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Post-irradiation morphea: An under reported complication

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Abstract
Post irradiation morphea (PIM) is a rare complication of radiotherapy, which occurs abruptly after an asymptomatic period of one month to three years and presents with painful sclerotic plaques associated with severe pain and disfigurement. We are reporting a 55-year-old patient of operated breast carcinoma, post chemotherapy; who developed PIM five months after completion of radiotherapy. PIM being a complication of radiotherapy with unpredictable risk factors is an underdiagnosed condition. Early suspiscion of the disease is necessary in order to avoid irreversible complications.

Keywords: morphea, radiotherapy

Introduction
Post irradiation morphea (PIM) is a rare complication of radiotherapy, which occurs abruptly after an asymptomatic period of one month to three years [1]. It presents with development of erythematous indurated plaques in the radiation field, associated with severe pain, and chronically progresses to become smooth and shiny as sclerosis develops causing severe morbidity as well as cosmetic disfigurement. Most skin changes after radiation exposure depend upon the dosage and duration of the radiotherapy, but no dose and duration relationship for PIM is known yet, hence making it difficult to predict the risk of development of PIM. We are reporting this rare condition in a 55-year-old patient of operated breast carcinoma, following radiotherapy.

Case Summary
A 55-year-old female, known case of triple negative Breast Cancer (Lt breast), underwent MRM (Modified Radical Mastectomy) in November 2019 followed by four cycles of chemotherapy with Docetaxel and cyclophosphamide from December 2019 to March 2020. The patient was then provided 25 cycles of radiotherapy over six weeks (8 June 2020 to 16 July 2020) at a dose of 50 Gy. After cessation of therapy, following an asymptomatic period of five months, patient developed tightening and thickening of skin over radiation area of mastectomy site. It was associated with redness and severe pain. Over a period of approximately one month, the pain extended beyond radiation area to involve left upper arm and back. She was also a known case of Diabetes Mellitus controlled on Insulin.
On examination, the patient had a large sclerotic plaque over radiation area with varying erythema. There were multiple erythematous small plaques measuring approximately 2*2 cm beyond the radiation area. All the plaques were indurated, firm to hard in consistency, with blanchable erythema. (Fig 1)
A biopsy from the plaque revealed epidermal atrophy, homogenization of dermis, with complete loss of appendages without any inflammatory infiltrate, consistent with morphea. [Fig 2 a) and b)]
Patient was started on potent topical steroid Clobetasol propionate 0.05% cream daily application for morphea, along with Injection Tramadol twice daily, Tab Gabapentin 300mg thrice daily, Buprenorphine transdermal patch, and Tab Nortriptyline 25mg SOS, for pain management. Patient was also given a trial of high dose steroids in the form of injection dexamethasone 100 mg in 500ml NS, but as her blood sugar levels could not be safely maintained, Dexamethasone was discontinued. NB UV-B (Narrow Band UV-B) alternate day therapy was initiated over localized area and provided some relief in pain and mild decrease in skin tightening, after which the patient was lost to follow up.

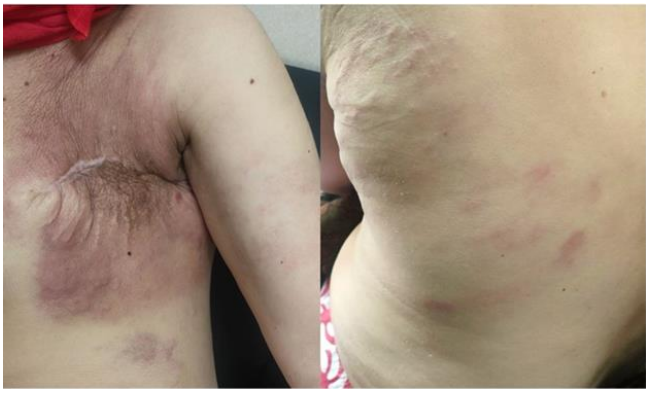

Fig 1: a) Large erythematous sclerotic plaque over previously irradiated area b) Multiple discrete, small, erythematous, indurated plaques over upper back

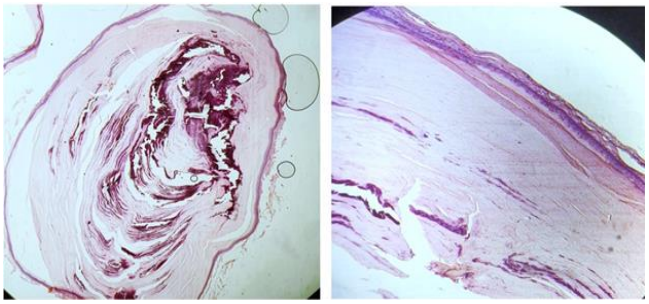

Fig 2 a) and b): Epidermal atrophy and homogenization of dermis, with complete loss of appendages without any inflammatory infiltrate, consistent with morphea; in 2x and 10x magnification respectively.

Discussion

The incidence of Morphea of any etiology have been reported to be 2.7 per 1, 00, 000 per year, and incidence of PIM has been estimated to be 1 in 500 [2]. This incidence rate of PIM suggests that significant number of PIM are underdiagnosed or misdiagnosed.

The pathological mechanism proposed suggests an increase in the expression of TGF-β and IL-4, IL-5 following trigger by radiation [3]. Leading to activation of fibroblasts and increased synthesis of collagen, glycosaminoglycans and extracellular matrix proteins. TGF –β also induces transformation of fibroblast precursors to myofibroblasts leading to sclerosis of the connective tissue.

Early inflammatory stage of PIM needs to be differentiated from radiation recall reaction or an inflammatory recurrence of the disease while late burnt-out stage needs to be differentiated from chronic radiodermatitis and Radiation induced fibrosis which is more common, occurs within 3 months of radiation exposure, is not associated with erythema and induration in the early stages, and does not extend beyond the area of irradiation.

Treatment modalities include topical calcineurin inhibitors, topical steroids, oral immunosuppressants like steroids, methotrexate, or cyclosporine, as well as phototherapy (UVA1, NB UVB) with variable results.

As discussed above, PIM being a relatively rare complication of radiotherapy as well as having overlapping clinical features with other commoner side effects, is often a missed diagnosis. Due to unpredictable risk factors of the disease, the treating doctor needs to consider and confirm this diagnosis early and begin treatment as soon as possible to prevent and delay irreversible fibrosis.

References

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