Abscopal Effect: Propitious or Pernicious?

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Effect of localized radiation on general body systems is a well-recognized phenomenon. In addition to routine commonplace effects like generalized fatigue, anorexia, and weight loss, regression of a malignancy at sites away from the irradiated organ is a rare clinical reply to localized radiotherapy and is usually acknowledged as abscopal effect. Abscopal is a Latin word wherein ‘ab’ means ‘position away from’ and ‘scopus’ means ‘a target for shooting at’. Mole in 1953 defined the term abscopal as ‘a tumor event occurring at a distance from the irradiated volume but within the same organism’. Thus it is a local irradiation of one tissue involved and a response of other or similar tissue remote from the irradiated site is seen. Thus, from the oncologist’s point of view, the term abscopal is regression of a distant tumor following localized irradiation, while from a biologist’s perspective, the term refers to initiation of genetic instability, cell senescence, and tumorigenesis alterations in a healthy tissue.

ABSCOPAL EFFECT AND TUMOR REGRESSION

Spontaneous regression of tumors is a captivating phenomenon and the five most common types of tumor that undergo spontaneous regression as per the annotated biography published in 1993 include renal cell carcinoma, neuroblastoma, leukemia and lymphoma, melanoma, and breast cancer. However, spontaneous regression of cancer metastasis is rare. Boyd suggested the term ‘Saint Peregrine tumors’ for spontaneously regressing malignancies for the young priest with a large bone malignancy that supposedly resolved without reported recurrence through intense prayer. Papac put forth several mechanisms influencing tumor regression including immunological, hormonal, and psychological factors, epigenetic factors and tumor cell death. These mechanisms may appear to be connected with those accountable for abscopal phenomenon. Nevertheless, in abscopal effect, their timing postdistant radiation therapy provides reasonable conjectural affirmation in regression of tumor. Cases of abscopal effects of spontaneous tumor regression by conventional...
therapeutic radiation therapy and stereotactic ablative body radiotherapy in patients with nonhematological malignancies have been well-documented. The extended timing of abscopal effects in the reported cases of cancer regression can be attributed to an adaptive humoral response that can be explained by development of a sequence of events of antitumor responses.\(^\text{3}\)

Regression of hematological tumors by abscopal effect differs than those of nonhematological tumors. Such regression of tumors is better explained as ‘pseudo-abscopal’ effect subordinate to the recirculation of lymphocytes. The abscopal effect of splenic radiotherapy on bone marrow and peripheral blood smears can be clearly elucidated by a cytotoxic consequence on circulating tumor cells passing through the irradiated spleen.\(^\text{7}\) Rees\(^\text{8}\) revealed abscopal effect in 10 cases out of 895 subjects with Hodgkin’s and non-Hodgkin’s lymphoma and suggested that the tumor regression can be due to direct damaging effect of radiation on the reactive lymphocyte populations.\(^\text{3}\)

**ABSCOPAL EFFECTS IN NORMAL TISSUE**

The surrounding normal tissue gets inevitably exposed to ionizing radiations during radiation therapy. The harmful effects of radiation exposure on normal tissues include direct killing leading to decrease of cell population and/or inhibition of cell proliferation in tissues with high cell turnover like skin and gut.\(^\text{9}\) Moreover, the susceptibility of adjacent tissues is increased by the tumor cell itself, which communicates with the local tissues by expressing signal molecules like reactive oxygen species that include long-lasting hydrogen peroxide,\(^\text{10}\) growth factors, and cytokines.\(^\text{11}\) These signaling molecules create chronic inflammatory microenvironment and overall genetic instability.\(^\text{12}\)

The effects of acute radiation-induced toxicity directly on gut tissues include enteritis, diarrhea, and ulceration of intestine and mucus secretion in rectum in addition to nausea, anorexia, or vomiting.\(^\text{9}\) Such effects are believed to be manifested through radiation-induced inflammatory cytokines.\(^\text{12}\) Evidences of discharge of soluble factors in the peripheral blood circulation on exposure to radiation were first reported in 1968. Such factors produced chromosomal injury in cultured cells that were not exposed to radiation directly and were called ‘clastogenic factors’ or chromosome breaking factors.\(^\text{13}\)

These aspects can produce ‘messenger’ effects at organs or parts of organs at distant site from the irradiated field. These ‘clastogenic factors’ are similar to soluble chemokines and cytokines that induce nausea and fatigue in radiation therapy.\(^\text{14}\)

Contrary to tumor regression, recurrence of distant metastases or presence of new metastases has been reported by oncologists.\(^\text{15}\) Secondly, treatment-related cancers are well identified in clinical practice and account for more than 1% of patients.\(^\text{16}\) Various justifications for this effect include internal radiation scatter or leakage from radiotherapy machines, remnants of micrometastasis, genomic vulnerability and intrinsic radio sensitivity, implantation of viable malignant cells from the surgical or irradiation process, secretion of growth factors related with wound healing, and numerous mechanisms of immunosuppression.\(^\text{15}\) The mechanisms governing anti-tumor abscopal effects are hypothesized to be involved in carcinogenesis as well. Genomic instability and secondary carcinogenesis can be partly attributed to chronic inflammation and oxidative stress.\(^\text{17}\)

**REFERENCES**


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