

A patient with renal cell carcinoma and thoracic pain

I.M.E. Desar*, M.J. Sonderen, C.M.L van Herpen

Department of Medical Oncology 452, Radboud University Nijmegen Medical Centre, Nijmegen, the Netherlands, *corresponding author: tel.: +31 (0)24-361 03 53, fax: +31 (0)24-354 07 88, e-mail: i.desar@AIG.umcn.nl

CASE REPORT

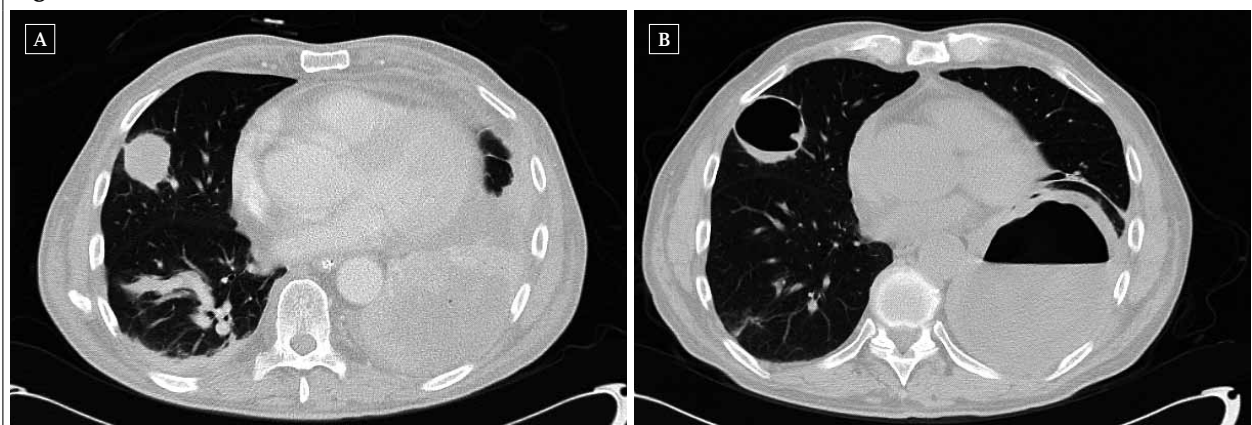
A 65-year-old man was diagnosed with metastatic clear cell renal cell carcinoma with sarcomatoid differentiation. Within weeks after a palliative nephrectomy, the patient's condition deteriorated. Computed tomography (CT) scan showed progressive disease of the pulmonary metastases (panel A) and we started treatment with the oral angiogenesis inhibitor sunitinib 50 mg once daily, 4 weeks on, 2 weeks off. Sunitinib is a multiple tyrosine kinase inhibitor targeting the vascular endothelial growth factor receptor, platelet derived growth factor receptor, c-kit, neurotrophic factor receptor RET and FMS-like tyrosine kinase 3. Three weeks after starting treatment,

the patient presented at the emergency ward with right thoracic pain, dyspnoea and cough. Laboratory studies showed a haemoglobin of 6.2 mmol/l (was 6.1 mmol/l 5 days before), leucocytes of $7.3 \times 10^9/l$ (was $9.7 \times 10^9/l$ 5 days before), C-reactive protein 176 mg/l (was 144 mg/l 9 days before) and a D-dimer of 6234 ng/ml. A new CT was performed (panel B).

WHAT IS YOUR DIAGNOSIS?

See page 232 for the answer to this photo quiz.

Figure 1.



DIAGNOSIS

The differential diagnosis of thoracic pain in this patient included a pulmonary embolus, pneumonia, pneumothorax, pleural effusion, and pleural metastases or bleeding within a metastasis. An angiographic CT scan excluded a pulmonary embolus and showed no signs of pneumonia, pneumothorax or pleural effusions. However, the CT scan showed extensive central necrosis of the lung metastases with cavitation (panel B), of which the largest was located in the area of the patient's pain. The CT image is characteristic for a good response of metastases of renal cell carcinoma to antiangiogenic treatment, although the size of the metastases did not decrease.

For the evaluation of treatment response of cancer, the Response Evaluation Criteria in Solid Tumours (RECIST) are used.¹ RECIST is based on the sum of one-dimensional measurements of the greatest diameter of the tumour and/or metastases. In the presented patient, according to RECIST, stable disease (+9%) was established. However, the sunitinib-induced extensive necrosis and cavitation illustrate the limitations of the RECIST guidelines for the evaluation of response to targeted therapies. The effect of targeted therapies as angiogenesis inhibitors and antivascular drugs can be underestimated by using the tumour size based RECIST guidelines.² In case of first-line treatment with sunitinib in RCC patients, the observed objective response rate is 47%, with a progression-free survival of 11 months, compared with five months for interferon alpha.³ However, first-line single-agent treatment with sorafenib⁴ in metastatic renal cell cancer failed to achieve significant objective response rates according to the RECIST criteria, but did result in a significant increase in progression-free survival, demonstrating its clinical efficacy.

Attempts are made to achieve more sophisticated imaging techniques or evaluation criteria. Striking examples are the PET criteria, also called PERCIST,⁵ and the Choi criteria for gastrointestinal stromal tumours (GIST).⁶ The Choi criteria add tumour density to tumour size, which makes it possible to assess tumour necrosis, an early feature of antiangiogenic therapies.

In this patient, the sunitinib was continued and analgesics were added. After this episode the condition of the patient gradually improved, the cough and pain disappeared and his weight increased. Unfortunately, five months later he developed cerebral metastases and died shortly thereafter.

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