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## Letter to the Editor

# Abscopal antitumor effect in a patient with melanoma and coronavirus disease 2019



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Received 20 February 2021; accepted 1 March 2021

Available online 14 March 2021

## KEYWORDS

Abscopal effect;  
COVID-19;  
Melanoma;  
Radiotherapy;  
Immunotherapy

## 1. Introduction

Abscopal effect has been described for the first time by Mole [1] in 1953 to define a tumor response at distance from an irradiated lesion. Several cases of abscopal effect have been reported in patients treated with radiotherapy while receiving immune checkpoint inhibitors (ICIs) [2]. However, this phenomenon unfortunately is a very rare occurrence. Infectious diseases are known to trigger the innate immune system and may even induce tumor responses [3]. We report here the first case of abscopal effect in a patient treated with radiotherapy for metastatic melanoma during the course of an infection by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

## 2. Case

An 84-year-old woman was diagnosed in February 2020 with peritoneal and nodal recurrence of a BRAF V600E–mutated melanoma. She was otherwise treated for atrial fibrillation, type II diabetes and chronic kidney disease, with a usual glomerular filtration rate of about 40 mL/min.

In July 2020, treatment with dabrafenib and trametinib was introduced but had to be discontinued after two months of therapy, in September 2020, for cardiac toxicity. Because of her poor general performance status, exclusive palliative care was then proposed.

In December 2020, she received symptomatic irradiation for a painful 4 × 3 cm metastatic cervical node, delivering 20 Gy in 5 fractions of 4 Gy.

One month later, she was admitted in our hospital for being symptomatic for coronavirus disease 2019 (COVID-

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19). Computed tomography (CT) evaluation revealed not only radiologic signs of pulmonary COVID-19 but also unexpected impressive objective tumor response with a shrinkage of 20–25% for all metastases (Fig. 1).

### 3. Discussion

In 1871, Coley described for the first time a case of tumor shrinkage in a patient with soft-tissue sarcoma after injection of streptococcal organisms [3]. Years later, the implication of the immune system, modulated by infectious agents via innate immune receptors such as Toll-like receptors (TLRs), was determined to be the

mechanism of tumor response [4]. On the other hand, since 1953, radiation therapy is known to have immunogenic capacity [1] and to induce an abscopal effect. The mechanism of abscopal effect is supposed to rely on a radiotherapy-induced increase in tumour-associated antigen (TAA) presentation by myeloid antigen-presenting cells of the stroma [5]. Radiotherapy can also release danger-associated molecular pattern ligands for TLR and cytokines that create an immunogenic microenvironment, further increasing the TAA presentation to CD8<sup>+</sup> cytotoxic T cells [6].

In the case of our patient, the deep tumor response could not be explained by a delayed effect

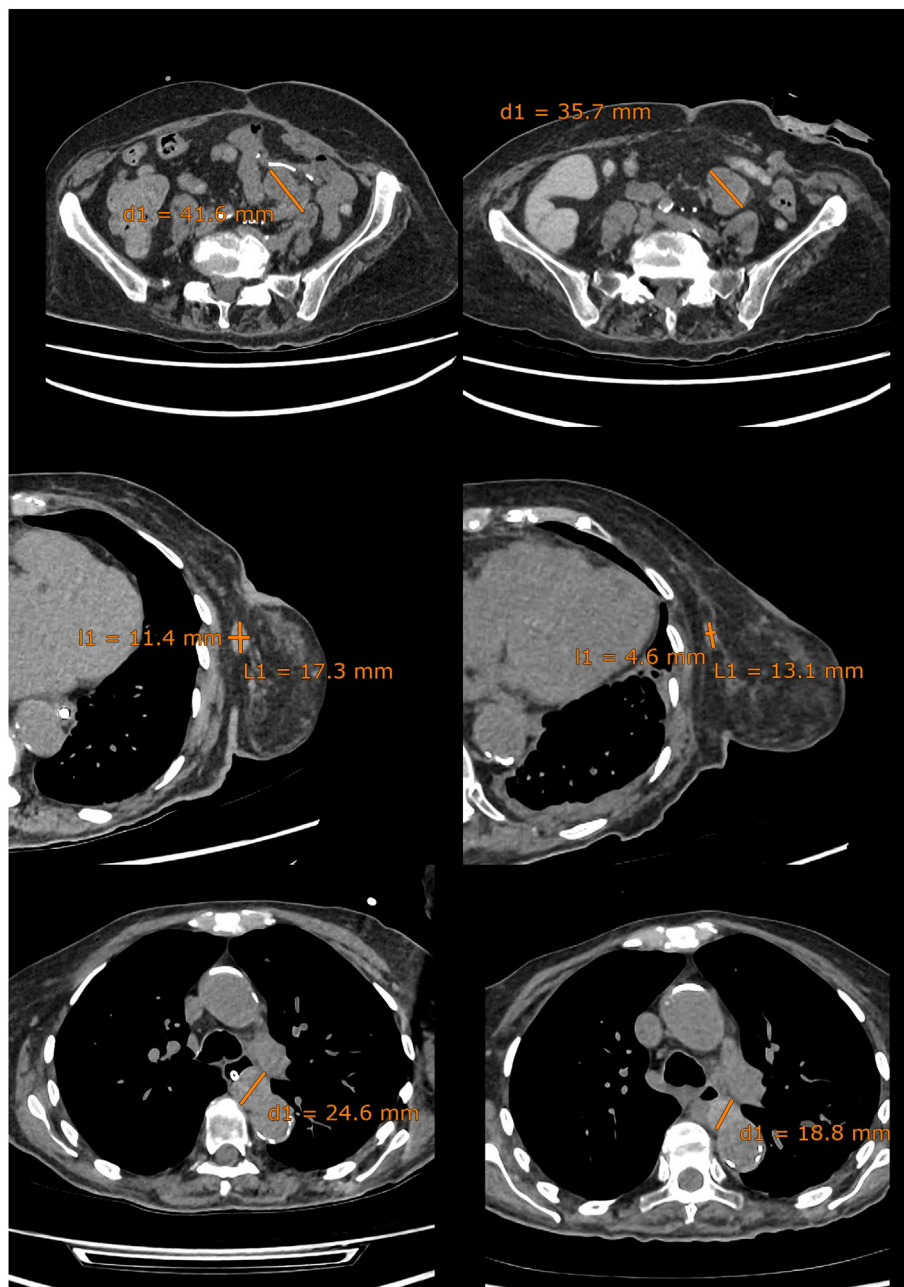


Fig. 1. Comparison of CT scans before (left side) and after (right side) cervical node irradiation and COVID-19. CT, computed tomography; COVID-19, coronavirus disease 2019.

of the treatment with dabrafenib + trametinib that had been stopped 3 months before because these targeted therapies, in contrast to what can be observed with ICIs, are not known to have any delayed efficacy after their interruption. Most cases of abscopal effects that have been described occurred in patients treated with ICIs [7]. Here, our patient had not received any ICI, and our hypothesis is that she developed an abscopal effect owing to the concomitant SARS-CoV-2 infection. Indeed, SARS-CoV-2 infection activates innate immune responses via TLRs and induces production of multiple proinflammatory cytokines and chemokines including interferon-alpha, tumor necrosis factor alpha, interleukin (IL)-1 and IL-6 [8,9].

Although abscopal effect can be induced by radiotherapy alone, this occurrence is so rare that our hypothesis is that COVID-19 triggering the immune system could have enhanced the antitumor immune response and explain the abscopal effect.

To the best of our knowledge, this is the first case of tumor abscopal effect potentially induced by COVID-19. More cases will be needed to validate this hypothesis.

#### 4. Conclusion

COVID-19 may increase antitumoral immune response against melanoma by enhancing abscopal effect in patients treated with radiotherapy.

#### Conflict of interest statement

H.H., B.S. and P.T. have no conflict of interest. C.R. has received honoraria for occasional consulting for BMS and MSD.

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