


Case Report

Hibernoma in the renal sinus: A case mimicking malignancy

Ayano Kashima,¹  Tsuyoshi Majima,¹ Tomoaki Muramatsu,¹ Haruka Kurosu,¹ Hideji Kawanishi,¹ Ikuo Kobayashi,¹ Keishi Kajikawa,¹ Taishi Takahara,² Takahiro Yamamoto³ and Naoto Sassa¹

Departments of ¹Urology, ²Surgical Pathology, and ³Radiology, Aichi Medical University, Nagakute, Aichi, Japan

Abbreviations & Acronyms

CT = computed tomography
 FDG = fluorodeoxyglucose
 HU = hounsfield unit
 IgG4 = immunoglobulin
 G4-related
 MRI = magnetic resonance
 imaging
 RCC = renal cell carcinoma
 UCP1 = uncoupling protein 1

Correspondence: Tsuyoshi Majima M.D., Ph.D., Department of Urology, Aichi Medical University, 1-1 Yazakokarimata, Nagakute, Aichi 480-1195, Japan. Email: majima.tsuyoshi.888@mail.aichi-med-u.ac.jp

How to cite this article:

Kashima A, Majima T, Muramatsu T *et al.* Hibernoma in the renal sinus: A case mimicking malignancy. *IJU Case Rep.* 2024; 7: 308–312.

This is an open access article under the terms of the [Creative Commons Attribution-NonCommercial-NoDerivs](#) License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

Received 13 December 2023; accepted 24 April 2024.
 Online publication 16 May 2024

Introduction: Hibernomas are benign tumors of brown adipose tissue. Hibernoma in the renal sinus is extremely rare. Herein, we present the third known case of renal hibernoma.

Case presentation: A 71-year-old man reported to our department with a left kidney tumor with an average growth rate of 5 mm/year and a progressive contrast effect on computed tomography. It was diagnosed as a hibernoma following a laparoscopic radical nephrectomy.

Conclusion: We encountered a rare case of a hibernoma in the renal sinus. Development of new and accurate diagnostic methods for hibernoma, without resorting to nephrectomy, is essential.

Key words: brown adipose tissue, hibernoma, nephrectomy, renal sinus.

Keynote message

Hibernomas found in the renal sinus are extremely rare. Here, we report the third documented case of hibernoma originating from the renal worldwide.

Introduction

Hibernomas are benign brown adipose tissue tumors and account for 1.1% of tumors originating from adipose tissues.¹ They are most common in the thigh, followed by the torso, upper limbs, head and neck, and <10% of cases occur in the abdominal cavity or thoracic cavity.² Hibernomas in the renal sinus are extremely rare, with only two previously reported cases.^{3,4} Here, we present the third known case of hibernoma originating from renal.

Case report

A 71-year-old man was referred to our department for evaluation of a left kidney tumor, initially detected on abdominal ultrasonography. He had no anamnesis or family medical history. Laboratory testing showed a mildly elevated IgG4 level of 129 mg/dL and interleukin-2 receptor level of 556 IU/mL; other laboratory values were within normal limits.

The tumor appeared heterogeneously hypointense on T1-weighted images (Fig. 1a), and hyperintense on T2-weighted (Fig. 1b), diffusion-weighted (Fig. 1c), and apparent diffusion coefficient images (Fig. 1d), without fat suppression. On T1-weighted images in the opposed phase, there were indications of signal drop and internal heterogeneity of the mass. Contrast-enhanced MRI showed subtle contrast enhancement in the renal tumor, indicative of gradual growth.

Contrast-enhanced CT revealed a 31 × 26 mm tumor in the left renal sinus, exhibiting progressive contrast enhancement but faint high density (simple phase 20 HU, corticomedullary phase 30 HU, and renal parenchymal phase 40 HU) (Fig. 2a,b). CT urography indicated that the tumor was located in the renal sinus fat rather than the renal pelvis (Fig. 2c,d). The CT image taken 3 years ago due to liver dysfunction showed a renal tumor size of 16 × 15 mm. Pathologic diagnosis without nephrectomy was impossible on account of the risk of post-biopsy hemorrhage owing to the tumor's location. Considering the elevated IgG4 level, we treated the patient with prednisolone 30 mg/day to exclude the possibility of inflammatory

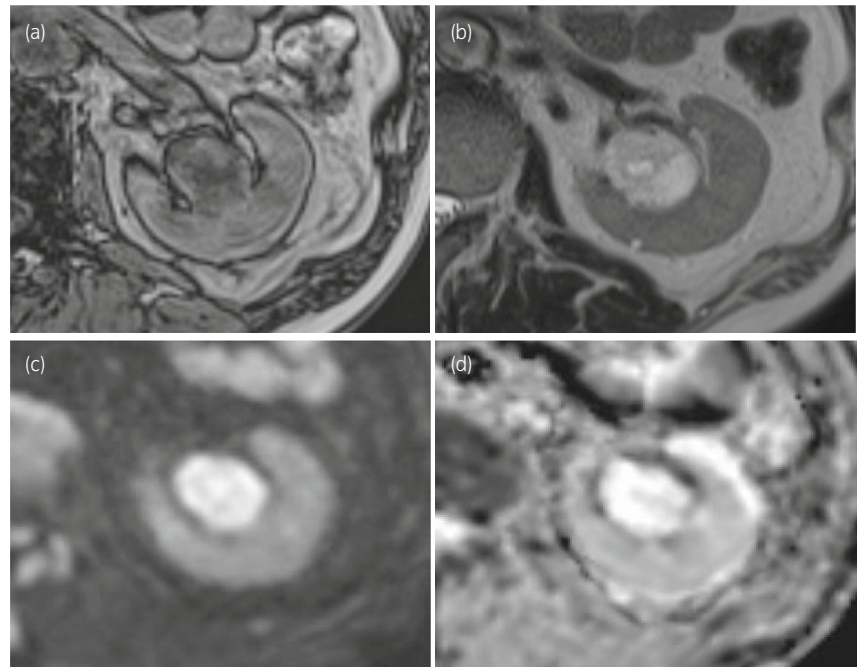


Fig. 1 On MRI, renal tumor exhibited hypointensity on the T1-weighted image (a), and hyperintensities on the T2-weighted image (b), diffusion-weighted image (c), and apparent diffusion coefficient image (d).

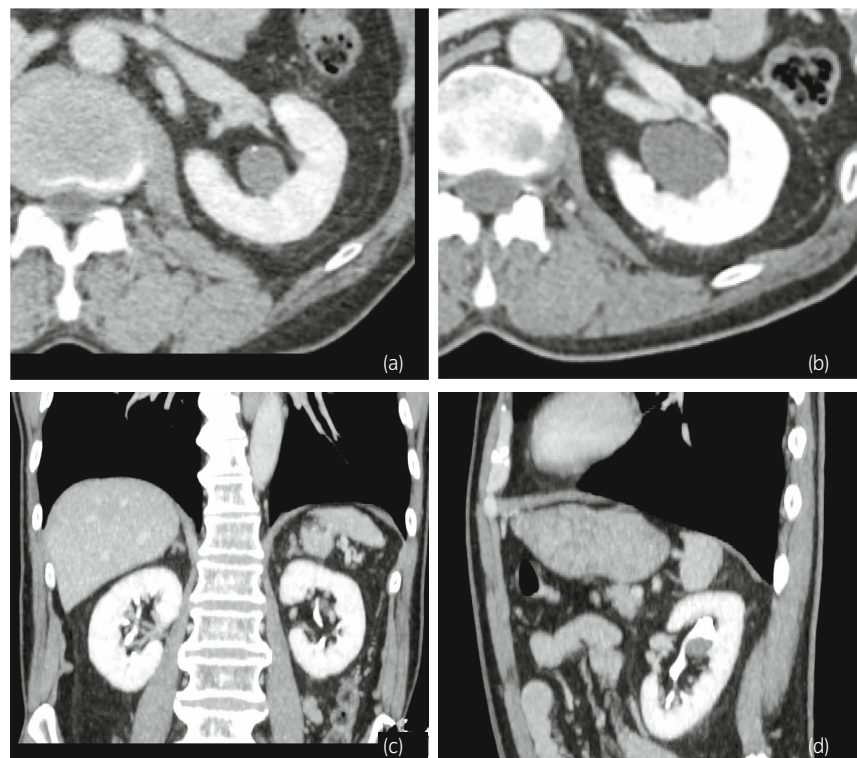


Fig. 2 The tumor was originally 16 × 15 mm in size, as seen on a CT scan from 3 years prior (a), and grew to 31 × 26 mm as seen prior to radical nephrectomy (b). The renal tumor was originated from renal sinus fat as seen on coronal (c) and sagittal (d) of CT urography at 3 years later.

diseases. However, 2 months of treatment showed no significant change in tumor size. Consequently, the possibility of malignancy could not be ruled out, and laparoscopic radical nephrectomy was performed. The operation lasted for 2 h and 48 min, with a blood loss of only 5 mL. Patient recovery was uneventful, and he was discharged from hospital on post-operative day 6. However, his creatinine clearance decreased

from 91.61 mL/min to 68.45 mL/min following the nephrectomy.

Macroscopic examination showed a well-circumscribed round brownish-red tumor (31 × 26 mm) located at the hilum (Fig. 3).

Microscopic examination revealed brown adipocytes with stromal spindle cells, myxoid stroma, and inflammatory cells.

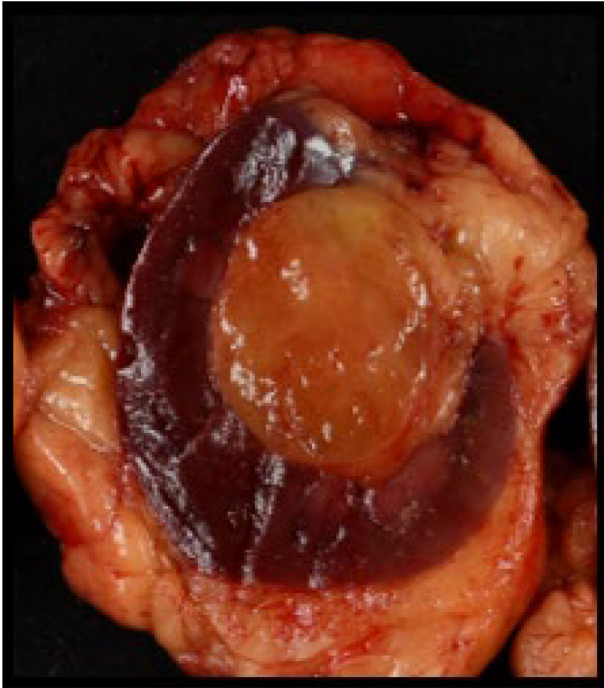


Fig. 3 Surgical specimen of the left kidney: Macroscopic examination showed a well-circumscribed round brownish-red tumor (31 × 26 mm) located at the hilum.

Against the background of abundant mucous stroma, spindle cells were heterogeneously distributed, brown fat cells were sparsely distributed, and white adipocytes were absent (Fig. 4a). The tumor was characterized by the presence of spindle cells positive for CD34 and brown adipocytes

positive for S-100 (Fig. 4b). CDK4 and MDM2 were negative, which are typically positive in liposarcoma (Fig. 4c,d). Based on these results, the tumor was diagnosed as a hibernoma.

Discussion

Hibernomas are rare benign tumors of the brown adipose tissue commonly found in hibernating animals and neonates.^{5,6} They are typically associated with translocations in chromosome band 11q13, with concomitant deletions of MEN1 and AIP.⁷ Hibernomas have four morphologic variants, namely typical, spindle cell, lipoma-like, and myxoid.¹

We present a case of renal hibernoma, which, to the best of our knowledge, is the third documented case worldwide (Table 1).^{3,4} Clinically diagnosing this rare benign tumor presents significant challenges. Its characteristics of rapid growth and contrast-enhancement on imaging tests often mimic those of malignant neoplasms. The average growth rate of our hibernoma was 5 mm/year, which is comparable to the mean growth rate of small renal cell carcinomas (2.8–4.0 mm/year^{8,9}). In terms of imaging, contrast-enhanced CT has proven exceptionally useful in distinguishing malignant tumors from benign ones. Phillip *et al.* investigated the actual enhancement mean HU in papillary RCC. They reported actual enhancement mean values in the corticomedullary, nephrogenic and delayed phases for papillary RCC as 37.6 HU, 56.8 HU, and 48.4 HU.¹⁰ In our case, the imaging characteristics of the renal tumor were analogous to the actual enhancement mean values of papillary RCC. Given these results, we decided to perform a radical nephrectomy, suspecting a probable malignancy. Brown adipose tissue contains more mitochondria than white adipose tissue. Thus,

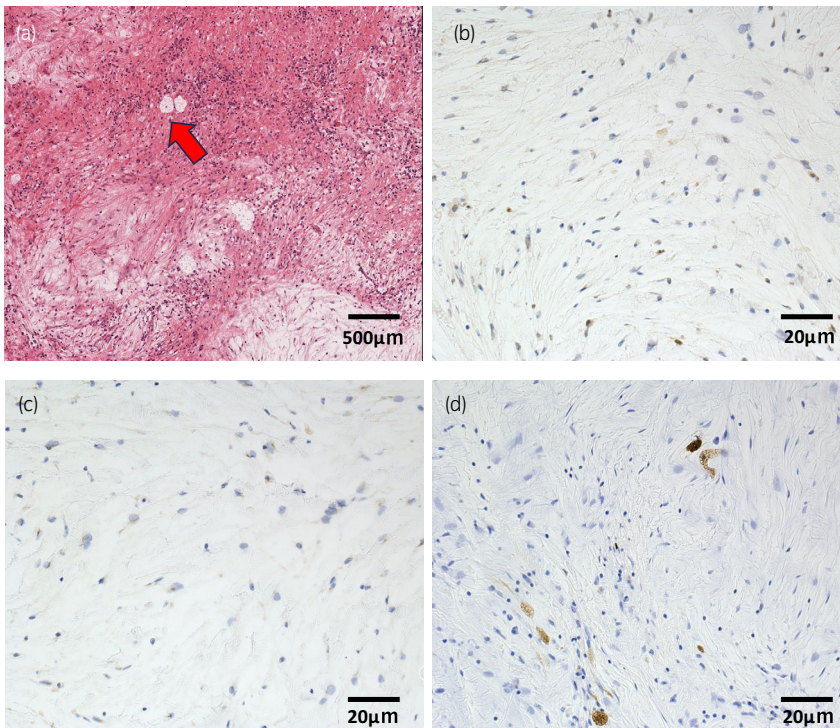


Fig. 4 (a) Hematoxylin and eosin staining shows brown fat cells (arrow head) with stromal spindle cells, myxoid stroma, and inflammatory changes. Immunostaining showed that (b) S100 was positive (arrow head), (c) CDK4 and (d) MDM2 were negative.

Table 1 Characteristics of the three previously reported cases of renal hibernoma, including our case

	Age	Size/site	Diagnostic method	Pathologic characteristics	Presence or absence of surgery
Our case	71	31 × 26 mm Left renal sinus	Pathologic diagnosis with nephrectomy	Stromal spindle cells Myxoid stroma, and inflammatory change	Radical nephrectomy
Lukas <i>et al.</i> (2020) ⁴	77	70 × 65 mm The lower pole of the right kidney	Pathologic diagnosis with nephrectomy	Adipocytes, hibernoma cells, and inflammatory cells	Radical nephrectomy
Larkin <i>et al.</i> (2022) ⁵	64	40 × 34 mm Left renal pelvis	Pathologic diagnosis with nephrectomy	Equal ratio of adipocytes to hibernoma cells with inflammatory cells	Radical nephrectomy

hibernomas may grow faster and show a progressive contrast effect due to the abundance of blood vessels that supply energy.¹¹

On immunohistochemistry, the tumor in this case was negative for MDM2 and CDK4, which ruled out the possibility of it being a liposarcoma. S-100 proteins, which are exclusively expressed in vertebrates, play a role in regulating cell proliferation.¹² Furlong *et al.* reported that S-100 proteins were positive in immunohistochemistry for the majority of hibernomas (85%).⁵ In this case, the tumor was tested positive for S-100 proteins. Based on these morphological and immunohistologic findings, we identified the tumor as a hibernoma.

In their study, Kelsey *et al.* conducted two percutaneous tumor biopsies on a hibernoma located in the renal pelvis and confirmed an inflammatory infiltrate with adipocytes. However, they ultimately performed a nephrectomy due to the inability to exclude malignancy, considering the tumor's growth rate and progressive contrast effect.⁴ As this report indicates, percutaneous tumor biopsy may be insufficient for diagnosing hibernoma. Hence, at present, it is difficult to diagnose renal hibernoma without resorting to nephrectomy.

Brown adipose tissue is typically found in the thigh, shoulder, neck, and back. It is abundant in newborns and hibernating animals, but its prevalence and metabolic activity in humans decreases with aging.² Brown adipose tissue expresses abundant UCP1, a class of mitochondrial proteins. UCP1 generates heat in newborns and hibernating animals by dissipating the proton gradient across the mitochondrial membrane.¹³ When UCP1 is activated by stimuli such as cold, energy is directly converted into heat, leading to increased anaerobic glycolysis and glucose uptake.¹⁴ Takahiro *et al.* reported a decrease in FDG uptake in malignant tumors and an increase in FDG uptake in UCP1⁺ brown adipose tissue under cold conditions.¹⁵ Several studies have also reported high FDG uptake in hibernomas,¹⁶ even higher than in liposarcomas.¹⁷ Therefore, ¹⁸F-FDG positron emission tomography might be useful in the diagnosis of hibernoma due to the difference of FDG uptake between hibernoma and malignant tumors under cold conditions. However, with regard to renal hibernoma, the usefulness of FDG PET may not be as high as in hibernoma in other tissues because FDG is accumulated in the urinary tracts due to the physiologic excretion of FDG. Nonetheless, a previous clinical study

reported that FDG uptake in brown adipose tissue increased under cold temperatures compared to warm temperatures.¹⁴ Hence, the temperature-dependent change of FDG uptake might be a useful diagnostic finding of renal hibernoma.

Consequently, the development of new diagnostic method is essential to prevent the loss of renal function due to nephrectomy.

Conclusion

We have reported a rare case of hibernoma in the renal sinus, representing only the third such case documented worldwide. To avoid loss of renal function, there is a pressing need to develop new, accurate clinical diagnostic methods for hibernoma that do not require a nephrectomy.

Acknowledgments

We thank all members from the Department of Urology, Dr. Taishi Takahara from the Department of Surgical Pathology, and Dr. Takahiro Yamamoto from the Department of Radiology, Aichi Medical University for discussions about the study.

Author contributions

Ayano Kashima: Conceptualization; writing – original draft; writing – review and editing. Tsuyoshi Majima: Conceptualization; supervision; writing – original draft; writing – review and editing. Tomoaki Muramatsu: Conceptualization; writing – original draft; writing – review and editing. Haruka Kurosu: Conceptualization. Hideji Kawanishi: Conceptualization. Ikuo Kobayashi: Conceptualization. Keishi Kajikawa: Conceptualization. Taishi Takahara: Data curation. Takahiro Yamamoto: Data curation. Naoto Sassa: Supervision.

Conflict of interest

The authors declare no conflicts of interest.

Approval of the research protocol by an Institutional Reviewer Board

Not applicable.

Informed consent

Informed consent was obtained from the patient.

Registry and the Registration No. of the study/trial

Not applicable.

References

- Merkel H. On a pseudolipoma of the breast (peculiar fat tumor). *Beitr. Pathol. Anat.* 1906; **39**: 152–7.
- Ahn C, Harvey JC. Mediastinal hibernoma, a rare tumor. *Ann. Thorac. Surg.* 1990; **50**: 828–30.
- Streich L, Yang X. Hibernoma with inflammatory features: a description of a new variant. *Hum. Pathol. Case Rep.* 2020; **22**: 200429.
- Larkin K, Chua KJ, Doppalapudi SK *et al.* Inflammatory hibernoma of the renal hilum mimicking a renal pelvis tumor. *J. Kidney Cancer VHL* 2022; **9**: 48–50.
- Furlong MA, Fanburg-Smith JC, Miettinen M. The morphologic spectrum of hibernoma: a clinicopathologic study of 170 cases. *Am. J. Surg. Pathol.* 2001; **25**: 809–14.
- Lidell ME. Brow adipose tissue in human infants. *Handb. Exp. Pharmacol.* 2019; **251**: 107–23.
- Nord KH, Magnusson L, Isaksson M *et al.* Concomitant deletions of tumor suppressor genes MEN1 and AIP are essential for the pathogenesis of the brown fat tumor hibernoma. *Proc. Natl. Acad. Sci. USA* 2010; **107**: 21122–2112.
- Li X-S, Yao L, Gong K *et al.* Growth pattern of renal cell carcinoma (RCC) in patients with delayed surgical intervention. *J. Cancer Res. Clin. Oncol.* 2012; **138**: 269–74.
- Chawla SN, Crispen PL, Hanlon AL, Greenberg RE, Chen DYT, Uzzo RG. The natural history of observed enhancing renal masses: meta-analysis and review of the world literature. *J. Urol.* 2006; **175**: 425–31.
- Pierorazio PM, Hyams ES, Tsai S *et al.* Multiphasic enhancement patterns of small renal masses (≤ 4 cm) on preoperative computed tomography: utility for distinguishing subtypes of renal cell carcinoma, angiomyolipoma, and oncocytoma. *Urology* 2013; **81**: 1265–71.
- Lazar MA. Developmental biology. How now, brown fat? *Science* 2008; **321**: 1048–9.
- Donato R, R cannon B, Sorci G *et al.* Function of S100 proteins. *Curr. Mol. Med.* 2013; **13**: 24–57.
- Malzahn J, Kastrenopoulou A, Papadimitriou-Olivgeri I *et al.* Immunophenotypic expression of UCPI in hibernoma and other adipose/non adipose soft tissue tumours. *Clin. Sarcoma Res.* 2019; **9**: 8.
- Saito M, Okamatsu-Ogura Y, Matsushita M *et al.* High incidence of metabolically active brown adipose tissue in healthy adult humans: effects of cold exposure and adiposity. *Diabetes* 2009; **58**: 1526–31.
- Seki T, Yang Y, Sun X *et al.* Brown-fat-mediated tumour suppression by cold-altered global metabolism. *Nature* 2022; **608**: 421–8.
- Burt AM, Huang BK. Imaging review of lipomatous musculoskeletal lesions. *Sicot J.* 2017; **3**: 34.
- Park JH, Ogura K, Fujiwara T *et al.* The values and limitations of FDG-PET/CT for diagnosis of hibernoma. *Case Rep. Orthop.* 2015; **2015**: 958690.