Journal of BUON **13:** 281-283, 2008
© 2008 *Zerbinis Medical Publications. Printed in Greece*

SHORT COMMUNICATIONS AND CASE REPORTS

Sarcomatoid differentiation of renal cell carcinoma: a clinical case with literature review

P. Kountourakis[1], K. Kandylis[1], D. Daskalopoulou[2], G. Rigatos[1]

[1]*First Department of Medical Oncology,* [2]*Department of Cytology, "Ag. Savvas" Anticancer Hospital, Athens, Greece*

Summary

A small percentage (1-10%) of renal cell carcinomas (RCC) belongs to the sarcomatoid variant. These malignancies are aggressive with worse prognosis and unfortunately the results following immuno- and / or chemotherapy administration are discouraging. A 62-year-old Caucasian male with advanced renal cell cancer and sarcomatoid component treated with sunitinib is presented. Better understanding of prognostic and molecular markers might help the selection of patients with a chance of benefiting from administration of new targeted drugs.

Key words: renal cell carcinoma, sarcomatoid differentiation, sunitinib

Introduction

Renal cell carcinoma is the most common histologic type of malignant tumors of the kidney [1]. Histologic subtypes of kidney cancer include conventional (clear cell) renal carcinoma (85%), papillary renal carcinoma (10%), chromophobe renal carcinoma, oncocytoma, collecting duct carcinomas and unclassified tumors. Obesity, smoking, diabetes mellitus, hypertension and renal dialysis have been associated with an increased risk of developing the disease [2].

Sarcomatoid differentiation occurs in 1-10% of RCC, and has a worse prognosis and rapid progression [3,4]. Response after administration of immunotherapy and/or chemotherapy is poor and for that reason there is no standard therapy [5,6].

Case presentation

A 62-year-old male Caucasian was admitted to our department because of pain in his left shoulder and fever lasting for 20 days. His medical history included type II diabetes mellitus and hypertension. There was no positive cancer family history.

Complete blood count was within normal limits. Erythrocyte sedimentation rate was 64 mm. Routine serum biochemistry was normal except elevated glucose (220 mg/dl). Serum immunoglobulins were within normal limits and no monoclonal paraprotein was detected. Physical examination showed a painless mass in his left back. Abdominal computed tomography (CT) revealed a mass involving the left kidney. A CT scan of the thorax revealed secondaries in both lungs. A bone scanning revealed secondary lesions at the left shoulder and 8th thoracic vertebra.

The diagnosis of clear cell renal carcinoma with a sarcomatoid component was established by CT-guided fine needle aspiration (Figure 1).

Initially, sunitinib 50 mg/daily was administered as a 6-week cycle consisting of treatment for 4 weeks followed by a 2-week rest period. The patient received one more cycle with 37.5 mg daily dose due to fatigue and grade IV diarrhea after the first cycle. The patient received 2 cycles of sunitinib in total and died after 3.5 months due to disease progression.

Discussion

The sarcomatoid component can occur with any histologic type of RCC and is associated with a worse

Correspondence to: Panteleimon Kountourakis, MD, PhD. 82a, Githiou Street, 185 44, Piraeus, Greece. Tel: +30 69366 00933, Fax: +30 210 6409508, E-mail:pantkount@hotmail.com; pkountour@med.uoa.gr

Received 03-10-2007; Accepted 13-11-2007

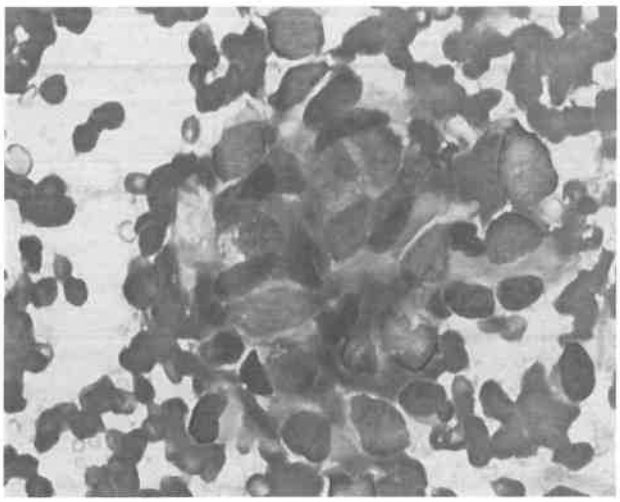


Figure 1. Aggregate of abnormal, polymorphic cells with spindle or fusiform nuclei, dense chromatin and in some areas nuclear convolution. None epithelial orientation (MGG × 400).

impact on prognosis and rapid progression [7]. Sarcomatoid differentiation is not a distinct histological entity and is reported that mutations of p53 gene that provoke overexpression of p53 protein are correlated with sarcomatoid transformation in RCC [8]. It is suggested that both sarcomatoid and clear cell components of RCC are derived from the same cell [9]. Loss of heterozygosity (LOH) of tumor suppressor genes has also been described [10,11].

The median survival of patients with sarcomatoid variant of RCC is only 7 months in comparison with a 19-month median survival of patients with non sarcomatoid component [12]. The response rates after cytokine or chemotherapy administration could reach 30 % but they are usually of short duration [13].

Doxorubicin - containing regimens and regimens used for soft tissue sarcomas (CYVADIC: cyclophosphamide + vincristine + doxorubicin + dacarbazine; DI: doxorubicin + ifosfamide; DECAV: cyclophosphamide + cisplatin + doxorubicin + dacarbazine + vindesine) are often administered to these patients, usually without significant benefit. A case of a 57-year-old male treated with adriamycin, ifosfamide (+mesna) and dacarbazine that presented complete remission and remains free of disease after 4 years has been reported but there is not as yet a standard therapeutic regimen [14].

Sunitinib is a multitargeted inhibitor of receptor tyrosine kinases including c-kit, RET, VEGFR-1, VEGFR-2, PDGFR-α, PDGFR-β [15]. *In vitro* and *in vivo* studies revealed renal tumor regression and growth inhibition with sunitinib [16,17]. In a phase II trial, sunitinib 50 mg/daily was administered to 63 patients with metastatic RCC in a 6-week cycle consisting of treatment for 4 weeks followed by a 2-week rest period. A response rate of 40 % with a median survival of 16.4 months and time to progression of 8.7 months was reported [18]. In a randomized phase III trial sunitinib therapy was superior to interferon-α (INF-α) in metastatic RCC (median progression free survival 11 and 5 months, and response rate 31% and 6% for sunitinib and INF-α arms, respectively) [19].

The patient presented in this communication was treated with sunitinib and died 3.5 months after initial diagnosis. It is intriguing to all clinicians why some patients' tumors respond and why some do not respond to a particular therapeutic regimen. Our ever-improving molecular understanding of the pathogenesis of malignancies is just beginning to shed light as to which of the patients could benefit from a particular agent. Certainly, new targeted therapies are active to selected but not to all patients. Molecular studies are needed to identify the markers that could distinguish the subgroup of patients that might benefit from new targeted therapies such as sunitinib, sorafenib, temsirolimus, everolimus.

References

1. Storkel S, Elbe JN, Adlakha K et al. Classification of renal cell carcinoma: Workgroup No. 1. Union Internationale Contre le Cancer (UICC) and the American Joint Committee on Cancer (AJCC). Cancer 1997; 80: 987- 989.
2. Redman BG, Kawachi M, Hurwitz M. Urothelial and kidney cancers. In: Pazdur R, Coia CR, Hoskins WJ, Wagman LD (Eds): Cancer management: a multidisciplinary approach (8th edn). New York, CMP United Business Media, 2004, Ch. 20, pp 412-413.
3. Tomera KM, Farrow GM, Lieber MM. Sarcomatoid renal carcinoma. J Urol 1983; 130: 657-659.
4. De Peralta-Venturina M, Moch H, Amin M et al. Sarcomatoid differentiation in renal cell carcinoma: a study of 101 cases. Am J Surg Pathol 2001; 25: 275-284.
5. Amato RJ. Chemotherapy for renal cell carcinoma. Semin Oncol 2000; 27: 177- 186.
6. Bleumer I, Oosterwijk E, De Mulder P et al. Immunotherapy for renal cell carcinoma. Eur Urol 2003; 44: 65-75.
7. Mian BM, Bhadkamkar N, Slaton JW et al. Prognostic factors and survival of patients with sarcomatoid renal cell carcinoma. J Urol 2002; 167: 65-70.
8. Oda H, Nakatsuru Y, Ishikawa T et al. Mutations of p53 gene and p53 protein overexpression are associated with sarcomatoid transformation in renal cell carcinomas. Cancer Res 1995; 55: 658-662.
9. Jones TD, Eble JN, Wang M et al. Clonal divergence and genetic heterogeneity in clear cell renal carcinomas with sarcomatoid transformation. Cancer 2005; 104: 1195-1203.
10. Morita R, Ishikawa J, Tsatsumi M et al. Allotype of renal cell carcinoma. Cancer Res 1991; 51: 820-823.
11. Anglard P, Tory K, Brauch H et al. Molecular analysis of genetic changes in the origin and development of renal cell carcinoma. Cancer Res 1991; 51: 1071-1077.

12. Dall' Oglio M, Cieberknecht M, Gouvera V et al. Sarcomatoid differentiation in renal cell carcinoma: prognostic implication. Intern Braz J Urol 2005; 31: 10-16.
13. Cangiano T, Liao J, Naitoh J et al. Sarcomatoid renal cell carcinoma: biologic behavior, prognosis and response to combined surgical resection and immunotherapy. J Clin Oncol 1999; 17: 523-528.
14. Bangalore N, Bhargava P, Hawkins MJ et al. Sustained response of sarcomatoid renal-cell carcinoma to MAID chemotherapy: Case report and review of the literature. Ann Oncol 2001; 12: 271- 274.
15. Pawson T. Regulation and targets of receptor tyrosine kinases. Eur J Cancer 2002; 38: S3-S10.
16. Hanahan D, Weinberg RA. The hallmarks of cancer. Cell 2000; 100: 57-70.
17. Mendel DB, Laird AD, Xin X et al. In vivo antitumor activity of SU 11248, a novel tyrosine kinase inhibitor targeting growth factor and platelet - derived growth factor receptors: determination of a pharmacokinetic/pharmacodynamic relationship. Clin Cancer Res 2003; 9: 327-337.
18. Motzer RJ, Michaelson MD, Redman BG et al. Activity of SU 11248, a multitargeted inhibitor of vascular endothelial growth factor receptor and platelet-derived growth factor receptor, in patients with metastatic renal cell carcinoma. J Clin Oncol 2006; 24: 16-24.
19. Motzer RJ, Hutson TE, Tomczak P et al. Sunitinib vs. interferon alfa in metastatic renal cell carcinoma. N Engl J Med 2007; 356: 115-124.