Coexisting Hybrid Malignancy in a Solitary Sporadic Solid Benign Renal Mass: Implications for Treating Patients Following Renal Biopsy

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Abbreviations and Acronyms

AML = angiomyolipoma
chRCC = chromophobe RCC
CK-7 = cytokeratin 7
PRB = percutaneous renal biopsy
RCC = renal cell carcinoma
RO = renal oncocytoma

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Purpose: Concern regarding coexisting malignant pathology in benign renal tumors deters renal biopsy and questions its validity. We examined the rates of coexisting malignant and high grade pathology in resected benign solid solitary renal tumors.

Materials and Methods: Using our prospectively maintained database we identified 1,829 patients with a solitary solid renal tumor who underwent surgical resection between 1994 and 2012. Lesions containing elements of renal oncocytoma, angiomyolipoma or another benign pathology formed the basis for this analysis. Patients with an oncocytic malignancy without classic oncocytoma and those with known hereditary syndromes were excluded from study.

Results: We identified 147 patients with pathologically proven elements of renal oncocytoma (96), angiomyolipoma (44) or another solid benign pathology (7). Median tumor size was 3.0 cm (IQR 2.2–4.5). As quantified by the R.E.N.A.L. (radius, exophytic/endophytic, nearness to collecting system or sinus, anterior/posterior and location relative to polar lines) nephrometry score, tumor anatomical complexity was low in 28% of cases, moderate in 56% and high in 16%. Only 4 patients (2.7%) were documented as having hybrid malignant pathology, all involving chromophobe renal cell carcinoma in the setting of renal oncocytoma. At a median followup of 44 months (IQR 33–55) no patient with a hybrid tumor experienced regional or metastatic progression.

Conclusions: In our cohort of patients with a solitary, sporadic, solid benign renal mass fewer than 3% of tumors showed coexisting hybrid malignancy. Importantly, no patient harbored coexisting high grade pathology. These data suggest that uncertainty regarding hybrid malignant pathology coexisting with benign pathological components should not deter renal biopsy, especially in the elderly and comorbid populations.

Key Words: kidney; carcinoma, renal cell; adenoma, oxyphilic; pathology; oncocytoma

Clinical management decisions in patients with an enhancing renal mass require a nuanced balance of risks, especially since only a minority of enhancing renal lesions prove to be biologically aggressive. Thus, accurate

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nonextirpative assessment of tumor histology is extremely desirable, especially in the elderly and infirm populations.

PRB has become the lynchpin strategy for nonextirpative pathological assessment.[1,2] Reliable biopsy results offer particular promise for patients who harbor benign masses. In fact, these patients comprise almost a quarter of modern renal mass cohorts and, arguably, can avoid treatment risks altogether.[3,4] However, the reliability of a benign renal biopsy result is called into question by reports of malignant histology harbored in otherwise benign tumors.[1,5] The existence of these hybrid tumors potentially deters renal biopsy and calls its validity into question.[1] Nevertheless, hybrid histology has been largely described in patients with multifocal tumors and known genetic syndromes with relatively sparse data on patients with sporadic solitary tumors.[6,7]

As such, we assessed the incidence of coexisting hybrid malignancy associated with solitary, sporadic, solid benign renal masses in a large cohort of patients undergoing renal surgery at a tertiary referral center.

MATERIALS AND METHODS

An institutional review board approved kidney cancer database maintained at our institution contains prospectively entered demographic, perioperative, pathological and imaging data as well as followup information. We queried the kidney cancer database to identify patients who underwent radical or partial nephrectomy between January 1994 and July 2012. We reviewed the records of those with lesions classified as benign, or who had oncocytoma or the term oncocytic as part of the pathological diagnosis. Patients with cystic lesions or synchronous multifocal lesions were excluded from analysis, leaving only those with a solitary solid lesion. Records were reviewed to exclude patients with a family history or diagnosis of genetic syndromes, thus, excluding those with renal oncocytosis or Birt-Hogg-Dubé syndrome.

Pathology reports were reviewed in detail and pathology slides were rereviewed by a urological pathologist as needed. All hybrid tumors were identified and corresponding slides were rereviewed. Hematoxylin and eosin stained slides were available in all hybrid tumor cases. Immunohistochemical staining, including CK-7 staining, was performed on all hybrid tumors at initial diagnosis. Karyotyping cytogenetic analyses were reviewed when available. Cases in which the primary lesion was described as oncocytic and did not contain a defined area of classic RO, such as oncocytic chRCC or papillary RCC with oncocytic features, were considered purely malignant and not hybrid. Therefore, they were excluded from analysis.

We performed a literature search of English language abstracts from 1990 until 2013 using the PubMed® and Web of Science® databases. Key words included chromophobe, oncocytoma, renal and hybrid tumors. We reviewed relevant articles and their bibliographies, and abstracted data. Descriptive statistics were generated using Excel® 2007.

RESULTS

Between 1994 and 2012 we identified 2,013 patients who underwent renal surgery at our institution, including 147 with renal masses containing any proportion of benign histology. Table 1 lists cohort demographic and histopathological characteristics. Median age at surgery was 61 years (IQR 53–70), 45.9% of patients were male and 81.7% were white. Median tumor size was 3.0 cm (IQR 2.2–4.5). As quantified by the R.E.N.A.L. nephrometry score,[8] tumor anatomical complexity was available in 96 cases (65.3%), and was classified as low in 27 (28.1%), moderate in 54 (56.3%) and high in 15 (15.6%). Nephron sparing surgery was performed in 109 patients (74.1%). Lesions included pathologically proven elements of RO in 96 cases (65.3%), AML in 44 (29.9%), metanephric adenoma in 2 (1.4%), and renomedullary interstitial cell tumor, medullary fibroma, juxtaglomerular cell tumor, inflammatory pseudotumor and hemangioma in 1 each (0.7%).

Adjunctive pathological evaluation, including immunohistochemical staining and/or karyotyping cytogenetic analysis, was available for 38% of RO containing specimens. After reviewing the pathology reports for morphological features, and immunohistochemical and cytogenetic analyses only 4 patients (2.7%) were found to have a hybrid malignant pathology. In this hybrid tumor subset all patients had tumors with features of chRCC

Table 1. *Demographic characteristics of benign and hybrid cohorts*

	Benign		Hybrid	
No. pts (%)	143	(97.3)	4	(2.7)
Median age (IQR)	62	(53–70)	50.5	(47–56)
% Male	45.5		50	
No. white (%)	116	(81)	4	(100)
Median cm tumor size (IQR)	3.0	(2.2–4.5)	6.0	(3.5–9.2)
No. pT stage (%):				
pT1a	107	(74.8)	2	(50)
pT1b	22	(15.4)	–	
pT2	8	(5.6)	2	(50)
pT3	6	(4.2)	–	
No. nephrectomy type (%):				
Partial	107	(74.8)	2	(50)
Radical	36	(25.2)	2	(50)
Median mos followup (IQR)	8.7	(5–31)	43.8	(33–55)
No. histological subtype (%):				
Chromophobe RCC	–		4	(100)
Oncocytoma	92	(64.3)	4	(100)
Angiomyolipoma	44	(30.7)	–	
Metanephric adenoma	2	(1.4)	–	
Renomedullary interstitial cell tumor	1	(0.7)	–	
Medullary fibroma	1	(0.7)	–	
Juxtaglomerular cell tumor	1	(0.7)	–	
Inflammatory pseudotumor	1	(0.7)	–	
Hemangioma	1	(0.7)	–	