Percutaneous Biopsy of the Renal Mass: FNA or Core Needle Biopsy?

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BACKGROUND: In recent years, there have been increasing indications for percutaneous renal biopsy. Fine-needle aspiration (FNA), with or without core needle biopsy (CB), has been used increasingly in the management of renal tumors at the study institution. METHODS: A computerized search of laboratory records was conducted to retrieve FNA cases of renal masses as well as the correlating CB and/or nephrectomy specimens. The cases spanned a period of 10 years (2006-2015). The diagnoses were classified into 5 categories: malignant, suspicious for malignancy, neoplastic, atypical, and negative/undiagnostic. Based on the results of the nephrectomy specimens, the diagnostic rate, sensitivity, and diagnostic accuracy were calculated among 3 groups of specimens: FNA only, CB only, and combined FNA and CB. RESULTS: A total of 247 cases of FNA with 123 correlating CB and 101 follow-up nephrectomy specimens were identified. The diagnostic rate, sensitivity, and diagnostic accuracy were 72%, 78%, and 96%, respectively, for FNA; 87%, 92%, and 94%, respectively, for CB; and 92%, 92%, and 94%, respectively, for the combined FNA and CB group. Renal cell carcinoma and its variants were the most common histologic diagnoses (112 of 174 cases; 64%). Significant diagnostic discrepancy was noted in one case: a malignant melanoma that was misdiagnosed as renal cell carcinoma in both the preoperative FNA specimen and in the CB specimen. CONCLUSIONS: In the current study, both FNA and CB demonstrated excellent diagnostic accuracy (96% and 94%, respectively). The combination of FNA and CB was found to significantly improve the diagnostic rate when compared with either FNA alone (92% vs 72%; P<.05) or CB alone (92% vs 87%).

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KEY WORDS: core needle biopsy (CB); cytology; fine-needle aspiration (FNA); renal cell carcinoma (RCC); renal tumors.

INTRODUCTION

The incidence of renal cell carcinoma (RCC) has increased over the past few decades, largely due to the improved detection of small (<4 cm) renal masses (SRMs). The widespread use of advanced imaging techniques including ultrasonography, computed tomography (CT), and magnetic resonance imaging for patients presenting with non-specific abdominal symptoms contributes to the increasing incidence of SRMs. Surgical resection of these early-stage, potentially malignant renal tumors also is on the rise.1,2 However, a significant percentage of SRMs removed by nephrectomy later are proven to be either benign neoplasms or low-grade RCC cases. These tumors usually have a relatively indolent biological and clinical behavior. Furthermore, early surgical intervention has not been shown to influence the mortality rate of patients with kidney cancers.1,3,4 Percutaneous renal biopsies before therapy can prevent overtreatment and unnecessary surgeries for patients with benign lesions. It also can provide useful information regarding patients with comorbidities who may not be good surgical candidates. These

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patients may benefit from alternative treatment options such as active surveillance and thermal ablative therapy. In addition, due to the advent of targeted biologic therapies, it is clear that pretreatment information regarding tumor pathology plays an important role in the management of patients with metastatic RCC. In view of the reasons mentioned above, the spectrum of use of percutaneous renal biopsy continues to expand in clinical practice, and it now plays an ever-increasing role in clinical decision making.

At the study institution, fine-needle aspiration (FNA) was the first diagnostic procedure performed for the majority of percutaneous renal biopsies. The cases were attended by a cytopathologist for rapid on-site evaluation. Concurrent core needle biopsies (CBs) also were obtained for some of the cases. If CBs were not obtained at the time of FNA biopsy, additional multiple FNA passes (2-4 passes) were collected for processing into cell blocks.

In the current study, we retrospectively reviewed 247 renal FNA cases with and without concurrent CB. Based on the results of the follow-up renal resection specimens, the sensitivity, diagnostic rate, and diagnostic accuracy were calculated and compared among 3 groups. These groups included specimens obtained with FNA alone, CB alone, and combined FNA and CB.

**MATERIALS AND METHODS**

The current study was approved by the Institutional Review Board of Indiana University (protocol 1607749519). A computerized search of the laboratory information system was performed over a 10-year-period from January 2006 to December 2015 to retrieve all FNA specimens of the kidney. All the renal aspirates were performed using 22-gauge to 25-gauge needles under CT or ultrasound guidance. Concurrent or subsequent CBs were obtained using 18-gauge needles. Paired air-dried (Diff-Quik stain) and ethanol-fixed (Papanicolaou stain) specimens were prepared. Rapid on-site evaluation routinely was performed by either a cytopathologist and/or a cyto-technologist to evaluate the adequacy of the specimen. Typically, 2 to 5 FNA passes were performed initially. If the FNA sample was considered adequate, additional aspirates (2-4 passes) for cell block preparation also were performed. If the specimens still were deemed inadequate after the on-site evaluation, the radiologist performing the procedure opted to obtain CBs in some cases. The decision to obtain CBs depended on many factors, including the on-site evaluation results and the preference of radiologists, urologists, or oncologists.

The FNA diagnoses were classified into 5 categories: malignant (M), suspicious for malignancy (SM), neoplastic (N), atypical (A), and negative/nondiagnostic (ND). Negative cases cannot simply be interpreted as “benign” because of the possibility of sampling errors. Therefore, we classified all the negative cases as ND. This category included samples containing normal glomeruli, tubular epithelial cells, blood only, or necrotic debris, among others. All correlating surgical pathology reports including CBs and nephrectomy specimens were reviewed. For the purposes of statistical calculations, we grouped M, SM, N, and A diagnoses as “positive.” ND diagnoses were considered “negative.” Based on the nephrectomy results, the sensitivity was calculated for the identification of both benign and malignant tumors. The diagnostic accuracy was determined using the rate of concordance between the diagnoses rendered for the biopsies compared with those rendered for the nephrectomy specimens.

**Statistical Analysis**

A chi-square test using an online calculator was performed to compare the diagnostic rate of FNA alone, CB alone, and the combination group. The result was found to be significant at \( P < .05 \) (http://www.socscistatistics.com/tests/chisquare/Default.aspx).

**RESULTS**

Renal FNA was performed for 247 patients, including 131 males and 116 females. The patients’ ages ranged from 3 to 96 years, with a mean age of 63 years. There were only 2 pediatric cases (<1%). The first case was a 3-year-old female patient who was diagnosed with Wilms tumor by both FNA and CB. These results later were confirmed by nephrectomy. The second case was a 14-year-old male patient with high-grade B-cell lymphoma diagnosed by both FNA and CB in conjunction with a flow cytometry study obtained during the FNA procedure. A follow-up nephrectomy was not performed for the second patient. Excluding these 2 patients, the age of the patients in the current study therefore ranged from 22 to 96 years, with a mean of 63.6 years. Correlating CBs were obtained for 123 patients and follow-up nephrectomy specimens were identified among 101 patients. Of the 124 cases for which
only FNAs were performed without a concurrent CB, 29 were consultation cases, 22 had no cell blocks prepared, and 73 had both direct smears and cell blocks prepared. Of the 73 cases with cell blocks prepared, 36 (49%) contained sufficient tissue within the cell block for further ancillary studies. Of these latter 36 cases, immunocytochemical stains were performed in 17 cases (47%).

Of the 247 FNA cases, a diagnosis of M was rendered in 132 cases (53%), SM in 9 cases (4%), N in 24 cases (10%), A in 12 cases (5%), and ND in 70 cases (28%). Of the 123 diagnoses rendered for the CBs, a diagnosis of M was noted in 83 cases (67%), SM in 1 case (1%), N in 23 cases (19%), and ND in 16 cases (13%). None of the CB specimens was diagnosed as A. Of the 123 cases for which both FNA and CB were performed concurrently, the final diagnoses for the combined samples demonstrated M in 84 cases (68%), SM in 2 cases (2%), N in 26 cases (21%), A in 1 case (1%), and ND in 10 cases (8%) (Table 1). The diagnostic rates for FNA, CB, and the combination group were 72%, 87%, and 92%, respectively. The diagnostic rate of the combination group was significantly higher than that of the FNA-alone group (92% vs 72%; P<.05). Using the nephrectomy diagnosis as the gold standard, the sensitivity for diagnosing renal neoplasia by FNA, CB, and both modalities combined was 78%, 92%, and 92%, respectively. The diagnostic accuracy was found to be 96%, 94%, and 94%, respectively (Table 2).

If the A category was excluded from the positive cohort, the sensitivity of FNA became slightly lower (77%) whereas the sensitivity for CB and both modalities combined remained unchanged. However our FNA diagnosis of A was highly associated with malignant tumors. Of the 11 FNA cases rendered as A for which there was histologic follow-up, 9 (82%) were malignant.

Follow-up nephrectomy specimens were identified in 101 FNA cases (Table 3), 51 of which included a concurrent CB (Table 4). All but one of the M diagnoses rendered on FNA or CB were found to be concordant with those rendered on the nephrectomy specimen. There were 4 additional cases with a minor diagnostic discrepancy. One case of unclassified RCC was diagnosed as an oncocytic neoplasm by both FNA and CB. One RCC of clear cell type was diagnosed as a renal epithelial neoplasm by CB and as ND by FNA. One case of leiomyosarcoma was diagnosed as a spindle cell neoplasm by FNA but was correctly diagnosed by the CB.

One case of papillary RCC was correctly diagnosed by FNA, whereas the CB was ND. Eleven nephrectomy-confirmed RCC cases were diagnosed by the CB whereas the corresponding FNA specimens were ND.

RCC and its variants accounted for the most common histologic diagnoses (113 of 174 cases; 65%) that were rendered by CB and/or nephrectomy. The most common subtype of RCC was the clear cell type (71 cases) (Fig. 1), followed by papillary (21 cases) (Fig. 2), unclassified (13 cases), chromophobe (4 cases) (Fig. 3), translocation (3 cases), and clear cell papillary (1 case).

FNA was able to accurately subclassify 40 of the 62 RCCs (65%) compared with CB, which was able to subclassify 30 of 36 tumors (83%). The tumor size was recorded in 170 renal masses, and ranged from 0.9 cm to 21 cm (mean, 5.02 cm). Approximately 48.8% of the tumors measured <4 cm in size. When the tumors were

**TABLE 1.** Subcategory of Diagnoses of Renal Masses Rendered by FNA Alone, CB Alone, and the Combination of Both FNA and CB

| Diagnosis               | FNA     | CB      | FNA Plus CB |
|-------------------------|---------|---------|-------------|
| Malignant               | 132 (53%) | 83 (67%) | 84 (68%)    |
| Suspicous for malignancy| 9 (4%)  | 1 (1%)  | 2 (2%)      |
| Neoplasm                | 24 (10%) | 23 (19%) | 26 (21%)    |
| Atypical                | 12 (5%)  | 0       | 1 (1%)      |
| Nondiagnostic           | 70 (28%) | 16 (13%) | 10 (8%)     |
| Total                   | 247     | 123     | 123         |

*Abbreviations: CB, core needle biopsy; FNA, fine-needle aspiration.*

**TABLE 2.** Comparisons of Diagnostic Rate, Sensitivity, Specificity, and Diagnostic Accuracy

| Procedure (Total No. of Cases) | No. of Follow-Up Nephrectomies (% of Total Procedures) | Diagnostic Rate | Sensitivity | Diagnostic Accuracy |
|--------------------------------|-------------------------------------------------------|-----------------|-------------|---------------------|
| FNA alone (247 cases)          | 101 (41%)                                             | 72%             | 78%         | 96%                 |
| CB alone (117 cases)           | 51 (44%)                                              | 87%             | 92%         | 94%                 |
| FNA plus CB (117 cases)        | 51 (44%)                                              | 92%             | 92%         | 94%                 |

*Abbreviations: CB, core needle biopsy; FNA, fine-needle aspiration.*
subcategorized into 3 size groups (<2 cm, 2-4 cm, and >4 cm), the diagnostic rates of FNA increased proportionally to the tumor size and were found to be 42.9%, 69.1%, and 80.2%, respectively, for each group.

**Case Report for Major Tumor Type Discrepancy**

In the one discordant case, a significant discrepancy was noted with regard to the tumor classification: a malignant melanoma was misdiagnosed as RCC in both the preoperative FNA and CB. In this case, the patient was a 62-year-old man with a right renal mass measuring 6 cm. He had no history of a prior malignancy. The patient underwent a CT-guided FNA biopsy of the mass and a CB also was obtained concurrently. The direct smears prepared from the FNA demonstrated numerous epithelioid tumor cells distributed singly and in loose clusters. The cells contained eccentrically located, round nuclei with prominent nucleoli and a moderate to abundant amount of eosinophilic cytoplasm (Figs. 4A and 4B). The concurrent CB demonstrated sheets of malignant cells with similar cytomorphologic features. In addition, frequent mitotic figures and tumor necrosis also were noted in the CB.

To further evaluate the malignant cells, immunocytochemical stains were performed on paraffin-embedded sections cut from the cell block prepared from the FNA sample. The tumor cells demonstrated immunoreactivity for CD10. They were negative for GATA binding protein 3 (GATA-3), CD117 (C-KIT), cytokeratin (CK) 7, E-cadherin, and carbonic anhydrase IX. Additional immunohistochemical stains were performed on paraffin-embedded sections cut from the CB. The tumor cells demonstrated immunoreactivity for CKAE1/AE3, vimentin, and paired box gene 8 (PAX8). They were negative for CK20, p63, and CD45. The immunoprofile of the tumor cells originally was believed to be consistent with an unclassified RCC. The patient subsequently underwent a right nephrectomy.

Histologic sections of the nephrectomy specimen again demonstrated a poorly differentiated epithelioid neoplasm with morphologic features similar to those described previously (Fig. 4C). Immunohistochemical staining also demonstrated positivity for CKAE1/AE3 and PAX8. However, additional staining for melan A, S100, homatropine...
methylbromide 45 (HMB-45), and tyrosinase also was positive. These findings were highly supportive of a melanocytic neoplasm. The tumor cells were not immunoreactive for p63, CK7, CK20, and CK5/6. These findings excluded a diagnosis of urothelial carcinoma. The tumor cells also were found to be negative for inhibin and synaptophysin, making a diagnosis of adrenal cortical carcinoma less likely.

Because of the unusual morphologic appearance of the tumor and the conflicting immunohistochemical staining results, the case was sent out for consultation at an outside institution. There, the immunohistochemical stains for pancytokeratin and PAX8 were repeated and were reported as negative. Repeat immunohistochemical stains for S100 and HMB-45 were confirmed to be positive. Therefore, the tumor ultimately was diagnosed as a metastatic melanoma. The diagnostic discrepancy in this case was attributed to the conflicting immunohistochemical results. The primary site of the patient’s melanoma was never identified, possibly due to tumor regression.

**DISCUSSION**

Percutaneous renal biopsy was not widely used in the past due to concerns regarding safety and accuracy. It was reserved for patients who had solid tumors with atypical imaging features, unresectable renal tumors, abscesses, or hematologic malignancies, or to rule out primary or secondary tumors in patients with a known extrarenal malignancy. However, a recent large series of renal needle biopsy studies demonstrated few or no major complications. This likely was due to better techniques, including the use of...
guiding cannules. The management of patients with SRMs (<4 cm) also has shifted away from traditional radical nephrectomy in favor of nephron-sparing surgeries such as partial nephrectomy and thermal ablation (radiofrequency or cryoablation). In addition, more conservative management such as active surveillance for patients with concurrent comorbidities has been adopted. For these reasons, urologists have relied on information obtained from percutaneous biopsies of renal masses for treatment-related decisions.

FNA and CB are 2 techniques that have been applied to obtain diagnostic material during percutaneous renal biopsy. Each technique has its own advantages. FNA may offer more extensive sampling from different areas within a mass and the cytologist can provide rapid on-site evaluation of specimen adequacy during the procedure. Furthermore, it guides the performing clinician in determining the

Figure 3. Fine-needle aspiration cytology of chromophobe renal cell carcinoma. (A and B) The cells were round to oval with a well-defined, thickened cell membrane and contained variegated cytoplasm ranging from dense, granular, and vacuolated to fluffy or flocculent with an occasional perinuclear clear zone. The nuclei were round to oval with an irregular nuclear membrane and occasional binucleation (A: Papanicolaou stain, original magnification ×400; B: Diff-Quik stain, original magnification ×400).

Figure 4. (A and B) Fine-needle aspiration cytology of metastatic melanoma to the kidney (A: Papanicolaou stain, original magnification ×400; B: Diff-Quik stain, original magnification ×400) and (C) a corresponding nephrectomy histological section (H & E stain, original magnification ×400).
correct location of the needle site. This helps to increase the diagnostic yield of the subsequent CB, if needed. Cell blocks prepared from the FNA samples may provide only limited information regarding tumor architecture, but can be useful for immunocytochemical studies. Optimal CB samples are comparable to nephrectomy specimens with regard to tumor architecture and histologic features. In addition, in the majority of laboratories, tissue from CB is required for the extraction of DNA or RNA. This material then can be used for genomic analysis, which can in turn guide the selection of new molecular targeted therapies.\textsuperscript{9–11} However, alternatively, FNA specimens also have been shown to provide adequate genetic material for molecular testing.\textsuperscript{12}

Compared with CB, the average sensitivity of FNA in diagnosing malignancy is reported to be lower (76% for FNA vs 97% for CB).\textsuperscript{6} The results of the current study also demonstrated that CB is more sensitive than FNA (92% vs 78%). Generally, CB is more likely to provide a definitive diagnosis and is better for subclassifying RCC.\textsuperscript{5,13,14} The current study results demonstrated fewer atypical and suspicious diagnoses were rendered by CB (1%) compared with FNA (9%). CB also correctly subclassified a higher percentage of RCC cases (30 of 36 cases; 83%) compared with FNA (40 of 62 cases; 65%).

It is interesting to note that FNA was found to be a reliable method for diagnosing papillary RCC. In the current study, the majority of papillary RCC cases (15 of 18 cases; 83%) were accurately diagnosed by FNA. FNA also correctly diagnosed 1 of 3 cases of chromophobe RCC (33%), 20 of 35 cases of clear cell RCC (57%), 0 of 2 cases of translocation-associated RCC, and 3 of 4 cases of unclassified RCC (75%).

In the current study, CB failed to provide correct subtyping in 6 cases due to limited diagnostic material. These included 2 cases of mucinous tubular and spindle cell carcinoma, 1 case of papillary RCC, 2 cases of clear cell RCC, and 1 case of translocation-associated RCC.

The use of both FNA and CB clearly has been shown to demonstrate superior diagnostic capabilities compared with FNA or CB alone.\textsuperscript{15–17} The data from the current study confirmed this and demonstrated a significantly higher diagnostic rate for the combination compared with FNA alone (92% vs 72%; \textit{P}<.05) and CB alone (87%). Of the 16 nondiagnostic CB cases in the current study, FNA was able to provide a diagnosis in 6 cases, including 2 RCCs, 2 oncocytic neoplasms, 1 angiomyolipoma, and 1 case that was suspicious for RCC. CB was able to provide a diagnosis in 27 of 36 cases reported as nondiagnostic by FNA. These cases included 17 RCCs, 6 oncocytic renal neoplasms, 3 angiomyolipomas, and 1 case suspicious for RCC.

The combination group also demonstrated a high sensitivity (92%) and diagnostic accuracy (94%) for renal neoplasms. In cases of complex cystic lesions, CB was likely to increase the diagnostic accuracy when combined with FNA compared with FNA alone. Conversely, when used alone, CB often was unable to obtain diagnostic material in large tumors with extensive tumor necrosis. FNA was able to accurately subtype 2 of 6 cases that were unable to be classified by CB (1 papillary and 1 clear cell-type RCC).

Full concordance of the Fuhrman grade between the CB and nephrectomy specimens was noted in 62% of the cases. When the tumors were classified into low-grade (Fuhrman grade I-II) and high-grade (Fuhrman grade III-IV) categories, concordance increased to 79%. Discordant grading results may be attributed to interobserver variability and/or tumor heterogeneity. Fuhrman grading was not performed for FNA specimens. Future studies for grading RCC by FNA are needed.

Tumor size may contribute to the success of the percutaneous biopsy. Lechevallier et al found that the biopsy failure rate was higher in tumors measuring ≤3 cm compared with tumors measuring >3 cm (37% vs 3%).\textsuperscript{17} In the current study, we subdivided the FNA cases based on 3 size groups: <2 cm, 2 cm to 4 cm, and >4 cm. We found that the diagnostic rate increased in proportion to the tumor sizes (42.9%, 69.1%, and 80.2%, respectively). For very small renal tumors (those measuring ≤2 cm), Li et al suggested that the combination of CB and FNA had a higher diagnostic success rate because FNA is able to provide more extensive sampling from different areas of the tumor whereas CB is more limited in regard to sampling.\textsuperscript{18}

In addition, the decision to perform a nephrectomy relied heavily on imaging data. Only 31% and 25% of nondiagnostic cases on FNA and CB, respectively, had a follow-up nephrectomy. Patients with small-sized tumors were more likely to be monitored via active surveillance.

The diagnosis of a renal oncocytic neoplasm is regarded as the most challenging of all the renal neoplasms. The differential diagnoses include renal oncocytoma; the eosinophilic variant of chromophobe RCC; and unclassified, low-grade oncocytic RCC. Ancillary studies such as
Hale colloidal iron and CK7 immunohistochemical staining performed on the CB or the cell block may be helpful in distinguishing between renal oncocytoma and the eosinophilic variant of chromophobe RCC. Renal oncocytomas usually are negative or only focally positive for Hale colloidal iron in a luminal distribution. In addition, oncocytomas usually are found to be only focally positive for CK7. In contrast, the eosinophilic variant of chromophobe RCC is positive for Hale colloidal iron in a reticular pattern and is diffusely positive for CK7. Occasionally, ancillary studies cannot be performed due to limited diagnostic material. In these circumstances, the tumor is best classified as an oncocytic neoplasm.\textsuperscript{15,19} In the current series, there were 11 oncocytic neoplasms and 8 oncocytomas diagnosed by either FNA or CB (Fig. 5). Of these, 3 cases underwent a follow-up nephrectomy. One of these cases was an oncocytoma diagnosed by FNA that later was diagnosed as an unclassified, low-grade oncocytic RCC on the nephrectomy specimen. The other 2 cases were diagnosed as oncocytic neoplasms by CB. The final nephrectomy diagnoses for these cases revealed one unclassified, low-grade oncocytic RCC and one renal cell neoplasm of oncocytosis.

Tumors that fall into the category of oncocytoma/oncocytic neoplasm with the absence of high-grade nuclear atypia are considered either benign or of low malignant potential. Regardless of the specific diagnosis, clinical management is similar and includes partial nephrectomy, active surveillance, and thermal ablative therapy. At the study institution, the majority of patients with these tumors (82%) received active surveillance.

Both FNA and CB are highly specific and have a high positive predictive value for the diagnosis of renal tumors. In the current study, there were no false-positive diagnoses found in either the FNA or CB cases. However, a major diagnostic discrepancy in tumor classification was noted in one case: a malignant melanoma was misdiagnosed as RCC in both the preoperative FNA and CB. Retrospective review of the FNA specimens demonstrated typical morphologic features of melanoma including a dishesive cellular pattern, epithelioid cells with eccentrically located round nuclei, prominent nucleoli, and occasional binucleation. Melanoma is a great mimicker and should be included in the differential diagnosis whenever a tumor with unusual morphologic features is encountered during the examination of renal biopsies.

Both FNA and CB demonstrate excellent diagnostic accuracy when diagnosing malignancy. The results of the current study demonstrated the synergistic diagnostic advantage of combining the FNA and CB techniques. The combination of FNA and CB was found to significantly improve the diagnostic rate when compared with the use of FNA alone (92% vs 72%; \( P < .05 \)), and also was better than CB alone (92% vs 87%).

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The authors made no disclosures.
AUTHOR CONTRIBUTIONS

Chi-Shun Yang: Investigation and writing–original draft. Euna Choi: Writing–original draft and writing–review and editing. Muhammad T. Idrees: Conceptualization, methodology, validation, investigation, resources, and writing–review and editing. Shaoxiong Chen: Conceptualization, methodology, validation, investigation, and writing–review and editing. Howard H. Wu: Conceptualization, methodology, validation, formal analysis, investigation, data curation, writing–original draft, writing–review and editing, supervision, and project administration.

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