Case Report

Metastatic Tubulocystic Renal Cell Carcinoma Treated with Targeted Therapies

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Abstract
A 64-year-old man was diagnosed with a right renal tumor and underwent radical nephrectomy. The pathological diagnosis was tubulocystic renal cell carcinoma. One month after surgery, metastases appeared in the para-vena cava lymph nodes and the patient began targeted therapy with sequential sunitinib, everolimus, and axitinib. The metastases progressed gradually and the patient died 10 months after surgery.

INTRODUCTION
Tubulocystic renal cell carcinoma is a rare renal malignancy. The prognosis is favorable when treated at the early stage, but poor for advanced cases. To date, few studies have assessed the efficacy of targeted therapies. Here, we report a case of a tubulocystic renal carcinoma that was treated with several different targeted therapies.

CASE REPORT
A 64-year-old man presented with dull pain and slight swelling in the right epididymis. CT scan revealed a poorly enhanced solid tumor in the right kidney (72 x 71 x 70 mm) with infiltration into the peri-renal fat (Figure 1) and metastasis to the right epididymis. The clinical diagnosis was T3aN0M1. He underwent laparoscopic radical nephrectomy and right orchidectomy. Histological examination showed multiple small- to intermediate-sized tubules and cysts lined by a single layer of large nucleic eosinophilic epithelial cells separated by fibrotic stroma (Figure 2). The patient was diagnosed with tubulocystic renal cell carcinoma and its metastasis. One month after nephrectomy, CT scan demonstrated multiple metastases in the para-vena cava lymph nodes and lungs. The patient was then treated with sunitinib (50 mg/day). CT scan revealed that the lymph node and lung metastases were stable at 3 months, but by 5 month they had grown and multiple liver metastases were also visible (Table 1). The treatment regimen was then changed from sunitinib to everolimus (10 mg/day). The lymph node metastases shrank, but the liver metastases progressed after 1 month. We consequently switched to axitinib (10 mg/day). The metastases were stable for 2 month, but then progressed after another 2 months. Subsequently, he suffered grade 2 interstitial pneumonia and stopped the targeted therapies. The metastases progressed gradually and he died 10 months after nephrectomy.

DISCUSSION

Tubulocystic carcinoma was categorized as a low-grade collecting duct carcinoma (Bellini duct carcinoma); however, recent studies have described this tumor as a separate entity [1-3]. This is a rare type of renal cell carcinoma that accounts for <1% of all renal cell carcinomas [2]. The mean patient age is 58 years (range, 34-94 years), with a male dominance of 4:7:1 [3]. On CT scan, tubulocystic carcinoma forms a solid tumor (72.7%), a cystic tumor (18.2%), or a complex structure (9.1%), which is poorly enhanced by imaging contrast [4]. Immunohistochemistry shows positivities for CD10 and P504S proximal tubule markers) as well as parvalbumin, CK19, CK7 and CK34βE12 (distal tubule markers) [1,2]. Despite the higher grade cytological features, most patients with tubulocystic carcinoma have a favorable prognosis when surgical resection is performed at the localized stage [2]. However, once it metastasizes, the carcinoma shows progressive and aggressive behavior.

Although there is no established salvage therapy, some authors have reported the effectiveness of targeted therapies. Teramoto et al. reported a case that metastasized to the lung and lymph nodes. Sunitinib treatment achieved a partial response with no disease progression 12 months after nephrectomy [5]. Steiner et al. evaluated the molecular pathways in tubulocystic renal cell carcinoma and reported no significant activation of angiogenesis via the VHL/HIF, RTK/MAPK, and PI3K/Akt/mTOR pathways; therefore, anti-angiogenic targeted therapy was not recommended [6]. The treatment course of our patient suggests that targeted therapy is effective for treating tubulocystic renal cell carcinoma metastases in the lymph nodes or lungs, but not in the liver.

REFERENCES


Table 1: Treatment response of targeted therapies for metastases.

<table>
<thead>
<tr>
<th>Pathology</th>
<th>Para-vena cava lymph node</th>
<th>Lung</th>
<th>Liver</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Duration</td>
<td>Response</td>
<td>%</td>
</tr>
<tr>
<td>Sunitinib</td>
<td>3 mo</td>
<td>SD</td>
<td>+10%</td>
</tr>
<tr>
<td></td>
<td>5 mo</td>
<td>SD</td>
<td>+10%</td>
</tr>
<tr>
<td>Everolimus</td>
<td>1 mo</td>
<td>SD</td>
<td>+5%</td>
</tr>
<tr>
<td>Axitinib</td>
<td>2 mo</td>
<td>SD</td>
<td>+4%</td>
</tr>
</tbody>
</table>

Treatment responses are expressed based on RECIST criteria.
CR, complete response; PR, partial response; SD, stable disease; PD, progress disease.