Renal cell carcinoma: complete pathological response in a patient with gastric metastasis of renal cell carcinoma

Rosario García-Campelo[a], Maria Quindós[a], Diana Dopico Vázquez[a], Margarita Reboredo López[a], Alberto Carral[a], Ovidio Fernández Calvo[a], José Manuel Rois Soto[d], Enrique Grande[c], Jesús Durana[b] and Luis Miguel Antón-Aparicio[a]

A 75-year-old-man, with a 2-month history of abdominal pain, underwent a standard diagnostic workup that included a CT scan that showed a large right renal mass and subcentimeter nodes in the right and left lung lobes. In December 2003, the patient underwent right nephrectomy with adrenalectomy and a diagnosis of renal cell carcinoma (pT3N0M0 stage) was made. No further treatment was proposed and patient was followed up regularly. In October 2006, the annual gastrointestinal endoscopy showed asymptomatic multilobulated and polypoid masses in the gastric fundus and gastric body that corresponded to metastasis of the renal carcinoma that had been resected three years ago. Surgical treatment was refused and oral treatment with sunitinib (50 mg/day consecutively for 4 weeks followed by 2 weeks off) was initiated. Patient completed one cycle and development of acute toxicity (grade 3 asthenia, anorexia and mucositis) led to treatment interruption. After recovering from acute toxicity, the patient was proposed to reinitiate treatment with dose reduction, but he refused any medical treatment. At the follow-up visit, three months later, the gastrointestinal endoscopy showed four unspecific 2 mm nodules without malignant evidence. The whole-body CT did not reveal any other abnormality except for the known lung nodes. PET scan six months after treatment confirmed complete gastric response. ***Anti-Cancer Drugs*** **21 (suppl 1): S13–S15 © 2010 Wolters Kluwer Health | Lippincott Williams & Wilkins.**

Anti-Cancer Drugs 2010, **21 (suppl 1):**S13–S15

Keywords: gastric metastasis sunitinib, renal cell carcinoma

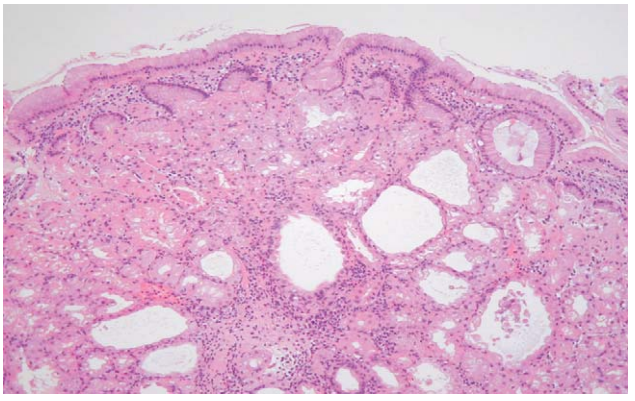
[a]Medical Oncology Service, University Hospital Complex, A Coruña, Spain, [b]Gastroenterology Unit, Juan Canalejo Hospital, A Coruña, [c]Medical Oncology Department, Ramon y Cajal University Hospital, Madrid and [d]Pathological Unit, Santa Teresa Hospital, A Coruña, Spain

Correspondence to Rosario García-Campelo, MD, C. H. U. A Coruña, Medical Oncology Unit, Jubias de Arriba 84, 15006 La Coruña, Spain
Tel: +34 981 17 83 53; e-mail: maria.rosario.garcia.campelo@sergas.es

Case report

A 75-year-old man presented with a 2-month history of abdominal pain. He had an earlier history of hypertension and hiatus hernia associated with gastroesophageal reflux disease, followed with annual endoscopic examination. He underwent a standard diagnostic workup that included hematochemical determinations and whole-body computed tomography (CT) scan, which showed a large right renal mass and subcentimeter nodes in the right and left lower lung lobes. In December 2003 he underwent right nephrectomy with adrenalectomy and pathology examination showed a renal cell carcinoma (RCC)_ of pT3N0M0 stage. No further treatment was proposed and the patient was regularly followed up with chest and abdominal CT showing no changes in the lung nodes size and number. In October 2006, the annual gastrointestinal endoscopy revealed several multilobulated and polypoid masses (between 6 and 15 mm in diameter) in the gastric fundus and gastric body. At that moment the patient was asymptomatic. The histopathologic examination showed a metastatic RCC consistent with a metastasis of RCC resected 3 years ago (Fig. 1). Thorax and abdominal CT only displayed lung nodes without changes compared with earlier studies. Positron emission tomography was carried out, confirming a 1.7 cm intense tracer uptake located in the gastric fundus (Fig. 2). Further uncertain uptake focuses were observed in both the lower lung lobes. Surgical treatment was proposed but the patient refused to undergo any aggressive treatment. Oral sunitinib malate therapy was started at

Fig. 1

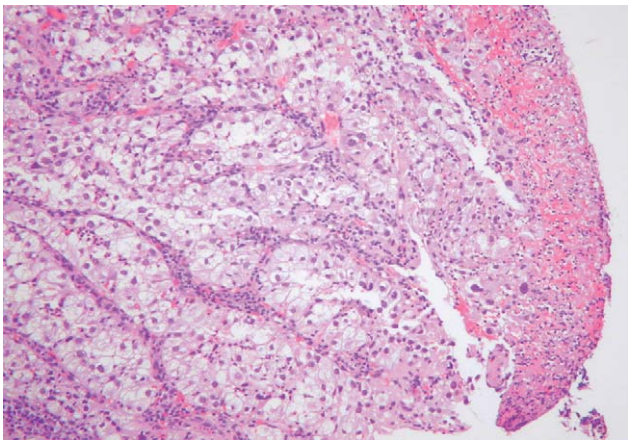


Pretreatment gastrointestinal biopsy: neoplasic proliferation of clear renal cell carcinoma, with ulceration and necrosis.

0959-4973 © 2010 Wolters Kluwer Health | Lippincott Williams & Wilkins

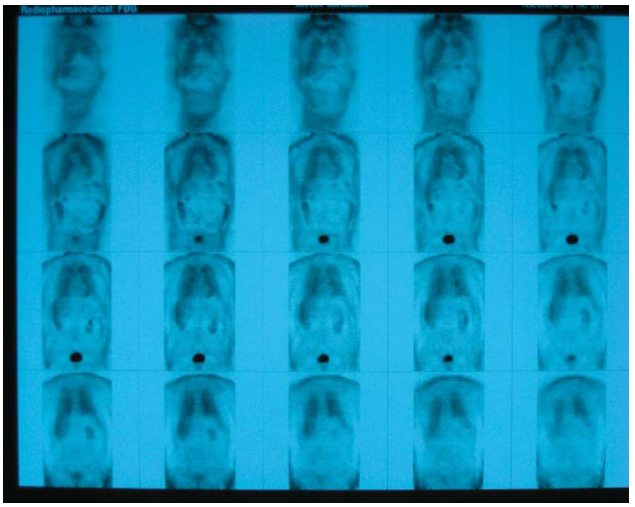
DOI: 10.1097/01.cad.0000361530.51675.60

Fig. 2



Posttreatment gastrointestinal biopsy: hyperplastic focal changes; no evidence of malignant cells.

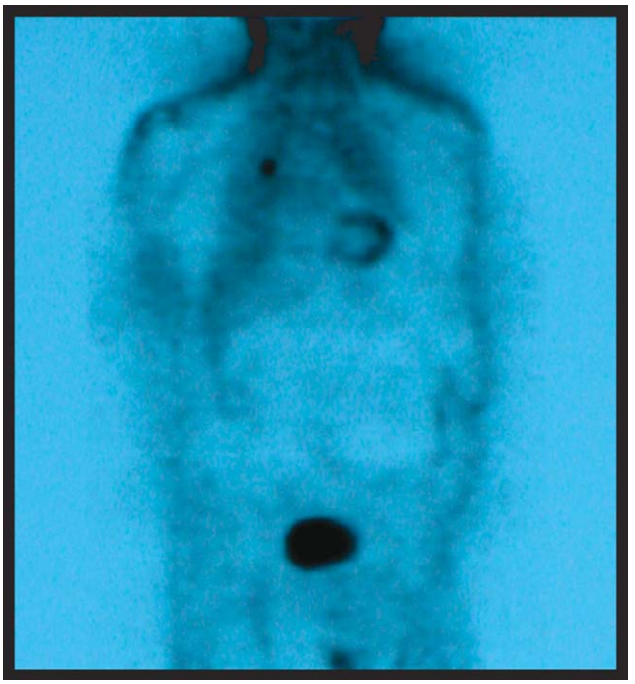
Fig. 3



Pretreatment PET scan: 1.7 cm tracer uptake located in gastric fundus; uncertain uptake focus in left lower lung lobe.

standard dose of 50 mg/day delivered consecutively for 4 weeks followed by 2 weeks off. The patient completed just one cycle developing grade 3 asthenia, grade 3 anorexia, and grade 3 mucositis. After recovering from the acute toxicity, he was proposed to begin the treatment again with dose reduction, but he refused any medical treatment. A follow-up visit was planned for 3 months later. The gastrointestinal endoscopy showed four unspecific 2 mm nodules with histopathologic examination showing hyperplastic changes without malignance evidence (Fig. 3). The whole-body CT did not reveal any other abnormalities except for the known lung nodes. Positron emission tomography also confirmed complete gastric response 6 months after treatment (Fig. 4).

Fig. 4



Posttreatment PET scan: uptake focus in right and left lungs; normal uptake traces in stomach.

Discussion

RCC is the most frequent cancer arising from the kidney. It accounts for 2–3% of all malignancies [1]. Although RCC is known because of its high potential of haematogenous spreading, RCC metastatic to the stomach following radical excision of the primary tumor is a very rare phenomenon [2,3]. Large autopsy series reported by different authors have not found any kidney metastases in the stomach [4,5]. Few cases of gastric metastases of RCC have been described in the literature [6–15]. In the majority of these cases, metastases often start as a submucosal lesion, single or multiple, grossly polypoid or plaque-like. The most common presenting symptom is abdominal pain although nausea, vomiting, or gastrointestinal bleeding may be present. The median time from surgery until the development of metastatic disease is 7.5 years. Surgical treatment is the best therapeutic option in those cases with solitary gastric metastasis, resulting in significant survival prolongation [16].

Sunitinib, a small molecule inhibitor of vascular endothelial growth factor and platelet-derived growth factor receptor has been approved for the treatment of patients with advanced or metastatic RCC. Clinical efficacy of sunitinib has been shown, with high-objective response rates, in a variety of solid tumor types, including RCC patients who failed to previous cytokine therapy partial response rates of 40% (95% confidence interval 28–53%) and 34% (95% confidence interval 25–44%) including

long-term responses to sunitinib [17,18]. In a large phase III trial, in first line setting, sunitinib showed longer progression free survival (11 vs. 5 months, $P < 0.001$) and higher response rates compared with standard interferon α (31 vs. 6%, $P < 0.001$) [19].

The present case involves a patient with RCC and solitary gastric metastatic disease 3 years after the initial diagnosis showing a radiological and pathological complete response after just one cycle of sunitinib treatment. Few cases have been described showing complete responses in metastatic RCC treated with sunitinib. Recently, a pathological response after neoadjuvant sunitinib treatment in a patient who developed a renal fossa recurrence has been reported [20]. Other two cases have been reported showing complete radiological and clinical response to sunitinib treatment. One of these reported cases showed complete cerebral radiological response and long-lasting partial response in pulmonary and nephrectomy area lesions after 21 months of sunitinib treatment [21]. Trinh *et al.* also reported a clinical response at the end of the second cycle of sunitinib in a metastatic RCC involving thoracic vertebras with spinal cord compression [22].

To our knowledge, this is the first case reporting a complete pathological response after just one cycle of sunitinib treatment in a patient with gastric metastasis of RCC. Molecular mechanisms underlying the impressive responses as the one showed here should be further evaluated to identify these patient subgroups highly sensitive to small molecule tyrosine kinase inhibitors.

Acknowledgements

Funding for the preparation of this manuscript was provided by Pfizer Spain. Medical writing assistance was provided by Sofia Perea, PhD on behalf of Wolters Kluwer Pharma Solutions. The authors have no conflicts of interest to declare.

References

1 Curti BD. Renal cell carcinoma. *JAMA* 2004; **292**:97–100.
2 Menuck LS, Amberg JR. Metastatic disease involving the stomach. *Am J Dig Dis* 1975; **20**:903–913.
3 Linda K. Hematogenous metastasis to the stomach. *Cancer* 1990; **65**:1596–1600.
4 Higgins PM. Pyloric obstructions due to a metastatic deposit from carcinoma of the bronchus. *Can J Surg* 1962; **5**:438–441.
5 Davies Gh, Zollinger RW. Metastatic melanoma of the stomach. *Am J Surg* 1960; **99**:94–96.
6 Mascarenhas B, Konety B, Rubin JT. Recurrent metastatic renal cell carcinoma presenting as a bleeding gastric ulcer after a complete response to high-dose interleukin-2 treatment. *Urology* 2001; **57**:168.
7 Sullivan WG, Cabot EB, Donohue RE. Metastatic renal cell carcinoma to stomach. *Urology* 1980; **15**:375–378.
8 Odori T, Tsuboi Y, Katoh K, Yamada K, Morita K, Ohara A, *et al.* A solitary hematogenous metastasis to the gastric wall from renal cell carcinoma four years after radical nephrectomy. *J Clin Gastroenterol* 1998; **26**: 153–154.
9 Blake MA, Owens A, O'Donoghue DP, MacErlean DP. Embolotherapy for massive upper gastrointestinal haemorrhage secondary to metastatic renal cell carcinoma: report of three cases. *Gut* 1995; **37**:835–837.
10 Tumours of the esophagus and stomach. *Atlas of tumour pathology 2nd series part 7.* Bethesda, Maryland: Armed Forces Institute of Pathology; 1973, pp. 253–255.
11 Nakamura R, Shimada A, Nakamura K. One case of intussusception due to intestinal metastasis of renal cell carcinoma. *Jpn J Clin Surg* 1984; **43**:1637–1640.
12 Green LH. Hematogenous metastasis to the stomach. *Cancer* 1990; **65**:1596–1600.
13 Otowa T, Muto I. A case of synchronous gastric metastasis from renal cell carcinoma with the chief complain of hematemesis. *Jpn J Surg* 1992; **53**:1219–1222.
14 Suárez C, Carballido J, González I, Sola I, Rodríguez G, Salas C. Gastric metastasis from renal cell carcinoma. Pathogenical hypothesis and literature revision. *Actas Urol Esp* 2004; **6**:472–476.
15 Saidi RF, Remine SG. Isolated gastric metastasis from renal cell carcinoma 10 years after radical nephrectomy. *J Gastroenterol and Hepatol* 2007; **22**:143–144.
16 Riviello C, Tanini I, Cipriani G, Pantaleo P, Nozzoli C, Poma A, *et al.* Unusual gastric and pancreatic metastatic renal cell carcinoma presentation 10 years after surgery and immunotherapy: a case report and a review of literature. *World J Gastroenterol* 2006; **28**:5234–5523.
17 Motzer RJ, Michaelson MD, Redman BG, Hudes GR, Wilding G, Figlin RA, *et al.* Activity of SU11248, 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.
18 Motzer RJ, Rini BI, Bukowski RM, Curti BD, George DJ, Hudes GR, *et al.* Sunitinib in patients with metastatic renal cell carcinoma. *JAMA* 2006; **295**:2516–2524.
19 Motzer RJ, Hutson TE, Tomczak P, Michaelson MD, Bukowski RM, Rixe O, *et al.* Sunitinib versus interferon alfa in metastatic renal-cell carcinoma. *N Engl J Med* 2007; **356**:115–124.
20 Baccala A, Hedgepeth R, Kaouk J, Magi-Galluzzi C, Gilligan T, Fergany A. Pathological evidence of necrosis in recurrent renal mass following treatment with sunitinib. *Int J Urol* 2007; **14**:1095–1097.
21 Medioni J, Cojorasu O, Belcaceres JL, Halimi P, Oudard S. Complete cerebral response with sunitinib for metastatic renal cell carcinoma. *Ann Oncol* 2007; **18**:1282–1283.
22 Trinh QD, Cardinal E, Gallina A, Perrotte P, Saad F, Karakiewicz P. Sunitinib relieves renal cell carcinoma spinal cord compression. *Eur Urol* 2007; **51**:1741–1743.