MUCOCUTANEOUS ADVERSE EFFECTS IN PATIENTS UNDERGOING CANCER CHEMOTHERAPYGarima Sharma¹, P. K. Nigam²¹Assistant Professor, Department of Skin, Pt. JNM Medical College, Raipur, Chhattisgarh, India.²Director, Professor and HOD, Department of Skin, Pt. JNM Medical College, Raipur, Chhattisgarh, India.**ABSTRACT****BACKGROUND**

New chemotherapeutic agents and new protocols in oncology have led to an increasing survival rate in patients affected by tumours. Traditional chemotherapy drugs as well as the newer targeted agents are associated with a wide array of cutaneous toxicities.^[1] Toxic effects on skin, hair and nails can negatively affect the quality of life and also lead to interruption or discontinuation of these drugs.^[2]

Aim- To study the various mucocutaneous adverse effects associated with cancer chemotherapy.

MATERIALS AND METHODS

A total of 200 patients with malignancies undergoing chemotherapy in the oncology ward and outpatient department were screened in this observational study. We have clinically examined 200 patients affected by cancer determining type, treatment and evolution of cutaneous side effects related to chemotherapy. It is a hospital-based observational study. All patients were counselled about the study and informed written consent was obtained. Patients were examined before start of chemotherapy treatment and after every cycle of chemotherapy. Data collected was analysed using SPSS version 16.0.

RESULTS

In this study, 200 patients including 118 females and 82 males were studied. Majority (56%) of the patients belonged to the age group of 41 - 60 years. The common indications for chemotherapy were carcinoma breast (29%), tongue (11%), buccal mucosa (10%), ovary (8%) and stomach (6%). Among the cutaneous adverse events noted, hair changes were the most common presentation and were reported in 156 (78%) patients. Skin changes were seen in 130 (65%) cases, nail changes in 102 (51%) cases and mucosal changes in 46 (23%) patients. Cisplatin, cyclophosphamide, 5-fluorouracil, carboplatin, paclitaxel and doxorubicin were the most frequently prescribed chemotherapeutic drugs.

CONCLUSION

Oncological therapies have become more selective and have low systemic toxicity because of their high specificity, but cutaneous side effects are common and may worsen the quality of life of these patients. Our observations necessitate a joint effort between dermatology and oncology for the early recognition and adequate treatment of the cutaneous adverse effects associated with cancer chemotherapy, which may help in reducing morbidity and improving compliance.

KEY WORDS

Chemotherapy, Skin Toxicity, Adverse Reaction.

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BACKGROUND

Cancer is a leading cause of mortality and morbidity in both developed and developing parts of the world with the disease burden projected to grow exponentially in the future. Anticancer drugs usually affect rapidly growing cells and hence the skin, hair follicles and nail matrix are the frequent targets of their toxicities.^[3] In recent years, targeted therapy has considerably increased survival rate in patients affected by important solid tumours of kidney, lungs, colon-rectum, breast and liver. Despite the benefits of all these chemotherapeutic agents, toxic effects on the skin may eventually result in poor compliance of patients and interruptions or discontinuation of antineoplastic therapy.^[4,5]

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MATERIALS AND METHODS

An observational study was conducted at our centre. A total of 200 patients diagnosed with cancer attending the Departments of Oncology and Dermatology in a tertiary care hospital between January 2018 and July 2018, who underwent chemotherapy and satisfied the inclusion and exclusion criteria were included in this study.

Inclusion Criteria

1. Patients above the age of 18 years and who gave consent for the study were included in the study.
2. Patients of both sexes who suffered from mucocutaneous adverse effects, which began after initiation of the anti-cancer drug.

Exclusion Criteria

1. Patients on radiotherapy.
2. Patients below the age of 18 years.
3. Patients who developed dermatological manifestations as a result of internal malignancy or before starting of chemotherapy.

All patients were counselled about the study and informed written consent was obtained. All patients underwent a complete dermatological examination.

Information including demographic data, cancer type, chemotherapeutic agents used, any significant dermatologic history and ongoing dermatologic treatment was collected using a structured proforma. Detailed descriptions of the clinical features as well as characterisation of the severity and evolution of cutaneous lesions were assessed and documented. Patients were examined before the start of chemotherapy treatment and at each clinical visit for every cycle of chemotherapy and the lesions were photographed. Data collected were analysed using SPSS version 16 (SPSS Inc. Chicago, USA).

Cutaneous lesions were diagnosed on the basis of typical clinical manifestations.

RESULTS

Out of 200 cancer patients studied, 82 (41%) were males and 118 (59%) were females. [Graph 1] They had 28 different types of malignancies.

Breast cancer was the most common cancer seen in 58 (29%) patients followed by tongue cancer in 22 (11%) patients, buccal mucosa cancer in 20 (10%) patients and ovarian cancer in 16 (8%) patients. The remaining types are depicted in figure below [Graph 2].

Common chemotherapeutic drugs used in this study were: cetuximab, gefitinib, imatinib, sorafenib, paclitaxel, vincristine, vinblastine, 6-mercaptopurine, 5-fluorouracil, cytarabine, capecitabine, gemcitabine, cisplatin, carboplatin, oxaliplatin, etoposide, cyclophosphamide, doxorubicin, daunorubicin, epirubicin, hydroxyurea, CHOP (cyclophosphamide, doxorubicin, vincristine, prednisolone) and ABVD (doxorubicin, bleomycin, vinblastine, dacarbazine) regimens.

Hair changes were the most common adverse effect noticed in 156 (78%) patients followed by skin changes in 130 (65%), nail changes in 102 (51%) and mucosal changes in 46 (23%) patients [Graph 3].

Graph 1. Distribution of Gender
Female (59%) - Male (41%)

Graph 2. Type of Cancer

Graph 3. Frequency of adverse effect
Hair (78%) > Skin (65%) > Nail (51%) > Mucosa (23%)

Hair changes were mainly in the form of anagen effluvium seen in 156 (78%) patients [Figure 1].

The skin changes were supragenous hyperpigmentation [Figure 2], generalised pruritis, facial pigmentation, acneiform (Papulopustular) eruptions, xerosis, hyperpigmentation of palm and sole, and toxic epidermal necrolysis, acral erythema, hand-foot syndrome, extravasation, erythema nodosum and flagellate dermatitis.

The most common nail finding observed was melanonychia [Figure 3], which was seen in 74 (37%) patients followed by onychoschizia [Figure 4], Muehrcke's lines, Mees' lines and Beau's lines.

Mucosal changes included pigmentation of tongue [Figure 5], oral ulcer, gingivitis [Figure 6] and stomatitis.

Figure 1. Anagen Effluvium

Figure 2. Supravenous Hyperpigmentation

Figure 3. Diffuse Melanonychia

Figure 4. Onychoschizia

Figure 5. Black Pigmentation of Tongue

Figure 6. Glossitis and Furrowed Tongue

DISCUSSION

Newer chemotherapy agents having specific targets in the pathogenesis of malignancies and older agents are associated with a variety of cutaneous adverse events. These drugs have a small therapeutic index and thus may be toxic to the rapidly proliferating cells of the skin, hair and nails at therapeutic doses resulting in a wide array of cutaneous side effects.^{[1],[6]}

In our study among all the cutaneous manifestation, most common ones were anagen effluvium followed by supravenous hyperpigmentation, xerosis and melanonychia of nail.

Hair loss has been rated as one of the most distressing side effects of chemotherapy along with vomiting and nausea.^[7] There have been reports of refusal of chemotherapy, especially among women, because of the risk of hair loss. Alopecia was the first most common adverse effect in our study [156 (78%) patients] similar to the study done by Kamil et al and Chiewchanvit et al.^[8] The mechanism involved is a sharp fall in mitotic activity of the matrix cells of the hair follicle due to cytotoxicity. The cessation of mitotic activity in the hair matrix results in a narrow weakened portion of the hair shaft known as Pohl-Pinkus constriction, which is prone to fracture.^[9]

Hair loss was seen within the first 1 month after the onset of chemotherapy in our study, which was also observed in a study by Chadha et al.^[10] Anagen effluvium is the most common cause of hair loss associated with anti-cancer drugs and it usually begins in 1 - 2 weeks after starting the drug, becoming more apparent in the subsequent 4 - 8 weeks. Drugs like doxorubicin, daunorubicin, docetaxel and cyclophosphamide are more likely to cause anagen effluvium. In our study, hair loss was seen in patients on paclitaxel and carboplatin, daunorubicin, cyclophosphamide and vincristine as noted in previous reports.

The severity of alopecia is directly related to the dosage, duration and regimen of therapy. Permanent hair loss is reported with certain drugs such as cyclophosphamide and busulfan.^[11] Minoxidil was found to be ineffective in preventing chemotherapy-induced hair loss.^[12] Hair loss is almost always reversible with good regrowth seen after cessation of treatment.^[12] It is therefore important to

reassure the patient regarding regrowth of hair after completion of treatment.

Hyperpigmentation has been reported to occur with anti-cancer drugs, which may be in the form of diffuse or localised involvement of skin, mucosa or nails. The mechanism remains unknown, but it is postulated to be due to accumulation of drug in skin or a direct toxic effect on melanocytes stimulating increased melanin production or elevated adrenocorticotrophic hormone and melanocyte stimulating hormone. The drugs commonly causing pigmentation are cyclophosphamide, hydroxyurea, doxorubicin, cisplatin, fluorouracil, etoposide, busulfan and bleomycin.^[1]

Along with cutaneous pigmentation, longitudinal and transverse bands or diffuse nail pigmentation and patchy pigmentation of tongue and buccal mucosa may also occur.

In our study we saw generalised hyperpigmentation of most of the body, both covered and exposed skin areas, results being consistent with some previous studies.^[13,14]

Xerosis was seen in 26% patients. Majority of them (53.9%) noticed skin lesions by 4 - 6th week of therapy. Abnormal keratinocyte differentiation, which leads to an impaired sebaceous gland function and loss of ability to retain water may be the cause of xerosis.^[15] A similar incidence of xerosis (22.2%) was reported by Pavey et al, but the onset of lesions was noticed earlier at 2 - 4 weeks.^[14]

Fabbrocini et al reported an incidence of 41.7% of xerosis in his study.^[16] The drugs found to cause xerosis in this study were cyclophosphamide, carboplatin, ifosfamide, mesna and vincristine. Liberal use of emollients and general hydrating measures should be explained to the patients to minimise this side effect.^[16]

Among nail changes, melanonychia was the most frequently seen adverse event and occurred in 15% cases followed by Beau's lines in 8% patients and Mees' lines in 4% cases. Paronychia and loss of nail were the complaints in 2% and 1% patients, respectively.

CONCLUSION

Oncological therapies have become more selective and have low systemic toxicity because of their high specificity, but cutaneous side effects are common and may worsen the quality of life of these patients. Our observations necessitate a joint effort between dermatology and oncology for the early recognition and adequate treatment of the cutaneous adverse effects associated with cancer chemotherapy, which may help in reducing morbidity and improving compliance.

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