Original Study

Hematologic Parameters to Predict Small Renal Mass Biopsy Pathology

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Abstract

Studies have shown that certain elevated hematologic parameters are associated with the presence of a malignancy. The present study of 475 diagnostic biopsy specimens of a small renal mass found that the hematologic parameters do not differ significantly between those with benign and primary renal malignancies. However, elevated platelet-to-lymphocyte ratios might be useful as a simple and inexpensive marker to help distinguish nonrenal malignancies in the workup of a small renal mass.

Background: Previous studies have demonstrated that elevated neutrophil-to-lymphocyte ratios and platelet-to-lymphocyte ratios (PLRs) are associated with the presence of various malignancies. The present study evaluated various hematologic parameters and their association with renal tumor biopsy pathology. **Materials and Methods:** The clinical, hematologic, and pathologic parameters were obtained through a retrospective review of 475 diagnostic biopsy specimens of small renal masses from January 2001 to December 2013. The complete blood counts closest to and before the biopsies were obtained. The biopsy pathologic findings were divided into 3 groups: benign, primary renal malignancy, and nonrenal malignancy. The hematologic parameters were compared among the 3 groups. Receiver operating characteristic curves were constructed for the parameters that were significantly different among the groups. Multiple logistic regression models were used to assess whether the clinical and hematologic parameters were associated with benign or malignant pathologic findings. **Results:** Hematologic parameters were available for 462 cases (97%). Pathologic examination of the biopsy specimens demonstrated benign, primary renal malignancy, and nonrenal malignancy in 114 (25%), 337 (73%), and 11 (2%) patients, respectively. The PLR was significantly ($P = .010$) different among the 3 groups and was significantly ($P = .013$) greater in those with nonrenal malignancies than in those with primary renal malignancies. Using a cutoff for the PLR of 202.9 gave a sensitivity of 63.6% and specificity of 82.2% for detecting a nonrenal malignancy. **Conclusion:** The hematologic parameters did not differ significantly between benign and primary renal malignant masses undergoing biopsy. The PLR might be useful as a simple and inexpensive marker to help distinguish nonrenal malignancies in the workup of a small renal mass.

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Introduction

Small renal masses (SRMs), typically defined as solid enhancing tumors < 4 cm in diameter, are being detected more frequently owing to the increased use of abdominal imaging.[1] It has previously been shown that up to 70% to 80% of SRMs are malignant, with 20% to 30% benign.[2,3] Although previously these masses were excised without a pathologic diagnosis, a percutaneous renal tumor biopsy has been proposed as a method to establish the histologic diagnosis preoperatively and avoid unnecessary interventions in patients with benign pathologic features.[4]

Previous studies have evaluated various hematologic parameters and their association with malignancy. The neutrophil-to-lymphocyte

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ratio (NLR), obtained by dividing the absolute neutrophil count by the absolute lymphocyte count, has been shown to be elevated in patients with various malignant diseases compared with those with benign disease.[5-7] The platelet-to-lymphocyte ratio (PLR) has also been shown to be a potentially useful marker for malignancy.[8-11] To date, however, no study has evaluated whether the hematologic parameters are associated with pathologic features found on biopsy of an SRM. The objective of the present study was to determine whether the hematologic parameters are associated with the histologic features of patients undergoing biopsy of a SRM. In some centers, up to 19% of biopsies will be nondiagnostic.[4] Thus, identifying noninvasive, simple, and reliable biomarkers for predicting biopsy pathology could help avoid biopsy-related complications, aid in decision-making of nondiagnostic biopsies, and be cost-effective.

Materials and Methods

After obtaining institutional research ethics board approval, the patients who had undergone an image-guided biopsy for an SRM to aid in treatment planning from January 2001 to December 2013 at the University Health Network (Toronto, ON, Canada) were identified retrospectively through a prospectively maintained database (eKidney). A medical record review was completed to exclude lesions that were mainly cystic and biopsies that had not been performed with the objective of aiding treatment planning. All patients had clinical and radiologic suspicion that the renal mass could represent a primary renal malignancy.

For the patients with >1 biopsy specimen available, the following criteria were used. First, if the findings from the initial biopsy were nondiagnostic, the hematologic parameters for the first diagnostic biopsy were obtained. Second, if the patients had undergone >1 diagnostic biopsy during the defined period, only the hematologic parameters from the first diagnostic biopsy were retained. Third, if they had undergone biopsy of >1 mass during the same session and the different masses had different pathologic features (1 mass being malignant and the other benign), the hematologic parameters were tested to reflect malignancy. Finally, if they had had >1 mass biopsied during the same session with identical pathologic findings, only 1 set of hematologic parameters was included for analysis.

Patients who had undergone biopsy for a mass in a transplanted kidney ($n=3$) were excluded, because their medications could have influenced their complete blood count (CBC) with differential. Of the remaining 530 biopsies, 54 (10.2%) were nondiagnostic. One patient had carcinoma of an unspecified type and was excluded. Of the 475 patients with a diagnostic biopsy, the CBC with differential was available for 462 (97%).

The clinical and pathologic parameters were abstracted from the database or ascertained from the electronic medical records. The parameters of interest included age, gender, body mass index (BMI), smoking status, CBC with differential, tumor size, and biopsy histologic findings. Tumor size was defined as the lesion's maximal axial diameter. The CBCs closest to, but before, the biopsy date were used. The NLR was calculated using the absolute neutrophil count divided by the absolute lymphocyte count. A similar calculation was used to obtain the PLR. The pathologic features were categorized into 3 groups: benign, primary renal malignancy, and nonrenal malignancy.

Statistical Analysis

The baseline characteristics were compared among the 3 groups using analysis of variance with Bonferroni's post hoc correction or the Kruskal-Wallis test with the post hoc Wilcoxon rank sum test for continuous variables and the χ^2 test and Fisher's exact test for categorical variables. Receiver operating characteristics (ROC) curve analyses were used for the sensitivity and specificity estimates for the hematologic parameters found to be significantly different among the 3 pathology groups. Appropriate cutoffs aimed at maximizing both sensitivity and specificity for the hematologic parameters were identified using the ROC curve.

Logistic regression analysis was used to assess whether the NLR and PLR were associated with the biopsy pathologic findings (benign vs. malignant) after adjusting for age, maximal tumor size, and gender. Given the limited number of patients in the nonrenal malignancy group, they were combined with the primary renal malignancy group in the logistic regression models. Furthermore, given the correlation between the various hematologic parameters, to avoid collinearity a decision was made a priori to only include the NLR and PLR in the logistic regression models. In a secondary analysis, the models were adjusted for BMI and smoking history. The fit of the models was assessed using the Hosmer and Lemeshow test and the c-statistic. Residuals were assessed using a case wise diagnostics method. The odds ratios are presented with their 95% confidence intervals (CIs).

All statistical analyses were performed using Statistical Analysis Systems, version 9.3 (SAS Institute, Cary, NC). A 2P value of .05 was considered statistically significant.

Results

Patient Characteristics

The patient characteristics are listed in Table 1. Of the final cohort of 462 patients, 114 (25%) were found to have benign pathologic features and 348 (75%) malignant pathologic features. Of those that were benign, 70 were reported as an oncocytic renal neoplasm consistent with oncocytoma, 31 were angiomyolipomas, 5 were inflammatory, 3 were metanephric adenomas, 2 were spindle cell lesions, 2 were hemangiomas, and 1 was leiomyoma. Of those that were malignant, 337 were primary renal malignancies and 11 were nonrenal malignancies. Of the primary renal malignancies, 205 were clear cell renal cell carcinoma (RCC), 90 were papillary RCC, 26 were chromophobe RCC, 2 were mucinous tubular carcinoma of the kidney, 1 was translocation RCC, and 13 were unclassified RCC.

Of the nonrenal malignancies, 2 were urothelial carcinoma, 2 were lymphoma, 2 were metastatic lung carcinoma, 2 were metastatic thyroid cancer, 1 had metastatic melanoma, 1 had metastatic squamous cell carcinoma, and 1 had metastatic colon adenocarcinoma. In the patients whose pathologic findings were consistent with metastasis, 4 (36%) had received previous chemotherapy and 5 (45%) had received previous radiation. The median time from the initial diagnosis of a nonrenal malignancy to SRM biopsy was 3.9 years.

Patients with a primary renal malignancy ($P=.01$) or nonrenal malignancy ($P=.046$) had significantly larger maximal tumor dimensions than those of the benign tumors. However, the maximal tumor dimension did not differ significantly ($P=.41$) between the primary renal malignancies and nonrenal malignancies. Patients

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