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Radiotherapy-induced abscopal effect on the metastatic carcinoma of unknown primary origin: a case report and literature review

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Abstract. – OBJECTIVE: Abscopal effect of radiotherapy refers to a clinical phenomenon that is characterized by the eradication of distant metastatic tumors following localized irradiation. Reports on the abscopal effect following pure radiotherapy have been relatively rare.

CASE REPORT: Herein, we reported a 70-year-old male patient, who has been subjected to swelling and pain in the left neck. Computed tomography examination presented a metastatic lymph node of the left cervical and an intra-abdominal mass which was located in hepatogastric space, upward of the pancreatic head. Histopathology of the left cervical lymph node further ensured a poorly-moderately differentiated form of squamous cell carcinoma. But the primary origin was not defined. This patient received radiotherapy on the metastatic lymph nodes of the left cervical (dose: 60 Gray in 30 fractions) only. After treatment, the pain in the left neck dramatically improved and the swelling of the radiation exposure site diminished gradually. Computed tomography examination also confirmed that the abdominal mass was significantly reduced.

CONCLUSIONS: The abscopal effect, in this case, may help us to get a better understanding of the impact of radiotherapy.

Key Words:
Abscopal effect, Radiotherapy, Metastases, Left cervical lymph node, Intra-abdominal Metastatic carcinoma.

Introduction

Radiotherapy (RT) has been applied as an effective local cancer treatment modality. It can trigger the phenomenon of the abscopal effect which refers to a clinical feature characterized as the eradication of distant metastatic tumors[1]. The detailed mechanisms underlying the abscopal effect of RT have not been clearly understood. Studies[2,3] have suggested that the immune system stimulated by radiation may play a vital role in mediating the abscopal effect. Although the abscopal effect was proposed in 1953, reports on the abscopal effect following pure RT have been relatively rare.

This report describes a case of a 70-years-old male patient who has been subjected to carcinoma with unknown primary origin. This patient was demonstrated to obtain systemic benefits from the local RT with an abscopal effect. The abscopal effect, in this case, may help us to get a better understanding of the impact of radiotherapy.

Case Report

A 70-year-old male was admitted to our hospital with swelling and pain in the left neck for nearly three months, with a limited movement of the neck. On physical examination, there was an enlarged, hard, and immovable lymph node in the left cervical. Histopathology of the left cervical lymph node showed poorly-moderately differentiated squamous cell carcinoma. Tumor markers were also detected: carcinoembryonic antigen (CEA) 0.14 ng/mL, squamous cell carcinoma (SCC) 0.45 μg/L, neurone-specific enolase (NSE) 5.74 ng/mL, cytokeratin 19 fragment (CYFRA21-1) 35.02 ng/mL, carbohydrate antigen 50 (CA50) 4.75 μg/L. Enhanced CT examination also demonstrated a metastatic lymph node in the left cervical (Figure 1A), and an intra-abdominal mass, located in hepatogastric space, upward of the pancreatic head, (Figure 1B-D) was discovered. It was presented as an uneven enhancement. However, no primary lesions were found. To identify the primary origin, we suggested a biopsy of the intra-abdominal mass of the patient, but the patient refused.

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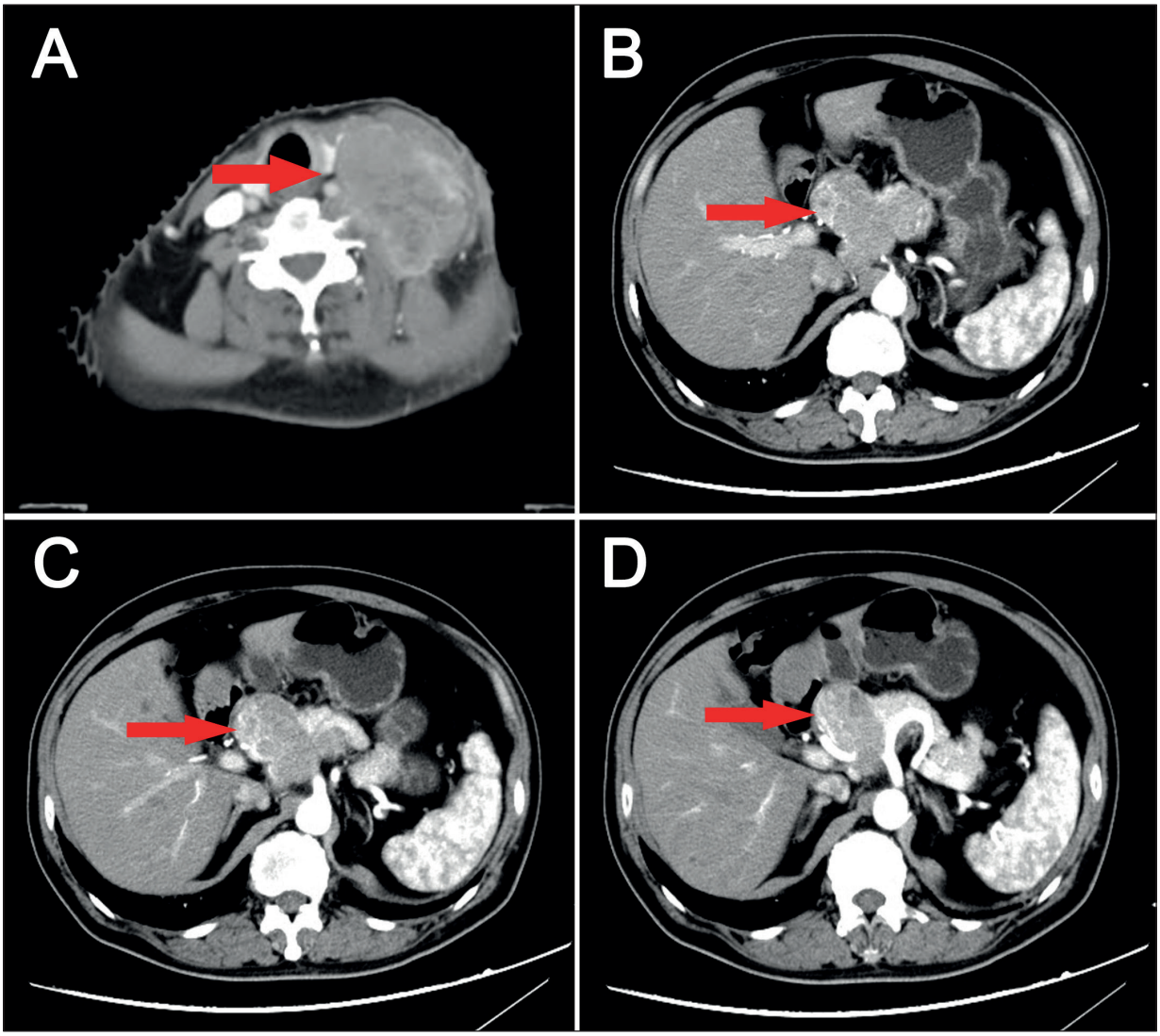

Figure 1. A, Metastatic lymph node of the left cervical and (**B-D**) an intra-abdominal mass which located in hepatogastric space, upward of the pancreatic head.

The patient was suggested to undergo systemic chemotherapy, but the patient and his family members rejected the therapeutic regimen. In consideration of the uncomfortable symptom of the patient, finally, a local RT was scheduled to execute. However, the metastatic lymph node of the left cervical and the intra-abdominal mass could not receive RT simultaneously due to the restriction of the apparatus. Taking the patient's major clinical symptoms into account, RT on the metastatic lymph nodes of left cervical (dose: 60 Gray in 30 fractions) was performed. The metastatic mass located in hepatogastric space, upward of the pancreatic head, was suggested to be observed regularly. After treatment, the pain in the left neck dramatically improved and the swelling of the radiation exposure site diminished gradually (Figure 2A). Unexpectedly, half a year later, CT examination showed that the abdominal mass was significantly reduced (Figure 2B-D).

Discussion

This study describes a case of a patient with a therapeutic effect on distant metastatic in carcinoma of unknown primary origin that responds to

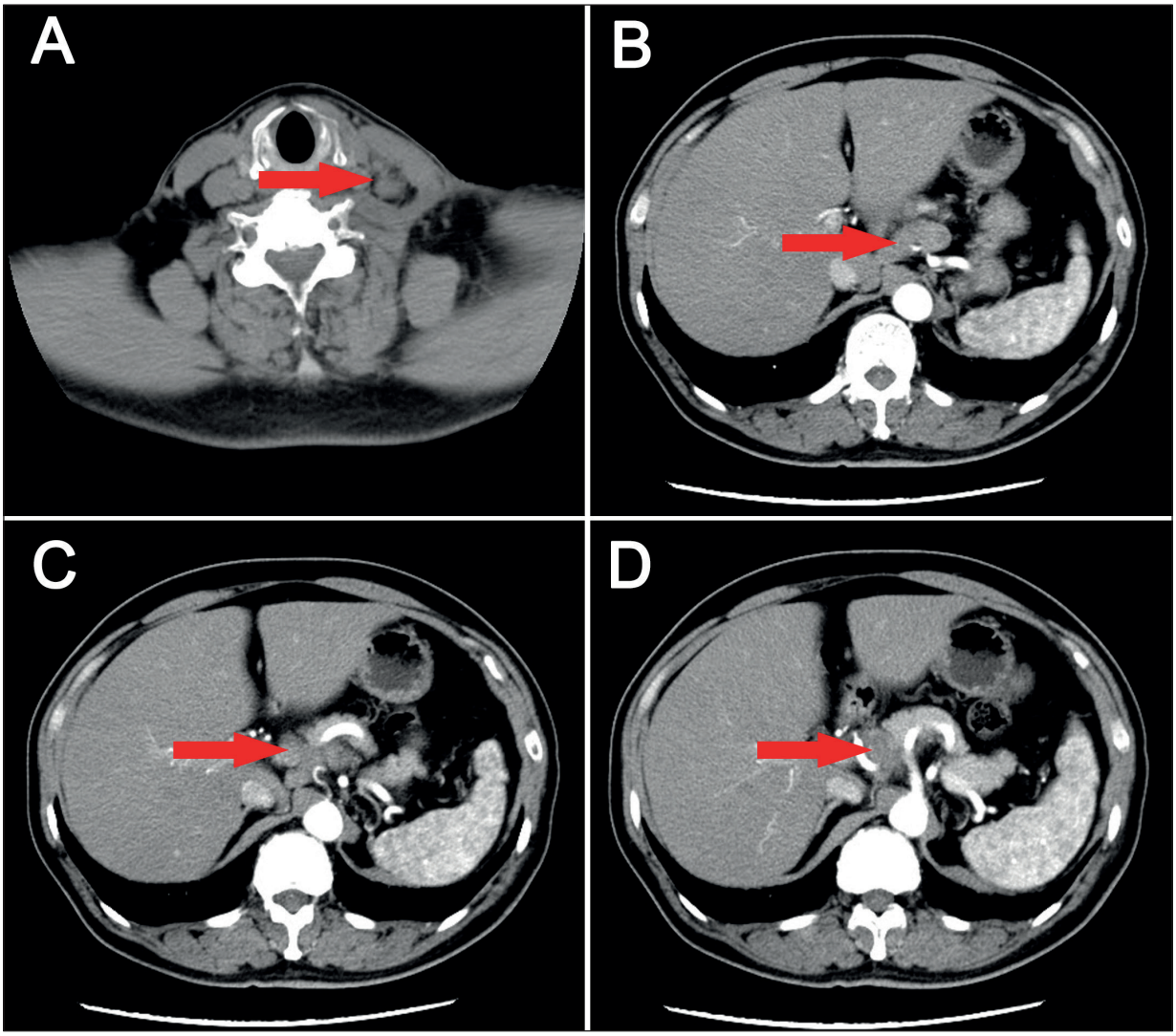

Figure 2. *A*, After radiotherapy, the radiation exposure site diminished gradually, (**B-D**) half a year later, metastatic mass which located in hepatogastric space, upward of the pancreatic head was significantly reduced.

the treatment with RT. This therapeutic outcome is highly suggestive of a true abscopal effect.

The abscopal effects have been first described[2-4] in 1953 by Mole, and they were characterized by an immune-mediated response to radiation by tumor cells located at a distant site from the site of irradiated site. Local RT increases the tumor-associated antigens presentation to $CD8^+$ T cells in the tumor microenvironment. Subsequently, these T cells recognized and attacked both the primary and the untreated malignant lesions[5]. In addition, the tumor cells after RT may also release cellular danger-associated molecular patterns and cytokines, which may enhance the traffic of immune cells[6]. The aforementioned explanations may help to elucidate the abscopal response of metastatic carcinoma to RT. In experimental animal models, scientists found that localized RT could stimulate the release of chemokines, such as CXCL10 and CXCL16, that might modulate immunological response by regulating the expression of adhesion molecules on the endothelial cells in the tumor microenvironment[7].

The abscopal effect of pure RT has only been described in sporadic clinical events maybe owing to the negation of pro-immunogenic effects of RT by counterbalancing with immunosuppressive effects in the tumor microenvironment. The phenomenon has recently revived considerable clinical attention since combining RT with immuno-

therapy showed the potential of boosting abscopal responses[8]. Recent studies[9] have demonstrated that immunotherapy can activate $CD8^+$ T cells by suppressing the inhibitors, eventually facilitating the abscopal effects. People with cancer benefit from the synergistic interactions between agents, such as anti-PD-L1 and RT-induced anti-tumor immune effects[10].

Limitations

Regrettably, the refusal of the patient to receive a further intra-abdominal mass biopsy due to personal reasons is considered a limitation of this study.

Conclusions

This study described a phenomenon of the abscopal effect, in which the intra-abdominal metastasis was ameliorated as a consequence of RT on the metastatic lymph nodes of the left cervical. The phenomenon might be due to the immunogenic response. The abscopal effect, in this case, may help us to get a better understanding about the impact of RT.

Conflict of Interest

The authors declare that they have no conflict of interest.

Acknowledgments

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Informed Consent

Written consent was obtained from the relatives of the patient.

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