

Abscopal effect of radiotherapy in a patient with metastatic diffuse-type giant cell tumor

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To the Editor,

A 19-year-old male presented in 1999 with anemia, increased inflammatory parameters and knee complaints, based on diffuse-type giant cell tumor (DGCT). In 2010, a low femoral amputation was performed after several functional joint sparing surgeries and a short unsuccessful period of imatinib 400 mg once daily (OD) therapy [1]. Histopathology showed destructive DGCT with secondary changes due to imatinib treatment, but no signs of malignancy.

Four years later, he presented with fever, sweating, anorexia, weight loss, palpitations and anemia. FDG-positron emission tomography (PET)-computed tomography (CT) scan showed new pulmonary lesions and mediastinal lymphadenopathy. A cytological lymph node biopsy proved metastatic DGCT. Imatinib 400 mg OD and prednisolone 30 mg OD were started. No other immune-modulating therapy has been administered. Two months after start of imatinib and prednisolone, his clinical condition deteriorated with weight loss, fever and inflammation (Table 1). FDG-uptake showed increased metabolic activity of metastases. To prevent atelectasis, the highly metabolically active right hilar metastasis was irradiated (30 Gy in 10 fractions; Figure 1(a)). During radiotherapy, his condition rapidly deteriorated with high fevers, profound anemia, hypoalbumenia, decreased sodium, hyperglycemia and pulmonary infection (Table 1). Unexpectedly, within two weeks after completing radiotherapy,

he clinically improved and his inflammatory laboratory values decreased (Table 1). FDG-PET-CT showed response of the right irradiated hilar lesion, volumetric and metabolic response of left-sided non-irradiated pulmonary metastases and an increase of uptake in one mediastinal lymph node (Figure 1(b) and (c)). This phenomenon is called *abscopal effect*. It persisted for six months, after which he progressed and died from disease three months later.

Discussion

The abscopal effect induced by radiotherapy is rare and is mostly reported in tumor types considered *immunogenic* such as melanoma, but has to our knowledge never been described in mesenchymal malignancies [2]. The immune system has been proposed as the key component of this abscopal effect [3]. Local radiotherapy induces cell death and release of immunogenic factors, leading to host immune responses. Damage-associated molecular patterns trigger dendritic cells, resulting in improved antigen presentation to T cells [2,4]. Pharmacological modification of the abscopal effect has been suggested for immune checkpoint inhibitors and granulocyte-macrophage colony-stimulating factor [4–7].

Here we report a patient with malignant DGCT with marked inflammatory symptoms and laboratory parameters, who demonstrated a systemic benefit from local radiotherapy by an abscopal effect. Tenosynovial giant cell tumors are rare

Table 1. Laboratory results.

Parameter (normal range)	Before start of radiotherapy	Day 5 of radiotherapy (10 × 3 Gy)	Last day of radiotherapy	3 weeks after completing radiotherapy
Hemoglobin (8.4–10.8 mmol/l)	5.1	5.1 ^a	5.8	6.7
Leukocytes (4.0–11.0 × 10 ⁹ /l)	17.4	15.1	13.2	16.8
Platelets (150–400 × 10 ⁹ /l)	811	609	567	445
Neutrophils (2–7.5 × 10 ⁹ /l)	12.7	12.4	11.4	
Lymphocytes (1–3.5 × 10 ⁹ /l)	2.4	0.6	0.5	
Monocytes (0.3–1.0 × 10 ⁹ /l)	2.3	2.0	1.3	
Sodium (135–145 mmol/l)	134	129	127	135
Albumin (35–50 g/l)	13	10	10	17
CRP (<10 mg/ml)	200	225		82

^aErythrocyte transfusion was administered after this measurement. CRP: C-reactive protein.

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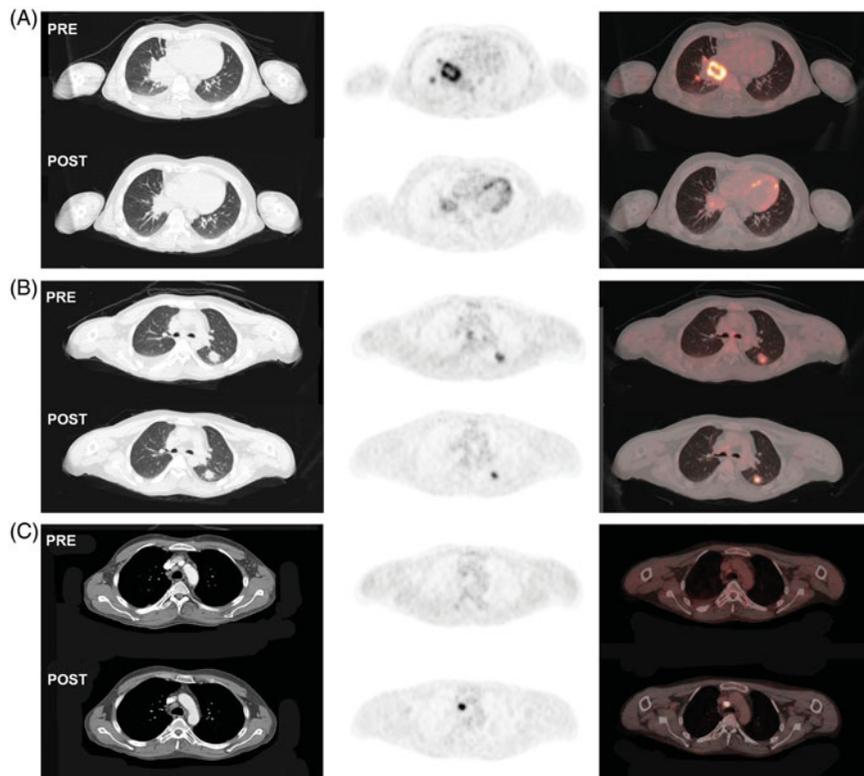


Figure 1. Computed tomography (CT) (left column), FDG-positron emission tomography (PET) (middle column) and combined FDG-PET-CT (right column) before the start (pre) and after completion (post) of radiotherapy. (a) showing high uptake of FDG in the right hilar diffuse-type giant cell tumor metastasis before the start of radiotherapy and impressive decrease in FDG-uptake, corresponding with metabolic response 3 weeks after completion of radiotherapy. Abscopal effect in the left pulmonary metastases (b) and mediastinal lymphadenopathy (c), showing a volume response on CT and metabolic response on FDG-PET-CT in the pulmonary lesions as well as increased uptake in a mediastinal lymph node on FDG-PET-CT, in keeping with an immunological reaction.

mesenchymal lesions that arise from the synovial lining of articular spaces, bursal sacs, and tendon sheaths. The diffuse-type is an aggressive multifocal proliferation of synovial-like mononuclear cells with inflammatory infiltrates. Metastases of DGCT are extremely rare. The current treatment strategies have recently been reviewed [8]. The inflammatory nature and the observed abscopal effect plea for considering immunotherapeutic approaches in this disease.

Disclosure statement

The authors report no conflict of interest. The authors alone are responsible for the content and writing of the paper.

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