Diagnosis of Renal Lymphoma by Percutaneous Image Guided Biopsy: Experience With 11 Cases

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Purpose: We reviewed an institutional experience with image guided percutaneous biopsy of focal renal masses that yielded a diagnosis of lymphoma.

Materials and Methods: We retrospectively reviewed the hospital records of patients undergoing percutaneous renal biopsy between September 1997 and February 2005. A total of 407 image guided focal renal lesion biopsies were identified. A diagnosis of lymphoma was made in 11 patients (3%). Biopsies were performed under computerized tomography guidance in 9 cases (82%) and under ultrasound guidance in 2 (18%). Core biopsies were performed in 11 cases, while fine needle aspiration was done in 10 (91%). Fine needle aspirations underwent cytological analysis in 10 cases and flow cytometry analysis in 9. The final combined pathological diagnoses were B-cell lymphoma in 10 cases and lymphomatoid granulomatosis in 1. Analysis of core biopsies yielded a diagnosis of B-cell lymphoma in 10 cases (91%) and lymphomatoid granulomatosis in 1. Analysis of fine needle aspirations yielded a diagnosis of B-cell lymphoma in 3 cases (30%), lymphoma in 4 (40%), suspicion of lymphoma in 1 (10%), atypical cells in 1 (10%) and a nondiagnostic sample in 1 (10%). Flow cytometry concurred with cytology in the diagnosis of B-cell lymphoma in 2 cases, allowed the identification of lymphoma subtype, which was not made on cytology, in 4, was insufficient in 2 and identified no abnormality in 1. No patients underwent surgery or an ablative procedure.

Conclusions: Core biopsy has a higher diagnostic yield than fine needle aspiration for diagnosing renal lymphoma. Flow cytometry analysis adds additional diagnostic information to cytological examination of fine needle aspiration samples. Accurate diagnosis of lymphoma in these cases allowed proper treatment without unnecessary surgery or other procedures.

Key Words: kidney; lymphoma; biopsy; nephrectomy; radiology, interventional

Secondary renal involvement in patients with known lymphoma is a common finding that is reported at autopsy in up to 60% of cases. Moreover, the prevalence of renal involvement in patients undergoing staging for lymphoma on CT has been estimated to be between 5% and 8%. Because renal lymphoma may assume various appearances on CT that mimic other types of renal malignancies, its conclusive diagnosis may prove challenging in the presence and absence of extrarenal disease. Studies have shown that percutaneous biopsy under CT and ultrasound guidance is a safe and accurate method of identifying and characterizing malignant lesions in the kidney. However, there are sparse data on percutaneous imaging guided biopsy of focal renal masses yielding a diagnosis of lymphoma.

We reviewed a single institution experience of 11 cases of focal renal lymphoma diagnosed by image guided percutaneous biopsy with particular emphasis on the technical aspects of percutaneous biopsy. We also analyzed the relative diagnostic value of core biopsy and FNA sampling in these procedures.

MATERIALS AND METHODS

Institutional review board approval was obtained for a retrospective review of medical records and diagnostic imaging. The requirement for patient informed consent was waived. A search of the institution computerized database of patients who underwent interventional radiology was performed to identify those with image guided percutaneous biopsy of a focal renal lesion in the 7-year period between September 1997 and February 2005. We identified 413 such patients. For each patient a review of diagnostic radiology reports, interventional radiology reports, pathology reports, outpatient notes and discharge summaries was performed to assess 1) imaging modality, 2) biopsy techniques, 3) histopa-
thology results, 4) cytology results and 5) the influence of biopsy results on patient treatment.

In this cohort all patients in whom biopsies yielded a diagnosis of lymphoma were identified. The final histopathology, cytology and flow cytometry results were analyzed to assess the diagnostic yield of each method of sampling and specimen analysis. The percutaneous technique used in all cases was analyzed for needle type, target lesion size and type of specimen retrieved (core biopsy and/or fine needle aspirate). The modality used for image guidance was also identified. Medical records were reviewed to determine the indication for each procedure, complications, extrarenal disease at presentation and the subsequent therapy method, including ultimate management of the focal renal mass. Pre-biopsy images were reviewed to determine the pattern of lymphomatous renal involvement.

Ten patients (91%) underwent biopsy under CT guidance and 1 (9%) underwent ultrasound guided biopsy. Core biopsy specimens were retrieved in all 11 cases and fine needle aspirates were obtained in 10 (91%). All FNAs were sent for cytological analysis, while in 9 flow cytometry examination was done based on suspicion of lymphoma.

A total of 402 patients in our initial cohort with renal mass biopsies negative for lymphoma were followed. In these patients initial biopsy results were recorded, as were histopathology data from subsequent nephrectomy or repeat biopsy. Patients without subsequent histopathology data available underwent clinical followup with review of electronic medical records for evidence of renal lymphoma. Patients without evidence of lymphoma at a minimum of 6 months of followup were considered to have had renalymphoma.

**Biopsy Procedure Technique**

For all renal biopsies the same coaxial technique was used to enable multiple specimens to be obtained via a single introducer needle. A 17 gauge Temno® coaxial needle was advanced into the lesions under CT guidance in 10 cases and ultrasound guidance in 1. The choice of imaging modality was at the discretion of the operator based on target lesion visibility on ultrasound vs CT. Fine needle aspirates and cores could be obtained via this coaxial introducer needle and each was usually obtained at operator discretion. Three to 4 fine needle aspirates were obtained through the introducer needle using a 22 gauge Chiba needle and 2 to 4 core biopsies were performed using an 18 gauge cutting needle.

**RESULTS**

Of the 413 image guided biopsies performed by interventionist radiologists for renal lesions at our institution during the study period we identified 11 patients (3%) in whom biopsy of the renal mass yielded a diagnosis of lymphoma. All of these patients had secondary lymphoma. In all 11 patients the initial percutaneous biopsy was definitive for lymphoma and there was no patient in whom repeat biopsy was required. Patient age at diagnosis was 5 to 88 years (mean ± SD 61 ± 7). Eight patients were male and 3 were female.

Based on cytology, flow cytometry and/or histopathology results a diagnosis of B-cell lymphoma was made in 10 cases, while lymphomatoid granulomatosis was diagnosed in the remaining case (see table). Core biopsy analysis yielded a diagnosis of B-cell lymphoma in 10 cases and lymphomatoid granulomatosis in 1. The subtype of B-cell lymphoma was diagnosed on core biopsy alone in 8 of the 10 lymphoma cases. Cytological analysis performed in FNAs yielded a diagnosis of B-cell lymphoma in 3 cases (30%), lymphoma in 3 (30%), suspicion for lymphoma in 1 (10%), atypical cells in 2 (20%) and no diagnosis in 1 (10%). B-cell lymphoma subtype classification was achieved by cytology in 1 case. Flow cytometry performed in FNAs differentiated B from T-cell lymphoma in 3 cases when cytology did not, identified B-cell lymphoma subtype in 1 when cytology did not, concurred with cytology in the diagnosis of B-cell lymphoma in 1 and yielded a diagnosis of B-cell lymphoma without subtype in 1 in which subtype classification was available on cytology. The flow cytometry specimen was insufficient in 2 cases and identified no abnormality in 1. No significant biopsy related complications were identified and no patient required hospital admission.

Of the 402 patients with biopsies negative for lymphoma biopsy results were diagnostic of another malignancy in 220 (54.7%) and of benign renal masses in 39 (9.7%). The remaining 143 biopsies (35.6%) were indeterminate. Lymphoma was not identified at pathology in any of the 113 patients (28.1%) in our study who later underwent nephrectomy. Similarly the 27 patients (6.7%) who underwent repeat biopsy were negative for lymphoma. Five patients underwent subsequent nephrectomy plus repeat biopsy, of whom none had evidence of lymphoma.

Of the 143 patients with indeterminate pathological findings on initial biopsy 43 underwent a subsequent histopathological examination that was negative for lymphoma. The remaining 100 patients were followed clinically for a minimum of 6 months with a review of electronic medical records. Of these patients 40 had less than 6 months of recorded followup available and no evidence of lymphoma, while 60 were followed more than 6 months (mean 1,077.7 ± 618.5 days). Evidence of renal lymphoma was found in 1 patient in the latter group in whom initial biopsy yielded unsatisfactory material for analysis.

**Imaging Appearances**

Three distinct patterns of renal lymphoma were identified on CT in 10 cases and on ultrasound in 1, including 1) a solitary focal mass in 8, 2) a posterior perinephric mass appearing as a contiguous plaque-like lesion applied to the
Indications for Biopsy

Two categories of indication for biopsy were identified. Category 1 consisted of 9 patients with a known extrarenal primary malignancy who presented with a renal mass suspicious for malignant neoplasm. Extrarenal primary tumors included non-Hodgkin's lymphoma alone in 7, non-Hodgkin's lymphoma with brochoalveolar cell carcinoma in 1 and melanoma alone in 1. Category 2 consisted of 2 patients who presented with a renal mass and widespread metastatic disease in whom renal biopsy was performed to identify the source of metastases.

Subsequent treatment for lymphoma was chemotherapy alone in 6 cases, chemotherapy with radiation in 3, radiation alone in 1 and unknown in 1 (lymphomatoid granulomatosis). Surgical treatment was not performed in any case. Average followup in the 8 patients in our study who underwent subsequent imaging at our institution was 694 ± 519 days. Mean clinical followup was 494 ± 655 days.

DISCUSSION

Image guided renal mass biopsy has previously been described in the literature as a safe and accurate means of characterizing indeterminate renal masses. Despite its potentially valuable role for directing treatment planning in patients with lymphomatous involvement of the kidney there is limited information regarding the usefulness of the procedure for diagnosing renal lymphoma. In the current study we present data regarding the diagnostic yield and safety of biopsy for histopathologically characterizing focal renal lymphoma lesions.

The diagnostic yield of core biopsy was compared with cytological and flow cytometry analysis of fine needle aspirates.
In our sample core biopsy differentiated B from T-cell lymphoma in all cases and achieved lymphoma subtype classification in 8 (80%). We found that cytological examination of FNA distinguished B from T-cell lymphoma in 30% of cases and identified lymphoma subtype in only 20%. The addition of flow cytometry studies improved the diagnostic yield of FNA, permitting the differentiation of B from T-cell lymphoma in 3 cases and allowing subtype classification to be made in 1. Moreover, flow cytometry supported the subtype cytodiagnosis of B-cell lymphoma in additional cases. Overall combined flow cytometry and cytological analysis of FNAs successfully identified B-cell lymphoma in 70% of cases and achieved subtype classification in 30%. FNA provided diagnostic information that was not obtained on core biopsy in 1 case.

This study suggests that core biopsy is likely to add incremental value to cytological and flow cytometry analysis of FNA for the diagnosis and classification of renal lymphoma presenting as a focal renal mass. The importance of this finding is underscored by the importance of lymphoma subtype classification for developing a prognosis and directing appropriate chemotherapy planning. Previous studies in the literature have assessed the relative value of performing FNA and core biopsy for lymphoma with varying outcomes. Silverman et al compared the results of core biopsy and FNA of abdominal lymphoma and concluded that core biopsy performed with larger needles is no more likely than FNA to yield diagnosis. However, to our knowledge our study is the first to present data on a series of patients with focal renal lymphoma. Our findings suggest that combined core biopsy and FNA is useful for the histopathological characterization of renal lymphoma when a renal lesion is present.

We performed followup in all patients without a diagnosis of lymphoma to assess the false-negative rate of diagnosis. Initial biopsy diagnosed 220 alternative malignant masses and 39 benign masses, while 143 patients had indeterminate histopathology. In the indeterminate group 43 patients had subsequent re-biopsy or nephrectomy that was negative for lymphoma. Clinical followup data available on 60 of the remaining 100 patients with indeterminate biopsy results yielded missed renal lymphoma in 1. In this woman with large cell lymphoma of the breast the renal lesion later responded to systemic lymphoma treatment. Therefore, our results document 1 definite and 40 potential false-negative results, yielding a false-negative rate of between 0.25% and 9.95%. Given the low prevalence of renal lymphoma, it is likely that most of the 40 patients with less than 6 months of followup did not have renal lymphoma and the true false-negative rate is likely to be at the lower end of this range.

Our series of patients underwent biopsy for 3 primary indications, including 1) a suspicious renal mass in the presence of a known extrarenal primary malignancy in 8, including lymphoma in 7, 2) an indeterminate renal mass with metastatic disease found elsewhere in 2 and 3) the incidental discovery of a suspicious renal lesion in the absence of previously identified malignancy elsewhere in 1. Subsequent treatment regimens included chemotherapy alone in 6 cases, chemotherapy with radiation in 3, radiation alone in 1 and an unknown course of therapy in 1. Surgical treatment was not performed in any case. Because it is accepted generally that initial management for an indeterminate solid renal mass is partial or radical nephrectomy, we conclude that biopsy diagnosis altered the course of treatment in all 11 of these patients since none underwent nephrectomy despite the presence of a focal renal lesion.

Some potential limitations of this study should be considered. The number of included patients with lymphoma was relatively small. Studies in larger sets of patients would certainly yield a more reliable assessment of the usefulness of percutaneous renal biopsy for diagnosing renal lymphoma. We relied on at least 6 months of clinical followup to verify the absence of lymphoma in many of our patients with indeterminate initial biopsies because pathological proof was not uniformly available. Since lymphoma can manifest clinically during a protracted period, no clinical followup duration can definitively exclude its presence.

**CONCLUSIONS**

We reviewed the diagnosis of renal lymphoma in 11 of 413 patients who underwent percutaneous image guided biopsy for indeterminate focal renal masses. Percutaneous renal biopsy was accurate and safe for diagnosing renal lymphoma. Making this diagnosis in advance of therapy may prevent unnecessary surgical or ablative procedures and it can facilitate appropriate treatment planning. We recommend the addition of core biopsy to flow cytometry and cytological analysis of FNAs to achieve the highest diagnostic yield and the most accurate lymphoma subtype classification.

**Abbreviations and Acronyms**

<table>
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<th>CT</th>
<th>computerized tomography</th>
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<td>FNA</td>
<td>fine needle aspiration</td>
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**REFERENCES**

This series of 407 image guided biopsies of focal renal lesions represents a large, well controlled series. The value of making the diagnosis of lymphoma is important to practicing urologists because nephrectomy or partial nephrectomy is not the appropriate form of therapy for these lesions. In fact, chemotherapy is the appropriate form of therapy, thus, making the diagnosis of lymphoma of the kidney before surgical intervention important.

The role of renal biopsy for other renal lesions is currently being debated by multiple groups (reference 13 in article). However, there is no question as to its value in making the diagnosis of renal lymphoma. We agree with these authors that core biopsies are much more capable of providing adequate tissue for pathological analysis than FNA.

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