Commentary

Radiation induced sarcoma: Everything comes with a price

The case illustration reported by the authors reiterates the fact "everything comes with a price". The advances in radiation therapy have resulted in improvement in the overall survival and disease free survival majority of solid tumors globally; however the improved survival has brought newer problems including the development of newer primary lesions and treatment related neoplasm besides local and distant treatment failures. Radiation induced sarcoma has been established as a real hazard of radiation therapy following numerous reports published in the literature since 1922.[1] The estimated incidence of RIS varies from 0.09% to 0.11% considering all cases of radiation therapy.[2] The key question remains whether the neoplasm developing in a pre-irradiated area is a result of sarcomatogenic effect of radiation or a new primary one. Cahan *et al.,*[3] described the criteria for defining RIS as histologically confirmed sarcoma in a previously irradiated field, where there was either no lesion or a microscopically or roentgenographically proved non malignant lesion, after a relatively long asymptomatic latent period of five years. The defining criteria have been modified many a times, a testimony to the fact that controversy is yet to come to rest. Arlen *et al.,*[4] modified the criteria by Cahan *et al.,*[3] by including pre-irradiation malignant tumors devoid of osteoblastic activity, and shortening the latency period to 3-4 years. The latency period is the one criterion which has been modified by most investigators as it is necessary to differentiate RIS from a second primary malignancy. A genetic expression profile "radiation signature" is yet to be found that can differentiate RIS from a second primary that may predate the radiation;[5] any spontaneous sarcoma appearing in the pre-irradiated field may not be related to radiation. Why do a subset of patients who receive radiation develop RIS still remains an unanswered question. Various risk factors have been identified for RIS which include young age at treatment, treatment- related factors including dose of radiation and simultaneous chemotherapy especially with alkylating agents, and genetic make-up of patients (Li-Fraumeni syndrome, familial gastrointestinal stromal tumor syndrome, retinoblastoma, Wermer syndrome, Neurofibromatosis type I, Costello syndrome, and Nijmegen syndrome).[5] RIS is likely to be induced in heavily radiated tissues or in the vicinity of the radiation fields, though a clear dose-response relationship for radiation-associated malignancies is yet to be established.[6]

Considering that radiation therapy is being used more and more frequently in the management of neoplastic conditions, further studies are needed to identify the risk factors for the development of RIS so as to be better able to select patients for radiation therapy vis-a-vis the pain and fear of a second malignancy.

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