Prediction of Carcinoma in Acquired Cystic Disease as a Function of Kidney Weight

Margaret L. MacDougall, M.D., Ph.D., Larry W. Welling, M.D., Ph.D., and Thomas B. Wiegmann, M.D.

ABSTRACT

Acquired renal cystic disease occurs in up to 80% of patients on chronic dialysis and is complicated by renal adenocarcinoma in about 6% of cases. This report suggests that acquired cystic kidneys weighing more than 150 g are six times more likely to contain carcinoma than are kidneys of smaller size. This relationship is true whether or not the large kidney contains a radiologically detectable tumor. Therefore, even in the absence of demonstrable tumor mass, strong consideration should be given to the removal of large acquired cystic kidneys.

Key Words: Cancer, cystic disease, dialysis

carcinoma in cystic kidneys and suggested a possible relationship between kidney size and the presence of malignancy.

CASE REPORT

A 49-year-old white male with end-stage renal disease secondary to hypertension was maintained on home hemodialysis. Renal sonography at the initiation of dialysis showed a right kidney 12 cm in length and a left kidney 7 cm in length. The smaller size of the left kidney was consistent with a partial nephrectomy some 30 years previously for “ectopic kidney.” Neither kidney showed any evidence of cysts. Eight years later, however, computerized abdominal tomography showed very large cystic kidneys (Figure 1). No discrete tumor masses were seen. Because of ureteral reflux, the patient underwent bilateral nephrectomy in preparation for transplantation.

The right kidney measured 22 x 12 x 12 cm and weighed 1,000 g. The left kidney was an approximately spherical mass measuring 10 cm in diameter and weighing 380 g. Numerous cysts from barely perceptible to approximately 3 cm in diameter were present in both kidneys at all levels of the cortex and medulla (Figure 2). A few cysts were septate, and a few appeared to be filled completely with blood clot. Some contained tan to yellow polyps up to 1 cm in diameter. In addition, there were several poorly circumscribed areas of tan discoloration, granular consistency, or mildly hemorrhagic necrosis, none of which were larger than 2 cm in diameter.

Microscopically, there was extensive interstitial fibrosis, tubular atrophy, glomerular sclerosis, arterial and arteriolar thickening, deposition of calcium oxalate crystals, and focal chronic inflammation. Many of the cysts contained proteinaceous material, while others showed hemorrhage in various stages of organization. Most cysts, particularly those of smaller size, were lined by a flattened, simple epithelium. In many of the larger cysts, however, the epithelium was thickened or markedly hyperplastic, frequently producing a thick papillary or cribriform layer. There also were large polyps that almost entirely filled a cyst cavity, and, in many of these, there were dense areas of compacted neoplastic tubule elements composed of cells with a somewhat granular, eosinophilic cytoplasm. These cells were focally quite atypical, with abnormal nuclear-cytoplasmic ratios and large nucleoli, consistent with renal cell carcinoma.
Figure 1. Noncontrast computed tomography showing markedly enlarged kidneys with numerous cysts (arrows).

Figure 2. Sagittal sections of kidneys demonstrating diffuse cystic disease and focal areas of neoplastic growth (arrows). Dark areas within the neoplastic growths indicate hemorrhage. The scale for kidney size is shown.

A para-aortic lymph node measuring 2 cm in length and approximately 1.5 cm in diameter was removed incidentally at the time of nephrectomy. It was enlarged primarily because of extensive fat infiltration. However, present in the peripheral sinuses were several small nests of granular cells in neoplastic tubule patterns resembling those within the kidneys.

METHODS

A computerized search of the literature for cystic disease, azotemia, dialysis, and carcinoma revealed 77 reports or reviews. All obtainable reports in English, French, and German were reviewed for information on single kidney weights. The sampling obtained represents all cases of acquired cystic kidneys with reported kidney weights, excluding two single kidneys containing massive hematomas. Reports with a single weight given for both kidneys together were also not included.

The relationship between single kidney weight and the presence of adenoma or carcinoma was evaluated by using receiver-operating characteristic curves. In this analysis, the true-positive rate of cancer (percent sensitivity) is plotted on the $y$ axis with the false-positive rate (100 percent minus specificity) plotted on the $x$ axis along the separator variable (kidney weight). A highly specific and sensitive test will show the resultant curve to be displaced towards the left upper corner of the diagram while a nonspecific test will show as a straight diagonal (7).

RESULTS

Single kidney weights were found for only 106 kidneys reported in the literature (Table 1). The weights ranged from 5 to 1,250 g, with only 25% exceeding 150 g (8–24). In 79 kidneys weighing 150 g or less, 11.4% were reported to contain carcinoma, 26.6% had adenomas, and 62.0% were tumor free. In contrast, of 27 kidneys weighing more than 150 g, 55.6% contained carcinomas, 22.2% had adenomas, and only 22.2% were tumor free. The smaller kidneys with carcinoma were not accompanied by metastases. However, in only four cases was this explicitly stated while five reports made no comment. Of 15 larger kidneys with carcinoma, 3 had metastases at the time of nephrectomy (8,9,11). Isolated lymph node metastases also occurred in these large kidneys (8,25). In the present case, node metastases also were associated with large kidneys. Further information regarding metastatic disease was not available on most of these cases because autopsy material was the primary source.

Receiver-operating characteristic curves showed a strong positive relationship between kidney weight and the presence of carcinoma (Figure 3). For example, at a discriminator weight of 350 g, the specificity for cancer was 100% with a corresponding sensitivity of 40%. At a kidney weight of 200 g, the specificity for cancer was 90% with a corresponding sensitivity of 65%. The straight line of the relationship between

<table>
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<th>Weight</th>
<th>$N$</th>
<th>No Tumor</th>
<th>Adenoma</th>
<th>Carcinoma</th>
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<tbody>
<tr>
<td>$\leq 150$</td>
<td>79</td>
<td>49</td>
<td>21</td>
<td>9</td>
</tr>
<tr>
<td>$&gt; 150$</td>
<td>27</td>
<td>6</td>
<td>6</td>
<td>15</td>
</tr>
<tr>
<td>Total</td>
<td>106</td>
<td>55</td>
<td>27</td>
<td>24</td>
</tr>
</tbody>
</table>

$^a$ Chi square, $F = 23.63, P < 0.001$. See references 1, 7–9, and 12–24.
Acquired Cystic Kidneys and Carcinoma

The diagnosis of renal cell carcinoma in acquired cystic kidney disease requires the use of ultrasound or computed tomography. Despite the lack of criteria to determine whether an acquired cystic kidney weighs more than 150 g on the basis of noninvasive tests, the size of these kidneys can be measured. Kidneys approaching or exceeding the size of normal kidneys should be considered enlarged.

Several relationships are now apparent regarding kidney weight and the presence of a neoplastic, proliferative process within the acquired cystic kidney. First, smaller kidneys have a low probability of proliferation, 62% being free of adenomas as well as carcinomas. Second, adenomas occur at about equal frequency at all kidney weights. There are several ways to interpret these findings. On the basis of the similar percentage of adenomas in the two groups and the marked difference in the number of carcinomas, we speculate that two pathologic stimuli are directed to these remnant kidneys, a concept consistent with other two-step stimuli for solid tumors (32).

In summary, a review of the literature on carcinoma in acquired renal cystic disease indicates that kidneys larger than 150 g are six times more likely to contain carcinoma than are kidneys of smaller size. They also are more likely to produce regional and generalized metastases. This is true whether or not the kidney contains a radiologically detectable tumor. Therefore, even in the absence of demonstrable tumor mass, strong consideration should be given to the presence of adenocarcinoma in situ in large acquired cystic kidneys. Whether this relationship will lead to increased screening or early nephrectomy remains to be investigated.

REFERENCES

2. Mickisch O, Bommer J, Bachmann S, Wald-
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