Recall pneumonitis during systemic treatment with sunitinib

A 49-year-old female patient was diagnosed with symptomatic metastatic clear cell renal carcinoma to the os ischii, right hip and left scapula and received upfront palliative radiation therapy (RTX) (6 MeV liniac photons, total dose of 30 Gy) to the left shoulder and the right hip. New lung and mediastinal lesions were detected on a computed tomography (CT) scan of the thorax and abdomen after completion of radiotherapy (Figure 1A), and systemic therapy with the tyrosine kinase inhibitor (TKI) sunitinib was considered appropriate for further anticancer treatment. Sunitinib (50 mg o.d. for 4 weeks, followed by 2 weeks rest) was initiated 3 weeks after termination of RTX. Tumor status evaluations were carried out every other cycle and included CT scans of the thorax and abdomen. During the fourth course of sunitinib, our patient complained of a dry cough. A CT scan of the thorax carried out within 4 days of initial presentation of cough revealed new ground glass opacity of the left upper lobe of the lung when compared with images taken at baseline (Figure 1B and C). Additional diagnostic investigations included a bronchoalveolar lavage, which revealed an increase in lymphocytes to 14% and supported the diagnosis of lymphocytic pneumonitis within previously irradiated areas. All further cytological and microbiological analyses remained unremarkable and did not support a neoplastic or infectious cause of the lung alterations.

Since our patient received RTX >6 months before onset of pneumonitis, a radiation-induced pneumonitis was considered to be unlikely. We have already observed pneumonitis in patients receiving therapy with TKI and suspected a sunitinib-induced pneumonitis. There are currently no reports of sunitinib-induced pneumonitis in the literature. However, treatment with inhibitors of the mammalian target of rapamycin (mTOR) such as temsirolimus and everolimus has been demonstrated to cause pneumonitis. The mTOR-inhibitor-induced symptomatic pneumonitis often requires dose reduction or discontinuation of therapy. In severe cases, the application of steroids may be necessary [1]. In our case, we reduced the sunitinib dose from 50 mg/day to 37.5 mg/day, and coughing completely resolved within 3 weeks (despite continuation of therapy). The interstitial lung changes remained detectable during follow-up CT scans (Figure 1D) restricted to the field, where radiation was carried out (Figure 1E). This observation led us to conclude that the pneumonitis was a result of sunitinib-induced radiation recall reaction.

Radiation recall describes an inflammatory reaction in a previously irradiated area after application of certain pharmacological agents [2]. The pathophysiological mechanism of radiation recall is unknown. It is most commonly observed on the skin but also reported in other tissues and organs [3, 4]. We describe a recall pneumonitis induced by systemic sunitinib treatment. Our report supports the notion that TKI may be associated with unforeseen adverse events, which in our case could be managed by dose reduction. The pathological mechanism of sunitinib interactions in the lung parenchyma remains unclear and warrants further studies. Thus, the combination of TKI and radiotherapy may lead to additional

Figure 1. Progressive disease was detected after irradiation of osseous lesions (A). Native lung is shown in (B) before initiation of sunitinib therapy. Newly occurring ground glass opacity (C) of the left upper lobe of the lung were detected on computed tomography (CT) scans after four courses of sunitinib and interstitial lung changes remained detectable during follow-up CT scans (D). Previous radiation field is shown in (E) and corresponds to the area of pulmonary changes.
toxicity when visceral organs are within the radiation field and should be avoided or limited whenever possible.

C. Seidel¹, S. Janssen², J. H. Karstens², T. Welte³, M. Morgan¹, A. Ganser¹ & V. Grünwald¹

Departments of ¹Hematology, Hemostasis, Oncology, and Stem Cell Transplantation, ²Radiation Oncology, ³Respiratory Medicine, Hannover Medical School, Hannover, Germany

(¹E-mail: gruenwald.viktor@mh-hannover.de)

funding
Novartis, Pfizer, Bayer and Roche to VG.

disclosure
VG is consultant for Novartis, Pfizer and Roche.

references

doi:10.1093/annonc/mdq444
Published online 18 August 2010