

Renal Oncocytoma: Clinical Experience of Taipei Veterans General Hospital

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Background: Renal oncocytoma has been reported mostly in the Western literature, and only a few cases have been reported in Eastern populations. In the present study, we review the clinical course of renal oncocytoma in our institution.

Methods: We obtained the files of 13 cases of renal oncocytoma between 1988 and 2006 from the pathological archives of Taipei Veterans General Hospital. We retrospectively analyzed the patients' characteristics, clinical manifestations, surgical technique and clinical outcome.

Results: The study population comprised 10 men and 3 women, and the mean age at diagnosis was 59.6 years (range, 37–75 years). Twelve patients (92%) were asymptomatic at presentation and were incidentally diagnosed to have renal tumor by sonography (9 patients), computed tomography (1 patient) or magnetic resonance imaging (2 patients), and 1 presented with hematuria. The clinical impression of oncocytoma was made preoperatively in only 3 patients by imaging studies, and most of the patients (76.9%) were diagnosed with renal cell carcinoma before surgery. Ten were treated with radical nephrectomy, 2 with partial nephrectomy, and 1 received excisional biopsy. All patients had unilateral solitary renal tumor; the right kidney was involved in 7 cases (54%) and the left in 6 (46%). Mean tumor size was 5.3 cm (range, 2.7–8.5 cm). Three patients were lost to follow-up in our series, and there was no recurrence or death (100% disease-specific survival) in the remaining 10 patients (77%) who were followed-up for a mean duration of 53.2 months (range, 10–117 months).

Conclusion: Renal oncocytoma has a benign clinical course with excellent long-term outcomes. Currently, nephron-sparing surgery is the mainstay of treatment, especially in patients with small tumors. However, accurate preoperative diagnosis based only on imaging studies is difficult, and radical nephrectomy was performed for most of the patients in our series. [*J Chin Med Assoc* 2008;71(5):254–258]

Key Words: kidney, oncocytoma, renal cell carcinoma, renal tumor

Introduction

Renal oncocytoma was first described in 1942 by Zippel and was grouped into renal malignancy at that time.¹ It was not until 1976 that it was accepted to be a distinct benign renal tumor with the report of 13 additional cases by Klein and Valensi.² The current 2004 World Health Organization classification of renal epithelial tumors recognizes benign lesions such as oncocytoma and angiomyolipoma.³ Oncocytomas are characterized by uniform polygonal or round cells with mitochondria-rich eosinophilic granular cytoplasm that occur in diffuse sheets or as islands of cells in an edematous stroma.³ The cells of origin are thought to be the intercalated

cells in the collecting duct.⁴ They account for 3–7% of all solid renal neoplasms.⁵ The majority (58–83%) are incidental findings on radiologic images from ultrasonography, computed tomography (CT) and magnetic resonance imaging (MRI).^{6–8} Most often, the diagnosis of renal oncocytoma is made after surgical removal of the tumor because of the lack of specific clinical features and imaging findings. Moreover, fine needle aspiration and biopsy are often not diagnostic due to oncocytoma having similar histopathologic characteristics as various eosinophilic variants of renal cell carcinoma (RCC).⁹ Consequently, most patients with these tumors are treated aggressively with either partial or radical nephrectomy.



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Renal oncocytoma has been reported mostly in the Western literature, and only a few cases have been reported in Eastern populations.¹⁰⁻¹² In the present study, we review the clinical course of renal oncocytoma in our institution.

Methods

A total of 13 cases of renal oncocytoma, diagnosed between January 1988 and June 2006, were retrieved from the surgical pathological archives at our hospital. In this retrospective chart-review study, clinicopathologic data including patient characteristics, clinical manifestations, surgical technique, pathologic findings and clinical outcome were analyzed.

Tumor size was evaluated by measuring the largest diameter of the tumor mass removed surgically. Tumor growth patterns were classified as exophytic or non-exophytic, and non-exophytic growth pattern was further subcategorized as with or without renal sinus involvement.

Results

The demographic and clinical features of the patients are shown in Table 1. There were 10 males and 3 females (male/female ratio of 3.3); mean age at presentation was 59.6 years (range, 37–75 years). Of the 13 cases, 12 (92.3%) were diagnosed incidentally as renal tumor by sonography ($n=9$), CT ($n=1$) or MRI ($n=2$), and 1 presented with microscopic hematuria. Preoperatively, the clinical impression of oncocytoma had been considered in only 3 (23.1%) patients following various imaging studies. Among them, 2 underwent CT which showed a centrally located stellate area of low attenuation (Figure 1), and the other underwent MRI which revealed a centrally located stellate area of low signal intensity on T1-weighted imaging. Most patients (76.9%) were suspected to have RCC and were treated accordingly. Ten (76.9%) patients underwent radical nephrectomy, 2 (15.4%) underwent partial nephrectomy and 1 (7.7%) received excisional biopsy. Radical nephrectomy was performed with the open method in 8 patients and laparoscopically in 2 patients.

The tumor location was right-sided in 7 (53.8%) cases and left-sided in 6 (46.2%). No bilateral or multifocal disease was observed. CT or MRI images were available for 10 patients; an exophytic growth pattern was noted in 2 cases and non-exophytic growth pattern was noted in 8, including 3 without and 5 with renal sinus involvement. Tumor size ranged from 2.7 cm to

Table 1. Demographic characteristics and clinical features of the patients*

Sex	
Male	10 (76.9)
Female	3 (23.1)
Presentation	
Incidental	12 (92.3)
Symptomatic	1 (7.7)
Laterality	
Right	7 (53.8)
Left	6 (46.2)
Surgery	
Radical nephrectomy	10 (76.9)
Partial nephrectomy	2 (15.4)
Excisional biopsy	1 (7.7)
Size	
< 4 cm	6 (46.2)
≥ 4 cm	7 (53.8)

*Data presented as n (%).

8.5 cm in greatest dimension (<4 cm in 6 patients, ≥4 cm in 7 patients), with a mean tumor size of 5.3 cm.

Most of the pathologic features of the tumors in our series were those of typical oncocytoma, i.e. oncocytes arranged in trabecular, acinar and glandular patterns. However, there was 1 patient who was initially diagnosed with chromophobe RCC; this diagnosis was revised to oncocytoma after further immunohistochemistry study with a panel of cytokeratin staining profiles (cytokeratin 7). In addition, the coexistence of oncocytoma and angiomyolipoma in the same lesion was noted in 1 case. No extension to perinephric fat tissue or lymphovascular invasion was observed.

Excluding the 3 patients who were lost to follow-up, there was neither recurrence nor death from oncocytoma during a mean follow-up of 53.2 months (range, 10–117 months). Accordingly, the disease-specific survival was 100%.

Discussion

Renal oncocytomas occur with an overall incidence of 3–7% among all renal tumors. Most (56–91%) are diagnosed incidentally, but symptomatic patients usually manifest with gross hematuria, flank pain or a palpable mass.¹³ The male/female predominance is 2–3:1, and peak occurrence is between the ages of 40 and 60. Average tumor size is 6 cm. In our series, the mean age at diagnosis was 59.6 years, and there was a male predilection with a male-to-female ratio of 3.3. Most

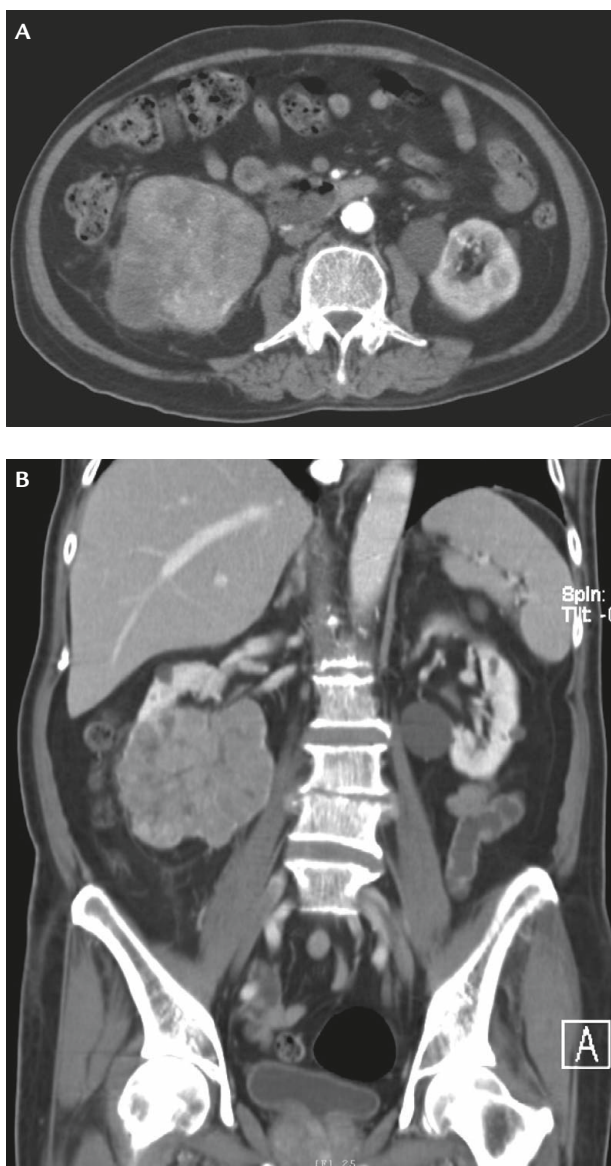


Figure 1. (A) Pelvic computed tomography, axial view, shows a right renal tumor with central stellate scar. (B) Pelvic computed tomography, coronal view, shows a right renal tumor with central stellate scar and renal sinus involvement.

patients presented with renal tumor incidentally except for 1 with hematuria. The mean tumor size was 5.3 cm. The demographic characteristics of our population, including gender distribution, peak occurrence, tumor size and clinical symptoms, are similar to the findings of previous studies. Moreover, the demographics of oncocytoma parallel those of RCC.¹⁴ Accordingly, clinical features cannot be used to discriminate oncocytoma from RCC.

The minimally invasive nature of imaging studies makes such techniques ideal for diagnosing benign tumors. However, no radiologic imaging techniques are currently available to reliably confirm a preoperative

diagnosis of oncocytoma. CT usually reveals a solid homogeneous lesion with a centrally located stellate area of low attenuation. On MRI, most oncocytomas demonstrate low signal intensity relative to the renal cortex on T1-weighted images. Twenty-seven percent of oncocytomas also demonstrate a central stellate scar on MRI.¹⁵ Angiography shows a spoke-wheel vascular pattern, but inconsistently. The degree of confidence with angiography is low. Hypovascular lesions may result in false-negative results, and hypervascular lesions may mimic RCCs. In our series, 2 patients presented with typical CT findings and 1 with typical MRI finding. However, these characteristics may suggest but cannot definitively diagnose oncocytoma.^{16,17} Gormley et al reported that the nuclear agent, technetium sestamibi, which was remarkably retained in mitochondria, showed increased uptake by oncocytomas compared to other renal lesions including RCC, angiomyolipoma and cysts.¹⁸ MR spectroscopy has been demonstrated to reveal different spectrographic signals from oncocytoma compared to RCC.¹⁹ Currently, few articles have reported the use of positron emission tomography (PET) for the diagnosis of oncocytoma. Blake et al reported a case of renal oncocytoma displaying intense activity on ¹⁸F-fluorodeoxyglucose PET.²⁰ It might be hypothesized that a benign tumor would behave metabolically differently from a malignant tumor, resulting in differential ¹⁸F-fluorodeoxyglucose uptake. Shriki et al described the first report of the I-11C acetate PET scan appearance of a renal oncocytoma. Possible mechanisms for increased uptake include dysfunctional but upregulated oxidative phosphorylation, or uptake through lipid biosynthesis pathways.²¹ All the novel imaging techniques were investigational, and further validated studies are required.

In our series, 1 patient was diagnosed with chromophobe renal cell carcinoma initially, which was revised to oncocytoma after further analysis of cytokeratin staining profiles. Differentiating oncocytoma from RCC histologically can be difficult, especially from chromophobe RCC, which originates from intercalated cells of the kidney tubules as well.²² The most common microscopic feature shared by oncocytomas and chromophobe RCC is the presence of abundant granular eosinophilic cells.²³ Oncocytomas mainly consist of eosinophilic cells arranged in an organoid, tubulocystic or mixed pattern; chromophobe RCC are always comprised of two cell types, with one type consisting of abundant eosinophilic cytoplasm and the other containing abundant, clear, and finely reticulated cytoplasm, which are arranged in diffuse sheets of cells aligned along fibrovascular septae.²⁴ Unlike the round and uniform nuclei typical of oncocytomas, chromophobe

RCC are significantly more likely to have irregular nuclear contour with bi- or multinucleation. With regard to Hales's colloidal iron stain, chromophobe RCC show strong diffuse positivity and oncocytoma show negative or weak focal staining. Recent data proposed that cytokeratin staining profiles may be useful for discriminating oncocytoma from its renal mimics: oncocytomas are typically CD7-, CD14+ and CD20+, while most chromophobe RCCs are positive for CD7; the various eosinophilic RCC are typically negative for CD14, and only 0–8% of RCCs are positive for CD20.^{25–27}

The finding of frequent coexistence of oncocytoma and chromophobe RCC is interesting,²⁸ suggesting a potential relation between these entities. In addition, both originate from the tubular intercalated cells and share common histologic findings. There is growing evidence that oncocytomas represent the benign end of a spectrum and chromophobe RCCs reside at the malignant end.²⁹ The phenomenon of renal oncocytoma with an increased risk of chromophobe RCC has only been described in Birt-Hogg-Dube syndrome, which is grouped as familial renal oncocytoma. This syndrome is a rare autosomal dominant condition characterized by benign skin tumors, pulmonary cysts and multiple renal tumors, particularly oncocytomas and chromophobe RCC,³⁰ resulting from the mutation of the Birt-Hogg-Dube gene on the short arm of chromosome 7.³¹ In this syndrome, oncocytomas are usually multifocal and bilateral.

The coexistence of oncocytoma and angiomyolipoma in the same lesion was noted in 1 case. Under the preoperative impression of oncocytoma, this male patient received excisional biopsy, and pathology revealed concurrent oncocytoma and angiomyolipoma. Although concurrence of RCC and oncocytoma within the same kidney is well recognized, the simultaneous existence of angiomyolipoma and oncocytoma is uncommon. To our knowledge, only 17 cases of concurrent angiomyolipoma and oncocytoma have been reported in the literature, and most of the patients were female.^{32,33} This observation parallels the female predominance of angiomyolipoma as opposed to the male predominance of oncocytoma. The mechanisms that cause a kidney to possess concurrent angiomyolipoma and oncocytoma are unclear at present.

The natural history of oncocytomas follows a benign and usually slow-growing course despite the occasional presence of invasive features such as lymphovascular and perinephric fat tissue involvement. Accordingly, conservative surgery, even for large tumors, should be performed, and the limit of conservative surgery is only technical.³⁴ In our series, most patients (76.9%)

underwent radical nephrectomy, which might be considered over-treatment. Because of the uncertainties with regard to the benign nature of the tumor before surgical intervention, radical nephrectomy was warranted in most patients. Currently, nephron-sparing surgery has been recommended as the standard of care for renal oncocytoma,³⁵ and is also considered the treatment of choice for cT1 clinically localized renal cell carcinoma.^{36,37}

In conclusion, renal oncocytoma behaves as a benign tumor, and the long-term prognosis is excellent. Nephron-sparing surgery is the mainstay of treatment, especially for patients with small tumors. However, as accurate preoperative diagnosis based on imaging studies was difficult, radical nephrectomy was warranted for most of the patients in our series.

References

1. Zippel L. Zur Kenntnis der oncocytem. *Virchow Arch Pathol Anat* 1942;308:360–82.
2. Klein MJ, Valensi QJ. Proximal tubular adenomas of kidney with so-called oncocytic features: a clinicopathologic study of 13 cases of a rarely reported neoplasm. *Cancer* 1976;38:906–14.
3. Eble JN, Sauter G, Epstein JI, Sesterhenn IA. World Health Organization classification of tumours. In: *Pathology and Genetics of Tumours of the Urinary System and Male Genital Organs*. Lyon, France: IARC Press, 2004.
4. Storkel S, Pannen B, Thoenes W, Steart PV, Wagner S, Drenckhahn D. Intercalated cells as a probable source for the development of renal oncocytoma. *Virchows Arch B Cell Pathol Mol Pathol* 1988;56:185–9.
5. Licht MR. Renal adenoma and oncocytoma. *Semin Urol Oncol* 1995;13:262–6.
6. Dechet CB, Bostwick DG, Blute ML, Bryant SC, Zincke H. Renal oncocytoma: multifocality, bilateralism, metachronous tumor development and coexistent renal cell carcinoma. *J Urol* 1999;162:40–2.
7. Amin MB, Crotty TB, Tickoo SK, Farrow GM. Renal oncocytoma: a reappraisal of morphologic features with clinicopathologic findings in 80 cases. *Am J Surg Pathol* 1997;21:1–12.
8. Licht MR, Novick AC, Tubbs RR, Klein EA, Levin HS, Strem SB. Renal oncocytoma: clinical and biological correlates. *J Urol* 1993;150:1380–3.
9. Renshaw AA, Zhang H, Corless CL, Fletcher JA, Pins MR. Solid variants of papillary (chromophil) renal cell carcinoma: clinicopathologic and genetic features. *Am J Surg Pathol* 1997; 21:1203–9.
10. Makita Y, Inenaga T, Kinjo M, Komatsu K, Onoyama K, Fujishima M. Renal oncocytoma developed in a long-term hemodialysis patient. *Nephron* 1991;57:355–7.
11. Peng CWB, Yip SKH, Tan PH, Ng LG. Bilateral synchronous renal oncocytoma. *Ann Acad Med Singapore* 2001;30:642–5.
12. Yen TH, Chen Y, Lin JL, Ng KF. Renal oncocytoma in Taiwan. *Ren Fail* 2006;28:141–7.
13. Chao DH, Zisman A, Pantuck AJ, Freedland SJ, Said JW, Belldgrun AS. Changing concepts in the management of renal oncocytoma. *Urology* 2002;59:635–42.
14. Motzer RJ, Bander NH, Nanus DM. Renal-cell carcinoma. *N Engl J Med* 1996;335:865–75.

15. Harmon WJ, King BF, Lieber MM. Renal oncocytoma: magnetic resonance imaging characteristics. *J Urol* 1996;155:863-7.
16. Tikkakoski T, Paivansalo M, Alanen A, Nurmi M, Taavitsainen M, Farin P, Apaja-Sarkkinen M. Radiologic findings in renal oncocytoma. *Acta Radiol* 1991;32:363-7.
17. Davidson AJ, Hayes WS, Hartman DS, McCarthy WF, Davis CJ Jr. Renal oncocytoma and carcinoma: failure of differentiation with CT. *Radiology* 1993;186:693-6.
18. Gormley TS, Van Every MJ, Moreno AJ. Renal oncocytoma: preoperative diagnosis using technetium 99m sestamibi imaging. *Urology* 1996;48:33-9.
19. Nurenberg P, Sartoni-D'Ambrosia G, Szczepaniak LS. Magnetic resonance spectroscopy of renal and other retroperitoneal tumors. *Curr Opin Urol* 2002;12:375-80.
20. Blake MA, McKernan M, Setty B, Fischman AJ, Mueller PR. Renal oncocytoma displaying intense activity on 18F-FDG PET. *AJR Am J Roentgenol* 2006;186:269-70.
21. Shriki J, Murthy V, Brown J. Renal oncocytoma on I-11C acetate positron emission tomography: case report and literature review. *Mol Imaging Biol* 2006;8:208-11.
22. Perez-Ordóñez B, Hamed G, Campbell S, Erlandson RA, Russo P, Gaudin PB, Reuter VE. Renal oncocytoma: a clinicopathologic study of 70 cases. *Am J Surg Pathol* 1997;21:871-83.
23. Tickoo SK, Amin MB. Discriminant nuclear features of renal oncocytoma and chromophobe renal cell carcinoma: analysis of their potential utility in the differential diagnosis. *Am J Clin Pathol* 1998;110:782-7.
24. Skinnider BF, Jones EC. Renal oncocytoma and chromophobe renal cell carcinoma: a comparison of colloidal iron staining and electron microscopy. *Am J Clin Pathol* 1999;111:796-803.
25. Stopyra GA, Warhol MJ, Mulhaupt HA. Cytokeratin 20 immunoreactivity in renal oncocytomas. *J Histochem Cytochem* 2001;49:919-20.
26. Chu PG, Weiss LM. Cytokeratin 14 immunoreactivity distinguishes oncocytic tumour from its renal mimics: an immunohistochemical study of 63 cases. *Histopathology* 2001;39:455-62.
27. Leroy X, Moukassa D, Copin MC, Saint F, Mazeman E, Gosselin B. Utility of cytokeratin 7 for distinguishing chromophobe renal cell carcinoma from renal oncocytoma. *Eur Urol* 2000;37:484-7.
28. Weirich G, Glenn G, Junker K, Merino M, Störkel S, Lubensky I, Choyke P, et al. Familial renal oncocytoma: clinicopathological study of 5 families. *J Urol* 1998;160:335-40.
29. Rowsell C, Fleshner N, Marrano P, Squire J, Evans A. Papillary renal cell carcinoma within a renal oncocytoma: case report of an incidental finding of a tumour within a tumour. *J Clin Pathol* 2007;60:426-8.
30. Pavlovich CP, Walther MM, Eyler RA, Hewitt SM, Zbar B, Linehan WM, Merino MJ. Renal tumors in the Birt-Hogg-Dube syndrome. *Am J Surg Pathol* 2002;26:1542-52.
31. Schmidt LS, Warren MB, Nickerson ML, Weirich G, Matrosova V, Toro JR, Turner ML, et al. Birt-Hogg-Dube syndrome, a genodermatosis associated with spontaneous pneumothorax and kidney neoplasia, maps to chromosome 17p11.2. *Am J Hum Genet* 2001;69:876-82.
32. Bahrami A, Schwartz MR, Ayala AG, Goldfarb RA, Brady JR, Takei H, Ro JY. Concurrent angiomyolipoma and two oncocytomas in the same kidney. *Ann Diagn Pathol* 2007;11:132-6.
33. Ou YC, Wu HC, Yang CR, Chang CL, Hwang TI, Chang CH. Renal angiomyolipoma: experience of 23 patients. *J Chin Med Assoc* 1991;48:217-23.
34. Neuzillet Y, Lechevallier E, Andre M, Daniel L, Nahon O, Coulanges C. Follow-up of renal oncocytoma diagnosed by percutaneous tumor biopsy. *Urology* 2005;66:1181-5.
35. Romis L, Cindolo L, Patard JJ, Messina G, Altieri V, Salomon L, Abbou CC, et al. Frequency, clinical presentation and evolution of renal oncocytomas: multicentric experience from a European database. *Eur Urol* 2004;45:53-7.
36. Lerner SE, Hawkins CA, Blute ML, Grabner A, Wollan PC, Eickholt JT, Zincke H. Disease outcome in patients with low stage renal cell carcinoma treated with nephron sparing or radical surgery. *J Urol* 2002;167:884-9.
37. Licht MR, Novick AC, Goormastic M. Nephron sparing surgery in incidental versus suspected renal cell carcinoma. *J Urol* 1994;152:39-42.