Prolonged natural progression from localized to symptomatic renal cell carcinoma

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Surgical excision is the gold standard therapy for clinically localized renal masses. Nevertheless, prognostication of the natural history of untreated renal cell carcinoma (RCC) remains a clinical challenge. While active surveillance (AS) has emerged as a viable treatment option in select patients with localized tumors and significant competing mortality risks, long term follow up data to assess the risk of disease progression are limited. We present a case of a localized, clinical stage T2 renal mass progressing to regional and systemic disease over 6 years, demonstrating that kinetics of disease progression may be prolonged and are yet to be fully understood.

Key Words: renal cell carcinoma, metastases, natural history, active surveillance

Introduction

It has been estimated that more than 64,000 men and women will be diagnosed with kidney cancer in the United States in 2012, with the majority of cases being renal cell carcinomas (RCC).[1] Due to the widespread use of cross-sectional imaging, earlier diagnosis of RCC has led to rising rates of treatment, but cancer-specific death rates are yet to improve.[2] With benign disease encountered at resection of as many as 20% of small renal masses (SRM), determination of tumor biology preoperatively may help guide treatment strategy. A number of studies have attempted to demonstrate an association between tumor size, anatomic location, and growth kinetics with the likelihood and severity of malignancy.[3] Yet, the natural clinical progression of asymptomatic, localized renal masses to symptomatic, non-localized disease remains poorly understood. According to a recent pooled analysis of 18 clinical series consisting of 936 renal masses, only 18 tumors were found to have metastasized while under expectant management, the largest of which was 8.8 cm.[4] Here, we present a case of a patient with a 9.5 cm left renal mass who was asymptomatic at presentation and over the course of 6 years progressed to symptomatic and widely metastatic disease. This case depicts that the natural progression of untreated RCC can be indeterminate and prolonged even with large renal masses at presentation, emphasizing the challenge of clinical trade off decisions facing contemporary urologists.

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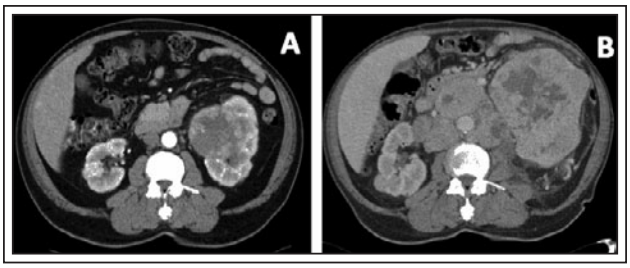

Figure 1. a) Contrast enhanced computed tomography (CT) of the abdomen at initial presentation demonstrating a 9.0 cm x 9.5 cm x 9.0 cm left renal mass without lymphadenopathy. **b)** CT scan 6 years later depicts interval growth of the patient's renal mass, retroperitoneal lymphadenopathy, and distant metastatic disease (not shown).

Case report

A 67-year-old African American male presented to an outside institution with an incidentally discovered asymptomatic 9.5 cm left localized renal mass, refused definitive therapy, and was subsequently lost to follow up, Figure 1a. He then re-presented symptomatically 72 months later with a 4 month history of weight loss and early satiety along with a 1 month history of gross hematuria. Radiographic evaluation revealed significant primary tumor growth (linear 1.1 cm/year; volumetric 1210 cm^3/year) along with progression to regional and systemic disease, Figure 1b. Compared to initial radiographic studies, interval imaging demonstrated a 16 cm primary tumor with development of extensive paraaortic (7 cm x 9 cm), renal hilar (5 cm x 6 cm), and retrocaval (4 cm x 6 cm) lymphadenopathy from the time of initial presentation, Figure 1b.

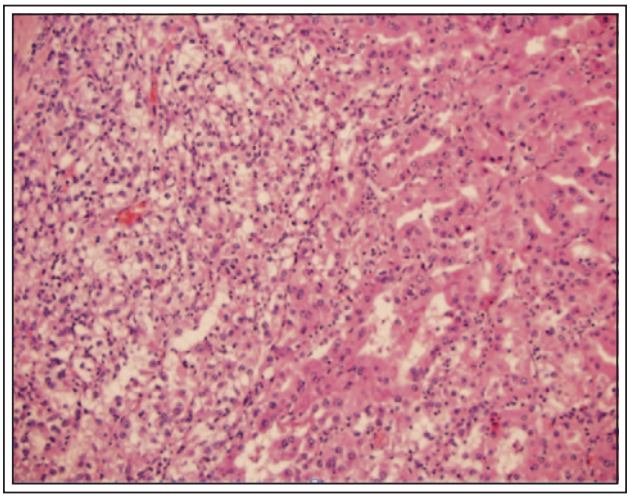

Figure 2. Hematoxylin and eosin staining of the tumor specimen at 10x magnification, showing mixed histology of clear cell (left) as well as papillary renal cell carcinoma (right) with < 5% sarcomatoid features (not pictured).

The patient underwent a cytoreductive nephrectomy and retroperitoneal lymph node dissection revealing a 16.5 cm pT3aN1M1 mixed papillary and clear cell RCC (Fuhrman grade IV) with < 5% sarcomatoid features, Figure 2. Three months after surgery, the patient developed brain metastasis and completed stereotactic brain radiation. Nine months following nephrectomy the patient was alive and receiving a course of intravenous temsirolimus targeted therapy.

Discussion

More prevalent use of routine abdominal imaging has led to an increase in both the number of incidentally diagnosed renal masses as well as the use of surgical therapy, while mortality outcomes remain essentially unchanged.[5] These data imply that a proportion of small renal masses may not require treatment and are thus overdiagnosed. As the cumulative experience with expectant management of renal tumors matures,[4,9] active surveillance (AS) or careful observation with serial imaging to guide the need for delayed intervention have emerged as attractive alternative management strategies to excision and ablation in select elderly and/or comorbid patients.

Current AS protocols lack well-defined predictors of malignant potential and triggers for intervention. While radiographic characteristics associated with malignant and high grade features include tumor size and anatomic complexity,[3] recent data suggest that a significant proportion of localized tumors can grow very large without progressing to other sites or causing symptoms. While individual cases of disease progression under observation have been reported,[6] institutional[7,8] and meta-analytic data[4,9] of renal masses managed expectantly suggest that disease progression in patients who present with localized disease is both an uncommon and delayed event.[10] As a result, the use of AS has evolved to include select cT1b-2 tumors in patients with significant competing risks. While large size at presentation, rapid primary tumor growth kinetics, and high grade features suggest aggressive tumor biology in lesions managed expectantly,[4] this case illustrates that progression from localized to symptomatic disease can be a prolonged process even in patients with large primary tumors. As such, objective decision-making and appropriate risk-counseling remain imperative. □

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