Paclitaxel-induced systemic muco-cutaneous reactions and radiation recall phenomenon

Sir,

We present here case of a 52-year-old female who developed muco-cutaneous toxicities and radiation recall phenomenon (RRP) after paclitaxel administration.

Paclitaxel is well known for its neurotoxicity and hypersensitivity adverse effects. But, mucositis with diffuse skin reactions and RRP are rare with paclitaxel. This lady underwent left sided modified radical mastectomy for her locally advanced breast cancer (pT3N1M0) in August 2012. She was treated with post-mastectomy radiotherapy by Co-60 conventional planning to a dose of 50 Gy (2 Gy per fraction) over 5 weeks. Thereafter, she received six cycles of adjuvant chemotherapy with 5-flurouracil (500 mg/m^2), adriamycin (50 mg/m^2), and cyclophosphamide (500 mg/m^2) on a 3-weekly basis. She complied well with this treatment and after remaining disease-free for 4 months, she developed ascites and hepatic metastasis was detected radiologically. She was started on 3-weekly paclitaxel monotherapy (175 mg/m^2). Two days after the second cycle, she developed generalized itchy rash, oral mucositis and stomatitis along with dysphagia and hematuria (all Common Terminology Criteria for Adverse Events (CTCAE) grade 2). Of particular, there was a noticeable erythema over her left chest wall precisely within the boundaries of the irradiated fields. Supportive management, especially topical and systemic steroids and anti-histaminics were promptly started and these complications gradually resolved over a week. Re-exposure to paclitaxel was not done.

Review of literature shows paclitaxel-induced skin disorders and stomatitis in 14.4% and 15.2% cases, respectively, when given as monotherapy in metastatic breast cancer,[1] whereas the rates were 12% and 15% when given in sequential dose dense combination chemotherapy.[2] Other dermatological toxicities of paclitaxel include pustular dermatosis,[3] fixed drug reactions,[4] and folliculitis.[5] To the best of our knowledge, there has been a few case reports of RRP with paclitaxel[6,7] till date, our case being the sixth one. RRP is probably related to localized hypersensitivity which involves direct activation of nonimmune inflammatory pathways; irradiation lowers the inflammatory response threshold. It has been suggested that this mechanism could be mediated by continued low-level secretion of the inflammation-mediating cytokines induced by radiation. The presence of a precipitating chemotherapy agent may then upregulate these cytokines, resulting in a radiation recall reaction.

Treatment of mucositis has not been standardised as yet. Oral glutamine, pre and probiotics, maintenance of proper hydration and nutrition, temporary cessation of offending agent(s)-chemotherapy or radiotherapy, etc., are usually advocated. For oral mucositis particularly, alcohol-free benzydamine-containing mouthwash and anti-fungal rinse, supersaturated solution of calcium and phosphate have been empirically proved to be effective. RRP is best managed by stopping the offending agent, corticosteroids, anti-histaminics, and emollients.

Such rare toxicities are imp ossible to predict at present and since there are no standard guidelines for re-challenge with or without dose reduction, the authors believe that re-exposure is not safe. Also, this case underscores the importance of being vigilant about the varied forms of hypersensitivity reactions paclitaxel may induce for which precaution and prompt action need to be ensured.

Paclitaxel-induced radiation recall phenomenon is very rare and difficult to diagnose. Once is gets diagnosed the offending agent must be withdrawn to prevent further aggravation of recall phenomenon. In our case, the lady in the metastatic settings got single agent paclitaxel, thereafter developed radiation recall, severe mucusitis as she received post mastectomy external beam radiotherapy more than 6 months back.

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