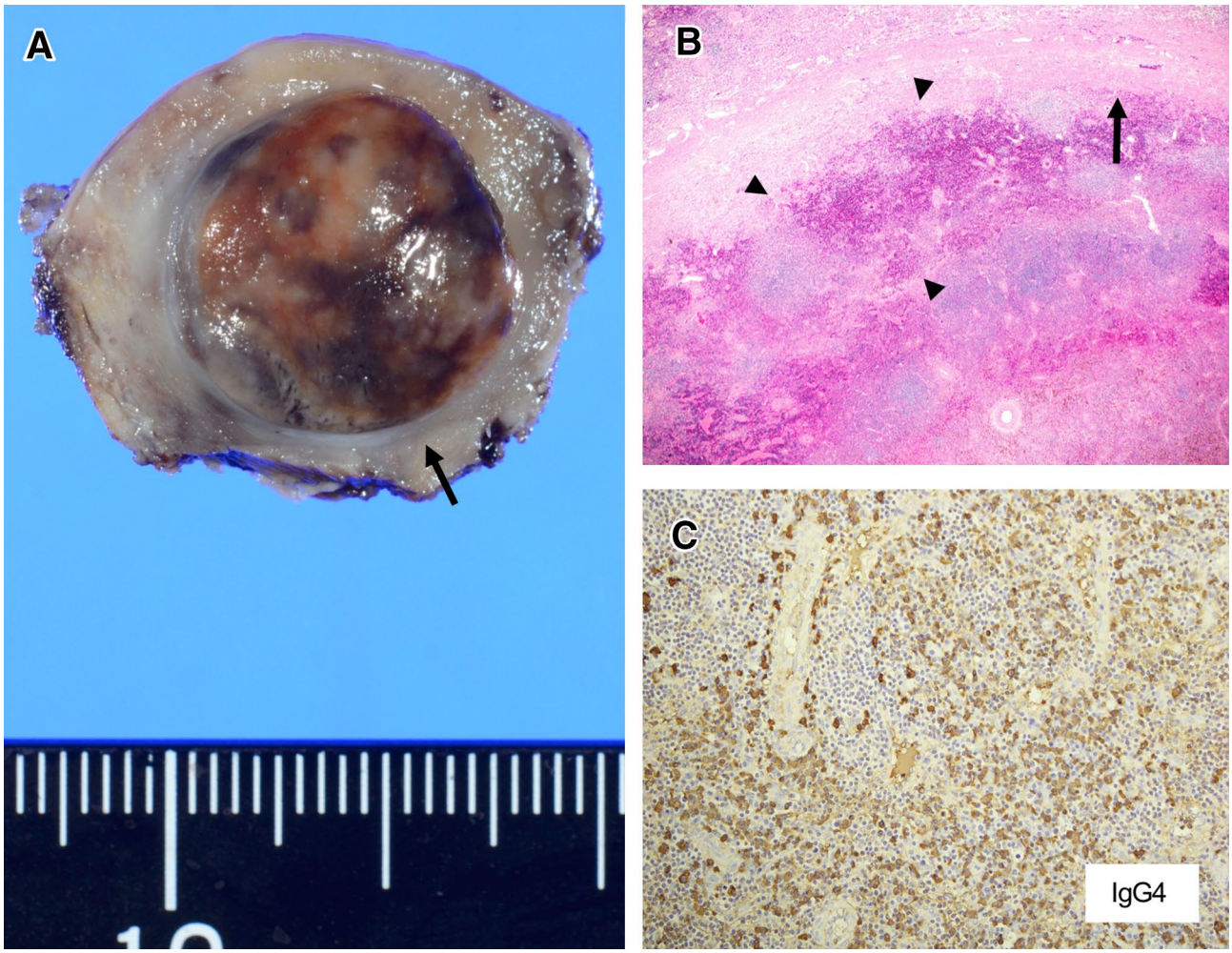

Fig. 5 The resected renal tumor shows mixed brownish and yellowish surfaces (**a**). A thick, whitish fibrous capsule surrounds the tumor (arrows in **a** and **b**). Histologically, diffuse infiltration of plasma cells is noted in the area covered by a thick fibrous capsule. Bleeding (arrowheads in **b**) and deposition of hemosiderin is conspicuous and numerous blood vessels are observed (**b** HE stain, 40×). IgG4-positive plasma cells are diffusely found in the mass at about 600 cells per HPF (**c** IgG4 stain, 400×)

Funding This study received no specific grant from any funding agency.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from the patient in the study.

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