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LETTER TO THE EDITOR

Memoirs of differential radiation doses: Gemcitabine induced radiation recall

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To the Editor

We present a 44-year-old lady with locally advanced carcinoma of the left breast. She was treated with left simple mastectomy and axillary clearance followed by systemic chemotherapy with cyclophosphamide, doxorubicin and 5 fluorouracil. Subsequently she received adjuvant radiotherapy to left chest wall and supraclavicular fossa. After a disease free interval of two years, she presented with symptomatic bone metastasis at Thoracic (Th) 6 and Lumbar (L) 3 vertebrae. In view of radiological features of impending collapse at Th6 region, she received palliative radiotherapy to Th5–Th7 region by Co^{60} gamma rays to dose of 20 Gy in 5 fractions by direct posterior portal, prescribed at 5 cm depth. The region of L2–L4 was treated by a similar technique albeit to a lower dose of 8 Gy in a single fraction at a depth of 5 cm. She experienced 70% relief of pain (as examined by visual analogue scale) one week after radiation and underwent subsequent vertebroplasty of involved vertebrae. After two months of completing her radiotherapy schedule, she was put on systemic chemotherapy with gemcitabine and carboplatin. At the start of the fourth cycle she presented with tightening and pain in upper back. Clinical examination revealed erythema, edema and induration at irradiated thoracic site while the lumbar region had minimal erythema only (Figure 1). She was treated with oral dexamethasone and showed regression of the erythema and induration after two weeks. On last follow-up she had only mild subcutaneous fibrosis at thoracic irradiated region.

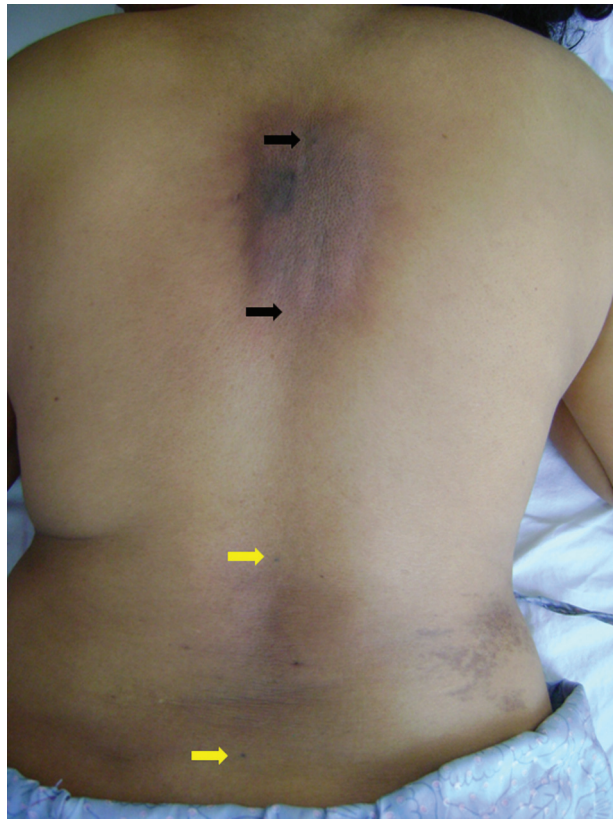

Figure 1. Differential "radiation recall" reactions at dorsal and lumbar regions. The area between the black arrows represents the portal for the dorsal spine (severe recall) while the area between the yellow arrows represents the portal for lumbar spine (very mild recall).

Radiation recall is characterized by an inflammatory reaction within a previously irradiated volume after subsequent exposure to antineoplastic drugs [1–3]. Dermatological manifestations include maculopapular eruptions, vesicle formation, desquamation

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and skin necrosis. For radiation recall to develop, the window period between completion of radiotherapy and administration of precipitating agent may vary from days to years [4].

Our case had received palliative radiotherapy at two different sites in the spine to different doses. The most apparent reason for a differential intensity of recall at these two sites was the different dose schedule to which these regions were treated, with the upper spinal region receiving more than twice the dose received by the lower spinal region. In radiobiological terms, although the dose was prescribed at 5 cm, the Biologically Equivalent Dose (BED) at subcutaneous tissue (i.e., at depth of maximum dose or D max) was generated from physics calculations. The BED for late reaction was 70 Gy for the upper spine radiotherapy as against 46 Gy for the lower spine (assuming $\alpha/ß=3$). For acute reactions the BED was 39 Gy and 21 Gy respectively (assuming $\alpha/ß=10$). Because of this uniqueness of treatment, the differential response in the intensity of recall was characteristic. In turn, this pointed to a dose-response relationship for radiation recall in our patient.

There have been suggestions in literature that patients who develop acute reactions are liable to develop radiation recall reactions as well. In our case, there was no reaction in the acute phase after completion of radiotherapy except for mild erythema in the upper spinal portal.

The principles of treatment of radiation recall reactions depend on the organ system involved and the severity of the recall. The agents used include withdrawal of the offending agent, corticosteroids (topical, oral, or i.v.) and non-steroidal anti-inflammatory agents. Masterly inactivity is an option when the reaction is not severe [5]. Another aspect of interest could be the effect of recall at non-dermatological sites. Our patient did not have any complaints related to effects on the spinal cord. The sensory and the motor examination were essentially normal. Although the spinal cord dose was well within tolerance limits, it would be interesting to see if she developed any recall sequelae related to the spinal cord or other viscera in her follow-up.

In summary our case has highlighted the importance of total dose as a factor for radiation recall. The late effects of this phenomenon are a subject of future examination and research.

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