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Two Cases of Advanced Renal Cell Cancer with Prolonged Survival of 8 and 12 Years

Nazim Turhal

Department of Medicine, Division of Neoplastic Diseases, Mount Sinai Medical Center, New York, NY, USA

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The prognosis of Stage IV renal cell cancer (RCC) is poor. Most of the long-term survivors are patients with resected solitary metastases. We report two cases of inoperable Stage IV RCC with survival of 8 and 12 years. While it is possible that the natural history of the disease contributed to such survival, the long duration of stable disease was remarkable.

Key words: renal cell cancer – vinblastine – carboplatin – long-term survivor

INTRODUCTION

Renal cell cancer (RCC) accounts for 2% of all cancers, with an estimated 28 800 new cases and 11 300 deaths in 1999 in the USA. The best chance of cure is seen at an early stage when surgery is feasible. Since symptoms are often delayed, however, a high proportion of patients present with advanced inoperable or metastatic tumors (1,2). We report here two cases of RCC, stage IV by American Joint Committee on Cancer (AJCC) staging criteria (1987 version), with exceptionally long survival of 8 and 12 years.

CASE REPORTS

CASE 1

A 66-year-old electrical repairman presented in March 1986 with right renal colic. The past medical history was significant for two myocardial infarctions that required bypass grafting in 1982 and non-insulin-dependent diabetes mellitus for 10 years. A CT scan showed a 7 cm solid left renal mass with mixed attenuation and small areas of necrosis. No lymph node enlargement, evidence of invasion of the renal vein or inferior vena cava or distant metastases were identified. At surgery, the tumor was deemed unresectable because of extensive local retroperitoneal spread (TNM: T4N0M0). The biopsies revealed renal cell carcinoma composed of lightly stained tumor cells with clear cytoplasm. The architecture was solid and cystic and thought to consist of conventional (clear cell) carcinoma. No sarcomatoid component or cytoplasmic staining with routine dyes was noted.

Chemotherapy was begun with megestrol acetate, 40 mg orally four times a day continuously, and vinblastine, 5 mg/m^2 given by bolus intravenously weekly for 2 weeks on and 2 weeks off. He tolerated this regimen well. Abdominal sonograms showed a slow decline in the size of the mass, down to 6 cm in greatest dimension in November 1990. The patient was able to continue this chemotherapy program regularly on an outpatient basis for 8 years. He had no symptoms attributable to his RCC, but developed increasing congestive heart failure. He died of another episode of acute myocardial infarction on April 1994, 8 years and 2 months after the diagnosis of his renal cell cancer. Consent for autopsy was not granted.

CASE 2

A 53-year-old secretary presented in 1976 with left renal colic. An intravenous pyelogram showed a left renal mass. Metastatic workup was negative and a left nephrectomy was performed for a large encapsulated tumor (TNM: T2N0M0). Pathology revealed renal cell carcinoma, clear cell type. The patient did not receive any adjuvant treatment and had no evidence of recurrence for 7 years. By September 1983, a CT scan of the chest showed a large 6 × 4 cm necrotic mass in the right lower lobe, and also several nodules in the right upper lobe, a right hilar mass invading the pericardium. An attempt was made to perform a pneumonectomy but the hilar tumor had invaded the inferior vena cava and the wall of the right and left atrium. The biopsies demonstrated a well-differentiated renal cell carcinoma with clear vacuolated cytoplasm with vacuoles containing cholesterol-like substances and characteristic delicate branching vascular component of the clear cell type. No sarcomatoid component or cytoplasmic staining with routine dyes was noted.

She was entered into a Phase I/II trial of single agent carboplatin, at a dose of 500 mg/m^2 intravenously every 4 weeks as an outpatient. She tolerated the treatment well except for two episodes of ulcerative esophagitis with gastrointestinal bleed-

For reprints and all correspondence: Nazim S Turhal, Division of Oncology, Marmara University Medical School, Tophanelioglu Cad. 13/15, Altunizade, Uskudar 81190, Istanbul, Turkey. E-mail: turhal@superonline.com

ing in April and October 1988, respectively. The patient had stable disease with the right hilar mass measuring 4 × 4.5 cm. She received a total of 54 cycles of carboplatin until May 1989. That last dose complicated with a Mallory–Weiss esophageal tear, blood transfusions, fluid overload and a short intubation. She recovered fully but treatment with carboplatin was then discontinued.

In August 1990, CT scan of the chest demonstrated a dominant mass in the right infrahilar region now measuring 6 × 7 cm with evidence of central necrosis. Multiple nodules were noted in the lungs, the largest of which was in the right upper lobe measuring ~1.6 cm. No treatment given at that time. She moved to another State in 1992. Her last available follow-up was in February 1995, 19 years after the initial diagnosis of renal cell carcinoma and 12 years after the onset of pulmonary metastases. She was lost to follow-up thereafter.

DISCUSSION

Stage is the most important prognostic factor in RCC. About 25–30% of patients present with overt metastases at diagnosis (2,3). The survival of patients with Stage IV RCC is poor, with 5-year rates varying between 0 and 10% and usually less than 5% (2). The great majority of long-term (>5 years) survivors with Stage IV RCC include patients with surgically resected solitary metastases (4,5). Among 337 patients with pathological stage IV RCC reported by Guinan et al. (6), 16% survived 5 years or more and all but one had surgical excision of a solitary metastasis. Spontaneous regression of metastases has also been reported, mostly pulmonary metastases following nephrectomy, but such an event is exceptional and has been observed in only 0.8% of patients (1,3).

Systemic treatments for inoperable patients have been disappointing because of the marked resistance of RCC to chemotherapeutic agents. In an exhaustive review by Yagoda et al. (7), vinblastine was the most extensively studied single chemotherapeutic agent, with an overall objective response rate of 6.4% in 250 adequately treated patients. Objective response rates for progestational agents such as medroxyprogesterone have been less than 10% using strict criteria of response (2). More recently, biological response modifiers have also been evaluated in RCC. The overall objective response rate of interferon alpha was 10% and of no clear superiority in response with addition of interleukin-2 with or without lymphokine-activated killer (LAK) lymphocytes (8). Response rates to organoplatinum compounds have been disappointing and no discernible response rates observed based on the early review by Yagoda et al. (7); more recent Phase II studies in early 1990s also confirmed these earlier findings (9).

These results and our two cases show that a subset of patients with metastatic RCC may experience prolonged survival and that some prognostic factors may portend a much better prognosis. There is, as yet, no clear explanation for these unusually long surviving patients' tumor cell characteristics, but activation of dendritic cell–T-cell interactions may create a powerful antitumor milieu that results in tumor regression or stabilization.

Looking only at rates of objective response and not survival may be misleading in RCC. It is highly desirable to include data on duration of responses, number of patients with stable disease and survival data overall and by subgroup in Phase II trials. For refractory tumors such as RCC, prolonged stabilization may lead to increased survival, as suggested by our two cases. A weak but sustained therapeutic effect can induce an important survival gain that is far superior to a short objective response, as shown by mathematical models (10). Strict emphasis on rates of objective regression for such refractory tumors may be a misguided goal that could deprive some patients from an important benefit in terms of survival gain.

CONCLUSION

Although similar prolonged survivals for RCC were reported earlier, we believe that reporting of such observations may help identify the common survival characteristics of such patients.

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References

1. Godley PA, Ataga KI. Renal cell carcinoma. *Curr Opin Oncol* 2000;12:260–4.
2. Richie JP, Kantoff PW, Shapiro CL. Renal cell carcinoma. In: Holland JF, Frei E III, Bast RC, Kufe DW, Morton D, Weichselbaum RR, editors. Cancer Medicine, 4th ed. Baltimore: Williams & Wilkins 1997;2085–96.
3. Uygur MC, Usubutun A, Ozen H, Ayhan A, Kendi S. Prognostic factors and the role of nephrectomy in metastatic renal cell carcinoma. *J Exp Clin Cancer Res* 1999;18:397–401.
4. Thrasher JB, Paulson DF. Prognostic factors in renal cancer. *Urol Clin N Am* 1993;20:247–62.
5. Althausen P, Althausen A, Jennings LC, Mankin HJ. Prognostic factors and surgical treatment of osseous metastases secondary to renal cell carcinoma. *Cancer* 1997;80:1103–9.
6. Guinan P, Stuhldreher D, Frank W, Rubenstein M. Report of 337 patients with renal cell carcinoma emphasizing 110 with stage IV disease and review of the literature. *J Surg Oncol* 1997;64:295–8.
7. Yagoda A, Abi-Rached B, Petrylak D. Chemotherapy for advanced renal-cell carcinoma: 1983–1993. *Semin Oncol* 1995;22:42–60.
8. Coppin C, Porzsolt F, Kumpf J, Coldman A, Wilt T. Immunotherapy for advanced renal cell cancer. *Cochrane Database Syst Rev* 2000;3:CD001425 (Medline record in progress).
9. Trump DL, Elson P. Evaluation of carboplatin (NSC 241240) in patients with recurrent or metastatic renal cell carcinoma. *Invest New Drugs* 1990;8:201–3.
10. Chahinian AP, Israel L. Survival gain and volume gain. Mathematical tools in evaluating treatments. *Eur J Cancer* 1969;5:625–9.