

Cutaneous manifestations of acute radiation dermatitis: a clinical study

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ABSTRACT

Background: Radiotherapy can result in common, inevitable cutaneous side effects such as acute radiodermatitis, chronic radiodermatitis and radiation induced dermatoses. There is paucity of clinical studies on skin manifestations of radiotherapy in the literature available. Even though there are isolated case reports, there have been no clinical studies on this subject in India.

Aims: The present study aims at studying the clinical pattern and manifestation of acute radiation dermatitis.

Materials and methods: Fifty patients (17 males and 33 females) were included in the study. Dermatological evaluation was carried out before commencement, after 24 hours, and weekly, till the completion of radiotherapy and one month after completion of therapy. Necessary investigations like scraping for fungus, Gram's staining and skin biopsy were carried out in selected patients.

Results: Various cutaneous manifestations of acute radiation dermatitis were observed in our study. The commonest manifestation was hyperpigmentation (74%) followed by dry desquamation (72%), erythema (70%), hair loss (34%), erosions (10%), moist desquamation (10%), edema (10%), and pustule (4%). The mucosal changes observed were erythema (10%), pain (6%), erosions (6%), and hyperpigmentation (4%). Risk factors associated with acute radiation dermatitis in our study were anemia, post operative radiotherapy, radiation at skin folds, smoking, diabetes and tobacco chewing. Majority of the patients in this study showed features suggestive of grade I acute radiation dermatitis (84 %) followed by grade II (10 %), grade 0 (6 %) changes whereas none of the patients had grade III and grade IV changes as per acute radiation dermatitis classification.

Conclusion: Hyperpigmentation and changes of grade I acute radiation dermatitis was the most commonly observed features of acute radiation dermatitis. Awareness of the signs and symptoms of acute radiation dermatitis is essential for better assessment and management.

Key Words: Acute radiation dermatitis, Cutaneous manifestations, Radiotherapy, Risk factors, Grading.

1. INTRODUCTION

Radiotherapy is a common modality in cancer treatment and more than 50 % of affected patients will eventually receive some form of radiotherapy as definite, preoperative, postoperative or palliative treatment (Omidvari et al. 2007). Radiotherapy can result in common, inevitable cutaneous side effects, such as, acute and chronic radiodermatitis (Venkatesan et al. 1998) and systemic side effects (Lichter, 2000). Even when the skin is not the primary target, it may be injured as an “innocent bystander” and develop profound alterations on functional, gross, and molecular levels (Hymes et al. 2006). Acute radiation effect is defined as changes occurring within 2 to 3 weeks of starting radiation and continuing 3 to 4 weeks after completion of therapy (Carper et al. 1999). Acute radiation dermatitis manifests as erythema, edema, burning or tingling, pruritus, pigmentation, desquamation, epilation, shedding of nails, vesiculation or bulla formation, erosion or ulceration. Chronic radiation changes include excessive wrinkling or atrophy of the skin, hyperpigmentation, permanent loss of hair, excessive dryness of skin, excessive longitudinal ridging of nails, keratosis and skin carcinomas (Price, 1978).

Very few studies are available on cutaneous affect of radiotherapy and majority of them are pertaining to chronic radiation dermatitis. There is paucity of clinical studies on skin manifestations of radiotherapy in the literature available. Even though there are isolated case reports, (Venkatesan et al. 1998) (Pavithran, 1998), there have been no clinical studies on this subject in India. Therefore, it is proposed to undertake this study.

2. METHODS

Patients attending the radiotherapy department at R.L. Jalappa Hospital and Research Center, Tamaka, Kolar were enrolled in the study. A total number of 50 patients were included in the study. A detailed history and clinical examination was carried out in all the patients with the special emphasis on indication for radiotherapy and histological diagnosis of underlying malignancy, type and total dose of radiation employed. A detailed dermatological evaluation was carried out in study subjects after 24 hours and weekly till the completion of radiotherapy and one month after completion of therapy and the findings were recorded in a proforma. The collected data was analyzed using descriptive statistical tools.

2.1. Inclusion criteria

All fresh cases planned for radiotherapy suffering from malignancy.

2.2. Exclusion criteria

1. Cases with dermatoses not due to radiation
2. Patients on chemotherapy in the past and concurrently.

2.3. Investigations

Investigations like scraping for fungus, Gram's staining, and skin biopsy were carried out in selected cases.

3. RESULTS

Fifty patients satisfying the inclusion and exclusion criteria were drawn for the study from the Department of Radiotherapy at R.L. Jalappa Hospital and Research Centre, Tamaka, Kolar. Among 50 patients, 33 (66%) were females and 17 (34%) were males with a male to female ratio of 0.52:1. The age range of patients was 15 – 75 years. Mean age was 51.54 years. 80 % of the patients were between 31 – 60 years of age, 18 % were above 61 years and 2 % below the age of 30 years. The most common occupation among the study population was agriculture (58%) followed by housewife (16%), coolie (14%), teacher (4%), carpenter (2%), tailor (2%), student (2%) and chef (2%) respectively. All the patients were given teletherapy in the total dose range of 30 – 64 Grays. (Mean 48.54 Grays) with 200 Centigray dose fractionation. Among the study population, the most common indication for radiotherapy was oral cancer (26%) followed by carcinoma cervix (24%), carcinoma laryngopharynx (18%), carcinoma oesophagus (10%), carcinoma breast (10%), carcinoma rectum (4%), carcinoma oropharynx (2%), carcinoma stomach (2%), sarcoma thigh (2%), and cerebral metastasis with unknown primary (2%).

3.1. Cutaneous manifestations of acute radiation dermatitis

3.1.1. Hyperpigmentation

It was the most common cutaneous manifestation observed in 37 patients, among which majority of them developed in 4th week (42%) followed by 5th week (20%), 3rd week (10%) during radiotherapy and 2% of patients developed within 1 month of completion of therapy. Punch biopsy of a hyperpigmented lesion was performed in 1 patient in this

Table 1

Onset of cutaneous manifestations

| Cutaneous Manifestations | Base-line | 24 hours | First week | Second week | Third week | Fourth week | Fifth week | One month |
|--------------------------|-----------|----------|------------|-------------|------------|-------------|------------|-----------|
| Hyperpigmentation | - | - | - | - | 5(10%) | 21(42%) | 10(20%) | 1(2%) |
| Dry desquamation | - | - | 5(10%) | 10(20%) | 10(20%) | 8(16%) | 3(6%) | - |
| Erythema | - | 13(26%) | 18(36%) | 4(8%) | - | - | - | - |
| Hair loss | - | - | 3(6%) | 4(8%) | 8(16%) | 2(4%) | - | - |
| Itching | - | 4(8%) | 5(10%) | 3(6%) | 3(6%) | - | - | 1(2%) |
| Erosions | - | - | - | - | 1(2%) | 3(6%) | 1(2%) | - |
| Pain | - | 1(2%) | 1(2%) | - | 1(2%) | 1(2%) | 1(2%) | - |
| Moist desquamation | - | - | - | - | 1(2%) | 4(8%) | - | - |
| Edema | - | - | - | - | 1(2%) | 3(6%) | 1(2%) | - |
| Burning sensation | - | 2(4%) | - | 1(2%) | - | - | 1(2%) | - |
| Pustules | - | - | - | 1(2%) | 1(2%) | - | - | - |

Table 2

Spectrum of clinical manifestations

| Dermatological manifestation | Skin Changes | | Mucosal Changes | |
|------------------------------|--------------|----|-----------------|----|
| | NUMBER | % | NUMBER | % |
| Hyperpigmentation | 37 | 74 | 2 | 4 |
| Dry desquamation | 36 | 72 | - | - |
| Erythema | 35 | 70 | 5 | 10 |
| Hair loss | 17 | 34 | - | - |
| Itching | 16 | 32 | - | - |
| Erosions | 5 | 10 | 3 | 6 |
| Pain | 5 | 10 | 3 | 6 |
| Moistdesquamation | 5 | 10 | - | - |
| Edema | 5 | 10 | - | - |
| Burning sensation | 4 | 8 | - | - |
| Pustules | 2 | 4 | - | - |

study group. The microscopic section studied shows thinned out epidermis with keratotic plugs and mild chronic inflammatory infiltrate in the superficial dermis (Table 1 & Figure 1).

3.1.2. Dry desquamation

Of the 72 % of patients who developed dry desquamation, 10 % developed it by 1st week, 20 % by 2nd week, another 20 % by 3rd week, 16 % by 4th week and only 6 % by 5th week of radiotherapy (Figure 2).

3.1.3. Erythema

26 % of the patients developed erythema within 24 hours whereas 36 % of the patients developed it in 1st week but only 8 % in 2nd week of radiotherapy.

3.1.4. Hair loss

Hair loss was noticed in 6 % of the patients in 1st week, 8 % in 2nd week. Majority of the patients (16 %) developed hair loss in 3rd week and only 4 % in 4th week of radiotherapy.

3.1.5. Itching

Itching localized to the site of radiation was a complaint in 8 % of the patients within 24 hours of radiotherapy followed by 10 % in 1st week, 6 % in 2nd and 3rd weeks each during radiotherapy whereas only 2 % of the patients developed it within 1 month of completion of therapy.

3.1.6. Erosions

Erosions were not observed till 2nd week of radiotherapy. However, 2 % of the patients developed erosions during 3rd week followed by 6 % in 4th week and 2 % in 5th week of radiotherapy.

3.1.7. Pain

Pain at the site of radiation afflicted 2 % of the patients in 24 hours, 1st week, 3rd week, 4th week, and 5th week each following commencement of radiotherapy. However, no patient complained of pain during 1 month of follow up after completion of radiotherapy.



Figure 1
Radiation induced Hyperpigmentation



Figure 2
Radiation induced Dry desquamation



Figure 3
Radiation induced Moist desquamation

3.1.8. Moist desquamation

Moist desquamation was a feature in 10 % of the total cases, majority of which (8 %) developed it in the 4th week while the remaining 2 % of the patients in 3rd week of radiotherapy (Figure 3).

3.1.9. Edema

Edema at the site of radiation was present in 2 % of the patients in 3rd week whereas in 6 % in 4th week followed by 2 % in 5th week of radiotherapy.

3.1.10. Burning sensation

Burning sensation at the site of radiation was experienced by 8 % of the total patients of the study population of which 4 % complained within 24 hours and 2 % in 2nd and 5th weeks each during radiotherapy. None of the patients complained during 1st week, 3rd week, and 4th week of radiotherapy and during 1 month following completion of radiotherapy.

3.1.11. Pustules

Pustules were seen in 2 % of the patients by 2nd and 3rd week each during radiotherapy. Gram's staining study in these patients revealed moderate number of pus cells and few Gram's positive cocci in pairs. The cutaneous symptoms found in 50 patients included in the study were itching (32%), pain (10%), and burning sensation (8%) as shown in table 2. The spectrum of cutaneous manifestations found in this study group is shown in table 2 and figure 1, the commonest being hyperpigmentation (74%). Other changes in decreasing order were dry desquamation (72%), erythema (70%), hair loss (34%), erosions (10%), moist desquamation (10%), edema (10%), and pustule (4%). The mucosal changes observed were erythema (10%), pain (6%), erosions (6%), and hyperpigmentation (4%). KOH mount was positive for candidial infection in 3 out of 5 patients with erythema and 2 out of 3 patients with erosions.

3.2. Grading of acute radiation dermatitis

Majority of the patients in the present study showed feature suggestive of grade I acute radiation dermatitis (84%) followed by grade II (10%), grade 0 (6%) changes whereas none of the patients had grade III and grade IV changes as per acute radiation dermatitis classification.

4. DISCUSSION

Since the discovery of ionizing radiation in 1895, it has played a crucial role in the treatment of various malignancies. Despite recent publication of reliable textbooks by qualified experts and of literature reports on the results and safety of radiotherapy, the majority of dermatologists today are still unaware with regard to risk afforded by this form of treatment (Caccialanza et al. 1999). There are many studies on chronic radiation dermatitis and radiation induced skin cancer (Vloten et al. 1987; Okumura et al. 2003; Stante et al. 2002; Landthaler et al. 1995; Lazar et al. 1963), however, there is paucity of clinical studies on acute

manifestation of radiotherapy in the literature available (Price, 1978; Schmuth et al. 2001; Caccialanza et al. 1999). Bearing this in mind, this study was conducted.

Among the 50 patients, 34 % were males and 66 % were females, showing strong female preponderance which differ with Norman's study which shows high male predominance (80 % males and 20 % females) (Price, 1978). The reason for this difference is not clear. The patient and treatment related factors like poor nutritional status, history of severe skin reaction to sun exposure, fair complexion, diabetes, smoking, pre existing connective tissue or auto immune diseases, burned skin, skin donor site, radiation at skin fold, post operative radiation and infectious diseases like HIV predisposes patients to radiation dermatitis (Hymes et al. 2006). Among the study population, the most common risk factor observed was anemia in 70 % of the patients followed by post operative radiotherapy in 54 %, radiation at skin fold in 42 %, smoking in 26 %, diabetes in 20 % and tobacco chewing in 14 % of the patients. Majority (94 %) of the patients in this study developed acute radiation dermatitis as compared to 100 % in the study conducted by Norman M. Price (Price, 1978) and 1.94 % in Massimo Caccialanza's study (Caccialanza et al. 1999). Thus, the finding of this study is more consistent with that of Norman's study. However, the wide difference between the present study and Massimo's study may be due to type, dosing, site of radiation, and protective devices used.

Clinically, human skin is known to exhibit erythematous changes after exposure to ionizing radiation (Schmuth et al. 2001). The erythematous response to radiation is composed of early erythema that begin within 24 hours after irradiation, main erythematous phase begins 7 – 8 days after radiation and the third delayed erythematous response occurs 6 – 7 weeks after irradiation (Jolles et al. 1966). In the present study, early erythema was observed in 26 % of the patients. The main erythematous response was noticed in 44 % of the patients whereas none of the patients developed delayed erythematous response. In a study by Mathias Schmuth in 2001, the early erythematous response was seen in 26.66 % of the patients which is similar to the present study. However, the main erythematous response in our study is comparatively less (44 % vs. 93.99 %). None of the patients in our study developed delayed erythema in contrast to 6.66 % of the patients in the Mathias's study.

Hyperpigmentation was the commonest manifestation observed in 74 % of the patients in the present study whereas dry desquamation and epilation were the commonest manifestations in Norman's study (Price, 1978). Majority of the patients (42 %) developed hyperpigmentation in the fourth week of radiotherapy which is also documented in the literature (Jolles et al. 1966). The occurrence of dry desquamation and erythema in the present study is consistent with Norman's study (72 % vs. 70 % and 70 % vs. 60 % respectively). However, the occurrence of other signs and symptoms was highly variable. Hyperpigmentation and itching was more (74 % vs. 40 % and 32 % vs. 20 %) compared with Norman's study whereas the occurrence of hair loss, erosions, burning sensation was less in the present study (34 % vs. 70 %, 10 % vs. 30 %, 8 % vs. 40 % respectively). Pain, moist desquamation, edema (10 % each) and pustules formation (4 %) was observed in the present study whereas none of the patients developed them in Norman's study. Mucosal changes included erythema (10 %), pain (6 %), erosions (6 %), and hyperpigmentation (4 %). None of the previously conducted studies described mucosal and skin changes separately (Price, 1978; Schmuth et al. 2001; Caccialanza et al. 1999). In the present study, microscopic section in one patient with hyperpigmentation showed thinned out epidermis with keratotic plugs and mild chronic inflammatory infiltrate in the superficial dermis which is consistent with the findings in Norman's study (Price, 1978).

Majority of the patients in the present study showed features suggestive of grade I acute radiation dermatitis (84 %) manifesting as erythema and or dry desquamation. Grade II changes were observed in 10 % of the patients characterized by moist desquamation confined to skin folds with moderate edema. The remaining 6 % of the patients did not show any changes of acute radiation dermatitis – Grade 0. None of the patients in the present study showed Grade III and Grade IV changes characterized by moist desquamation not confined to skin fold and skin necrosis or ulceration of full thickness dermis respectively. None of the previous studies correlated the skin lesions with acute radiation dermatitis grading. There are isolated reports of lichen planus confined to a radiation therapy site (Kim JH et al. 2002) , radiation induced Stevens-Johnson syndrome (Nawalkha et al. 1972), erythema multiforme (Arnold, 1949) , cutaneous lymphangiectasis (Kaya et al. 2001), Dariers disease (Chopra et al. 2004), bullous pemphigoid (Venkatesan et al. 1998), discoid lupus erythematosus (Pavithran et al. 1998), localized acneiform eruption (Stein et al. 1972), Sweet's syndrome (Vergara et al. 2003), pemphigus, asteototic eczema, non specific hypersensitivity reaction including urticaria, delayed breast cellulitis (Hymes et al. 2006). None of the patients in the present study developed these radiation induced dermatoses. Awareness of the signs and symptoms of acute radiation dermatitis is essential for its better assessment and management.

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