Intestinal Metaplasia of the Renal Pelvis

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INTRODUCTION
Renal pelvis is normally lined by urothelium and contains neither squamous nor intestinal epithelium. However, transitional cell epithelium undergoes phenotypic changes usually in the form of squamous metaplasia.1 We report a rare case of intestinal metaplasia of the renal pelvis with cytokeratin profile and assessment of the tumor markers to set light to understand the pathogenesis of the multistep pathway through metaplasia to neoplasia.

CASE REPORT
A 32-year-old man presented with left flank pain and dysuria. He had a history of urolithiasis for 3 years. Physical examination revealed a nonpalpable left kidney. An intravenous pyelography showed a nonfunctioning left kidney. No calculus was identified within the urinary tract. Ultrasonography revealed a small kidney with dimensions of 9.5 × 5.3 cm.

Left nephrectomy was performed. Gross examination of the surgical specimen revealed a shrunken kidney with dimensions of 6 × 3 × 2 cm. Cut surface showed destruction of the normal parenchyma and thinning of the cortex (Figure 1). The corticomedullary border was obscured with fatty infiltration. Light microscopic examination revealed features of chronic pyelonephritis, including tubular atrophy with thyroidization of the remaining tubules, loss of glomeruli, interstitial fibrosis, and lymphoplasmacytic infiltrate. The epithelial lining of the renal pelvis showed intestinal metaplasia with abundant goblet cells. Gradual transition from urothelium to

Figure 1. Cut surface of the nephrectomy specimen showing thinning of the cortex, dilatation of the calices, and fatty infiltration of the medulla.
the intestinal epithelium was seen in the form of pyelitis glandularis (Figure 2). No squamous metaplasia was observed. Histologic examination did not reveal any dysplastic foci or invasive adenocarcinoma. Immunohistochemical studies were performed and summarized in Table.

Immunohistochemical staining pattern in transitional and metaplastic epithelium.

<table>
<thead>
<tr>
<th></th>
<th>Transitional epithelium</th>
<th>Pyelitis glandularis</th>
<th>Intestinal epithelium</th>
</tr>
</thead>
<tbody>
<tr>
<td>CK5/6</td>
<td>+ (basal cells)</td>
<td>+ (basal cells)</td>
<td>-</td>
</tr>
<tr>
<td>CK7</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>CK8</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>CK18</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>CK19</td>
<td>+ (focal)</td>
<td>+ (focal)</td>
<td>-</td>
</tr>
<tr>
<td>CK20</td>
<td>+ (superficial layer)</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>P16</td>
<td>-</td>
<td>+ (few cells)</td>
<td>+</td>
</tr>
<tr>
<td>P53</td>
<td>-</td>
<td>+ (few cells)</td>
<td>+</td>
</tr>
<tr>
<td>Ki67</td>
<td>&lt;1 %</td>
<td>&lt;1 %</td>
<td>10% to 20%</td>
</tr>
</tbody>
</table>

After 3 months of follow-up, the patient was asymptomatic and free of disease.

**DISCUSSION**

The intestinal metaplasia of the renal pelvis is very rare and to the best of our knowledge, only 15 subjects have been reported in English literature. The ages ranged from 24 to 79 years old. The sex ratio is 3.6 to 1 (male to female ratio is 11 to 3) with a male predominance. Almost all of the subjects have been reported to be associated with pyonephrosis or pyelonephritis. Of reported subjects, 14 (93%) had calculi. Six of the 15 subjects had both intestinal and squamous metaplasia, and the remaining cases had only intestinal metaplasia. Intestinal metaplasia of the renal pelvis is an incidental histologic finding and the clinical presentation is nonspecific and mainly...
depends on the underlying kidney disease.

Urothelium has a potential to undergo metaplastic changes, and chronic inflammation and irritation play critical roles in development of metaplastic changes. However, the mechanism of the glandular metaplasia is not well understood.\(^5\)

Urothelium normally expresses simple epithelial cytokeratins such as CK7, CK8, CK18, CK19, CK20, and other isoforms in small amounts of CK5, CK4, and CK17. Simple epithelial cytokeratins are present in all urothelial cell layers. Cytokeratin 5 is expressed in basal cells and CK13 and CK20 are expressed in superficial umbrella cells.\(^6\) In the present case, CK7, CK8, CK18, CK19, CK20, and CK5/6 expression are preserved in normal urothelium whereas metaplastic epithelium lost CK7, CK19, and CK5/6 expression and gained stronger CK20 expression. Pyelitis glandularis showed a cytokeratin expression profile similar to the normal urothelium. These findings further support that pyelitis glandularis is a transition step in this metaplastic process.

Precancerous changes are thought to be present in the metaplastic changes and adenocarcinomas may arise from metaplastic changes of potentially unstable epithelium.\(^7\) Alterations in cell cycle regulators such as p16 and p53 are found in significant fractions of urothelial and nonurothelial carcinomas.\(^7\) The p53 expression indicates loss of cell cycle control and is in favor of progression into dysplasia. The p53 gene product is known to modulate the transition from premalignant to malignant condition. It plays an early role in the neoplastic changes and its accumulation might occur in the nondysplastic gland before the phenotypic changes of neoplasia become apparent.\(^8\) The p16 (CDKN2A) is frequently involved in urinary bladder carcinogenesis and plays a role similar to p53.\(^9\)

In conclusion, urothelium begins to loss of cell cycle control assessed by p53 and p16 accumulation during the intestinal metaplasia and our study proves the hypothesis that metaplastic epithelium of the renal pelvis is at least potentially premalignant.\(^1\) Monitoring of the renal pelvic urothelium in the context of the pyelonephritis is difficult; therefore, nephrectomy will be the safest therapeutic strategy in long lasting cases.

CONFLICT OF INTEREST

None declared.

REFERENCES


