Dilemmas in diagnosis and natural history of renal oncocytoma and implications for management

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Abstract

Introduction: Oncocytomas have traditionally been treated with surgical excision; however, their excellent long-term prognosis has popularized conservative and minimally invasive ablative techniques. We evaluated the evolving management and natural history of renal oncocytomas and investigated the relationship between radiological and histopathological diagnosis.
Methods: We performed a 17-year retrospective cohort study on all patients with a confirmed histopathological diagnosis of renal oncocytoma. The primary outcome variables were long-term outcomes, coexistence with renal cell carcinoma, and development of metastatic disease.
Results: A total of 38 oncocytomas were reported in 36 patients. Of the 36 patients, 29 (81%) were diagnosed incidentally. Oncocytoma was considered in the differential diagnosis in 4 oncocytomas (10.5%). In total, 34 patients underwent early surgical intervention; of these, 27 (79.4%) underwent radical nephrectomy and 7 underwent partial nephrectomy (20.6%). Four patients (11.1%) were managed conservatively with surveillance. No patients developed recurrence or metastatic disease after a median follow-up of 84 months (range: 4–178).
Conclusions: The diagnostic accuracy for imaging modalities in renal oncocytoma is poor. Surveillance or minimally invasive ablative techniques are appropriate in selected patients with biopsy-proven oncocytoma that are not increasing in size.

Introduction

Oncocytomas represent 3% to 7% of all solid renal tumours and their incidence increases to 18% when tumours <4 cm are considered.[1,2] Although most oncocytomas behave in a benign manner, rare cases of metastases have been reported.[3] Currently, no imaging modalities can accurately predict the diagnosis of renal oncocytoma.[1,4] Renal mass biopsy is the most reliable diagnostic modality, but can be complicated by histopathological similarities between oncocytoma and eosinophilic variants of chromophobe renal cell carcinoma (RCC).[1,2] Renal oncocytoma may coexist with RCC as hybrid tumours,[4] which has further implications for diagnosis and in particular for conservative management.

Traditionally, the standard treatment for renal oncocytoma has been surgical excision by radical nephrectomy. More recently, with improved radiological and biopsy techniques and evidence-based follow-up data suggesting excellent long-term prognosis, minimally extensive and ablative renal sparing techniques, such as partial nephrectomy, cryotherapy, or radiofrequency, have become alternative options.[4] The objectives of this study were to evaluate evolving management and natural history of renal oncocytomas at our institution, and to investigate the correlation between radiological and histopathological diagnosis.

Methods

A retrospective cohort study was performed on patients diagnosed with confirmed pathological diagnosis of renal oncocytoma in Tallaght Hospital Dublin from January 1998 to June 2015. Patients were identified from pathology and clinical HIPE (Hospital In-Patient Enquiry) databases. Patients were excluded if pathological diagnosis was not confirmed. Recorded patient demographics included age, gender, preoperative radiological diagnosis, biopsy reports, management (surgery or other modalities), surgical histopathology, and long-term follow-up. Tumour size was recorded at imaging and at final histopathology (if excised). Details regarding tumour size at diagnosis, growth rate and final outcome were recorded in cases managed conservatively.

Statistical analysis was performed using a two-tailed Student *t*-test with unequal variances. Differences were considered significant at $p < 0.05$.

Results

Patient demographics

A total of 820 renal tumours with confirmed histopathology were recorded (1998–2015). Of these, 38 were oncocytomas (4.6%) diagnosed in 36 patients. The median age was 57 (range: 19–79) years and the male-to-female ratio was equal.

A total of 8 patients (21%) presented with flank pain and 1 patient had a palpable mass. The remaining 27 (74%) patients were diagnosed incidentally with either ultrasonography or computed tomography (CT). Right-sided tumours were present in 21 patients (58.3%) and 2 patients (5.3%) presented with bilateral tumours. Oncocytoma was present in 1 patient with Birt-Hogg-Dube (BHD) syndrome. No patients had metastasis at diagnosis.

Investigations and differential diagnosis

All patients underwent contrast-enhanced triphasic CT. Oncocytoma was considered in the differential diagnosis in only 4 tumours (10.5%). Thirty-two tumours (84.2%) were diagnosed as neoplastic RCCs on imaging, 2 tumours were diagnosed as angiomyolipoma (n = 1) and cystic adenoma (n = 1), respectively. Renal biopsy was performed on 4 tumours (10.5%). All 4 were not the same cases in whom imaging was suspicious for oncocytoma. The median tumour size on imaging was 4.65 (range: 1.5–18) cm.

Management

In total, 34 tumours (89%) underwent early surgical intervention; including radical nephrectomy (27 oncocytomas, 71%) and partial nephrectomy (7 oncocytomas, 18%). The median tumour size at surgical histopathology in the partial nephrectomy and radical nephrectomy groups were 3 cm (range: 2.3–6.5) and 4.8 cm (range: 2.3–16), respectively

(p = 0.002). The median histopathological tumour size was 4.8 cm (range: 2.2–16). One radical nephrectomy specimen revealed multifocal oncocytomas. Vascular invasion or perinephric fat extension was reported in 2 tumours (5.2%). There were no coexisting RCCs in this series of oncocytomas.

Four patients underwent CT surveillance and the median tumour size by radiology was 3.65 cm (range: 2–6.1 (Table 1). The indications for surveillance in these patients were a high suspicion of oncocytoma on imaging, oncocytoma in solitary kidney, and patients that were unfit for surgery. The median follow-up for these patients undergoing surveillance was 3.75 years (range: 1–8). The mean interval size increase of 0.4 cm/year was noted in 2 patients. One patient with an increase of only 0.19 cm/year continues on surveillance and the second patient with an interval increase of 0.6 cm/year underwent radiofrequency ablation. In the other 2 patients, tumour size remained stable during follow-up (2 years) and both continue on follow-up (Table 1).

Follow-up in patients undergoing surgery

None of the patients who underwent surgical intervention developed recurrence or metastatic disease after a median follow-up of 84 months (range: 4–178).

Discussion

The incidence of oncocytoma from all renal tumours (benign and malignant inclusive) on histopathology at our centre (4.7%) is comparable to previous studies reporting an overall incidence of 3% to 7% and with most patients having an incidental radiological diagnosis.[5] Oncocytomas demonstrate solid, well-demarcated homogenous features on CT and therefore often mimic RCC. A central stellate scar, observed in 27% to 54% of cases, can also be difficult to differentiate from central tumour necrosis.[6] Other relevant, but not distinctive, diagnostic findings on CT for renal oncocytomas may include hemorrhage, calcification and necrosis.

Table 1. Patient follow-up and tumour characteristics of 4 cases with oncocytoma undergoing surveillance				
Parameters	1	2	3	4
Age, gender	57, male	71, female	51, female	71, male
Tumour size at diagnosis	4.2 cm	2.3 cm	5 cm	2 cm
Indication for conservative management	High suspicion of oncocytoma on CT scan, confirmed on biopsy	Unfit for surgery	Bilateral oncocytomas, second tumour in solitary kidney	Bilateral oncocytomas, second tumour in solitary kidney
Total follow-up period	8 years	4 years	2 years	1 year
Growth velocity	0.19 cm/year	0.6 cm/year for 2 years	0	0
Outcome	Continued observation	RFA at 2 years (size 3.5 cm), continued observation post-RFA (2.7 cm after RFA)	Continued observation	Continued observation
RFA: radiofrequency ablation.				

Thus, in the present study (as in other reports) the diagnostic accuracy for multiphasic CT in renal oncocytoma remains low at 10.5%.

Reported growth rates for oncocytomas are similar to RCC.[7] In our study, tumours in 2 of the 4 patients conservatively managed increased in size, with a mean growth rate of 0.4 cm annually. The etiology for local growth is poorly understood and metastatic progression is unclear.[2,8] Kawaguchi and colleagues concluded that 80% oncocytomas grow in size at an average of 0.2 cm annually over a 40-month period.[2] Neuzillet and colleagues reported a mean (standard deviation [SD]) growth rate of 0.7 (SD 0.5) mm and 2.4 (SD 2.1) mm annually for non-surgically and surgically treated oncocytomas, respectively.[9] The indications for surgery in their study was initial tumour size more than 10 cm, growth velocity more than 0.5 cm/year, and patient preference. Patient age (older age associated with increased growth rate) was a predictor for an increased tumour growth rate, as was an association with RCCs in patients who subsequently underwent surgery. Another study reported no growth in a total of 12 oncocytomas that were followed-up over a mean of 7 years.[10]

Oncocytomas are classified as benign tumours by the World Health Organization classification and updated European Association of Urology guidelines.[11] Kwast and colleagues suggest there may be a subset of oncocytomas sharing the genetic and molecular features of chromophobe RCC, thus explaining the rare occurrence of metastasis.[8] The malignant potential of renal oncocytoma remains controversial, as hybrid tumours with concomitant RCC and oncocytomas are found in up to 32% of cases.[1] None of the patients in our study developed metastatic disease after a median follow-up of 7 years.

Bilateral or multifocal renal oncocytomas should prompt clinicians to investigate for Birt-Hogg Dube (BHD) syndrome. Stamatakis and colleagues demonstrated that about 27% of patients with BHD had renal lesions, including oncocytomas and RCC, and 65% of these tumours were multifocal.[12]

The coexistence and histopathological similarity of oncocytoma and chromophobe RCCs can complicate a definitive diagnosis on renal biopsy. The sensitivity of needle biopsy for malignancy is between 70% and 100% and specificity is almost 100%, with reported accuracy at almost 100%.[13] Dogan and colleagues concluded that renal biopsy can be safely performed in patients with suspected renal malignancy that have a solitary kidney or are considered high-risk for treatment.[13] This protocol is followed at our centre.

Two of 4 renal biopsies were performed in patients with solitary kidneys: one in a patient unfit for aggressive surgical treatment and one in a patient with high-index of suspicion for oncocytoma. The threshold for renal biopsy will reduce in the future because biopsy is increasingly employed in the preoperative diagnosis of small renal masses (SRMs, ≤4 cm) due to the high incidence of benign tumours among SRMs (nearly one-third at surgery).[14-16] There is little data on minimally invasive ablation therapy for oncocytoma.[12] Ablative intervention is an attractive alternative to surgery, in that it stabilizes tumour volume. However, nephron-sparing and ablative techniques for renal oncocytoma cannot be universally adopted considering the definitive incidence of coexisting RCC.

Conclusions

As current radiological imaging remains unreliable for diagnosing renal oncocytoma, renal biopsy (histopathology) has become a definitive diagnostic modality. None of the patients in this study undergoing surveillance developed metastatic disease. Surveillance or minimally invasive ablative techniques are thus attractive alternatives to surgery in patients (especially with a solitary kidney and/or comorbidities) with biopsy-proven oncocytomas that are not increasing in size.

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