Original Article

Mucocutaneous Findings in Hematolymphoid Neoplasms: An Observational Study

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Abstract

Background: Cutaneous manifestations of hematological neoplasms can be divided into three broad categories – direct infiltration, paraneoplastic conditions, and those due to the treatment of hematological cancers. **Objectives:** To study the frequency and patterns of mucocutaneous manifestations in patients with hematolymphoid neoplasms and those due to chemotherapy. **Materials and Methods:** This was an observational study done with 172 patients. Categorization of mucocutaneous manifestations was done into malignancy-associated and chemotherapeutic drugs-associated and data was analyzed. **Results:** Out of a total of 172 patients, 15.6% (27/172) had malignancy-related mucocutaneous manifestations. Among these, 4.6% (8/172) had direct infiltration of malignant cells into the skin and 11% (19/172) had paraneoplastic manifestations. The most common chemotherapy-related mucocutaneous manifestations were nail changes – 47.1% (81/172), of which transverse melanonychia was the most common (20.9%). About 44.2% (76/172) had a cutaneous infection, the commonest of which was a fungal infection (15.1%). Chemotherapy-induced alopecia was noted in 46.5% (80/172) and found to be significantly associated with cytarabine, daunorubicin, doxorubicin, methotrexate, and vincristine. Cutaneous hyperpigmentation was found to be significantly associated with cytarabine, doxorubicin, and vincristine. **Conclusion:** Mucocutaneous manifestations cause additional discomfort to a patient undergoing chemotherapy. Early recognition and timely and appropriate management facilitate symptom control and prevent treatment-related morbidity. A multidisciplinary approach involving hemato-oncologists and dermatologists can help achieve this target.

Keywords: *Chemotherapy, hematolymphoid, mucocutaneous, neoplasms*

Introduction

Cutaneous manifestations of hematological neoplasms can be divided into three broad categories:[1] (a) Direct infiltration of skin with malignant cells or their products (e.g., paraproteins) (b) Paraneoplastic conditions or dermatological syndromes associated with underlying malignancy (c) Treatment-related cutaneous manifestations, mainly adverse effects of chemotherapeutic agents and infections secondary to immunosuppression. Diagnosis of hematological malignancy is usually established before skin lesions appear (e.g., leukemia cutis) or skin lesions may be the presenting feature (e.g., sweet's syndrome and purpura). Given the varying presentations, mucocutaneous findings associated with hematolymphoid neoplasms can pose diagnostic challenges for hemato-oncologists and dermatologists. In this study, we attempt to describe the cutaneous findings in patients with various hematological malignancies and those due to chemotherapy regimens.

Materials and Methods

This cross-sectional study was conducted in the department of dermatology and hematology between September 2019 and February 2021. The study protocol (No. 290/IEC/PGM/2019) was approved by the Institutional Ethics Committee. A confirmed case of hematolymphoid neoplasm of any age and gender on chemotherapy regimens as per WHO guidelines[2] with mucocutaneous involvement was included after written consent. Patients with cutaneous findings secondary to thrombocytopenia or after blood product transfusion were excluded. Clinical and laboratory details were entered in a pre-designed proforma. Appropriate

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treatment for all dermatological conditions was offered as per standard protocol.

Statistical analysis was done using Statistical Product and Service Solutions [SPSS v23 (IBM Corp., Chicago, USA)] software. Descriptive statistics were represented as mean/standard deviation and median/interquartile range for continuous variables and frequencies and percentages for categorical variables. Proportions were compared using Chi-squared or Fisher's exact test, whichever was applicable. All statistical tests were two-sided and performed at a significance level of $P = 0.05$.

Results

A total of 172 patients were enrolled in the study. Mean age of the study population was 32.52 ± 21.26 years with a male:female ratio of 1.5:1. Diagnosis and treatment details of the study population are summarized in Table 1. Hematological malignancy-related mucocutaneous manifestations were noted in 15.6% (27/172) [Table 2], of which 4.6% (8/172) patients had direct infiltration of malignant cells into the skin and paraneoplastic manifestations were seen in 11% (19/172). There was no association between any mucocutaneous lesion and type of hematological malignancy. Chemotherapy-related mucocutaneous manifestations are summarized in Table 2. Among the cutaneous non-infectious manifestations, the commonest was cutaneous hyperpigmentation (31.4%, 54/172) followed by xerosis (18.6%, 32/172). Others noted were papulopustular eruptions (4.7%), melasma-like pigmentation and drug-induced urticaria (1.7% each), palmoplantar erythrodysesthesia, and maculopapular drug rash (1.2% each). Cutaneous infections/infestations were noted in 44.2% (76/172), the commonest being fungal infection (15.1%, 26/172) [Figure 1a]. Nail findings were noted in 47.1% (81/172), the commonest being transverse melanonychia (20.9%, 36/172) [Figure 1b]. Up to 24.4% (42/172) had findings in oral mucosa, the commonest being mucositis (11%, 19/172) [Figure 1c], and 46.5% (80/172) had chemotherapy-induced alopecia (CIA) [Figure 1d].

Association between individual chemotherapeutic drugs and mucocutaneous manifestations due to chemotherapy is shown in Table 3. Cutaneous hyperpigmentation was found to be significantly associated with cytarabine ($P = 0.039$), doxorubicin ($P = 0.004$), and vincristine ($P = 0.028$). Transverse melanonychia was significantly associated with 6-mercaptopurine ($P = 0.046$), cytarabine ($P = 0.002$), methotrexate ($P = 0.007$), and vincristine ($P = 0.03$).

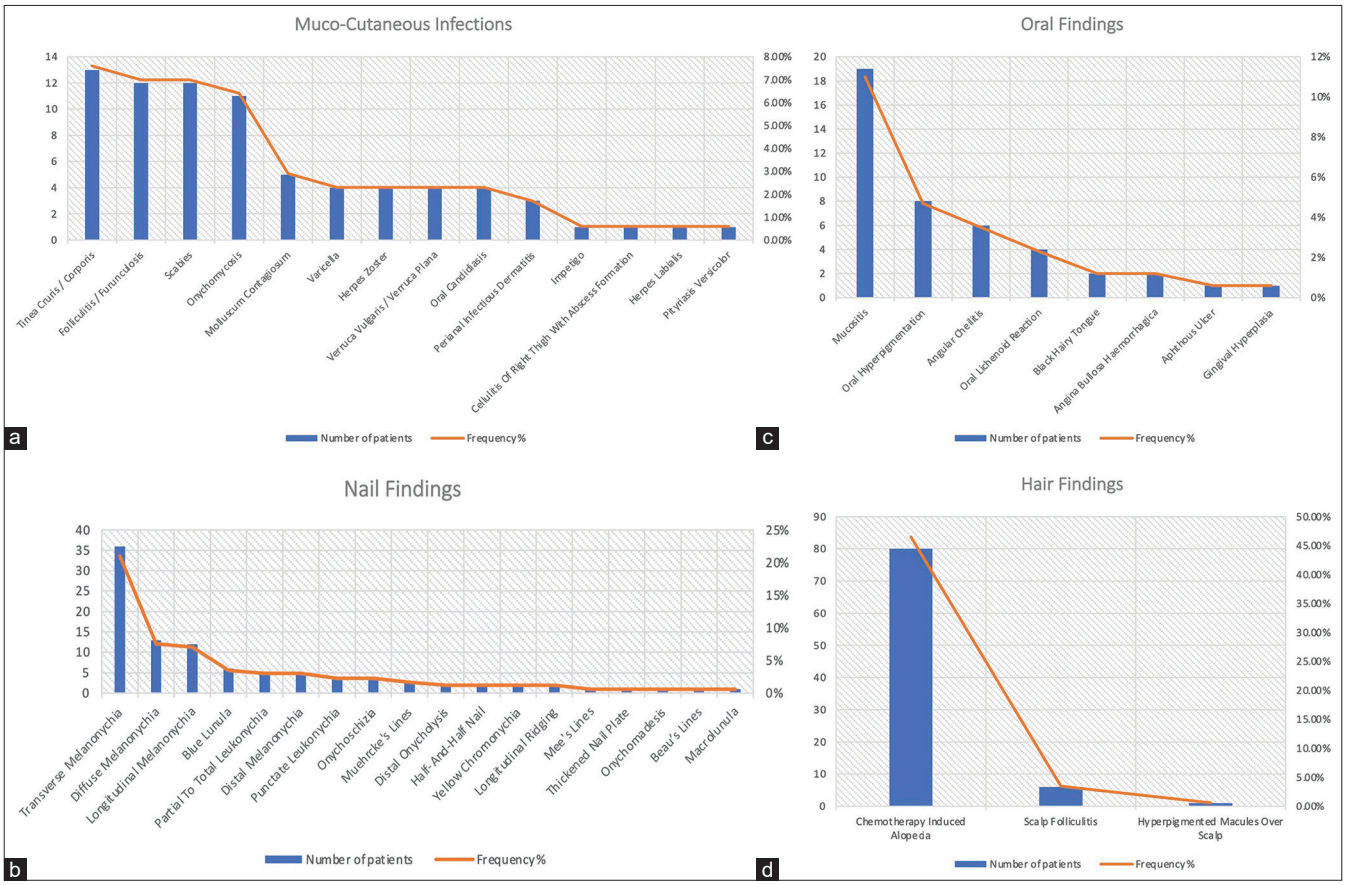

Figure 1: (a) Chart showing mucocutaneous infections in terms of number of patients and frequency found in the study. (b) Chart showing nail findings in terms of number of patients and frequency found in the study. (c) Chart showing oral findings in terms of number of patients and frequency found in the study. (d) Chart showing hair findings in terms of number of patients and frequency found in the study

Table 1: Distribution of the participants in terms of hematological malignancy and treatment (*n*=172)

Hematological malignancy - Frequency (%)	Subcategory -Frequency (%)	Treatment protocol - Frequency (%)
ALL - 69 (40.1%)	B Cell ALL - 50 (29.1%)	ALL IC-BFM 2009 (modified) protocol - 39 (22.6%)
		Hyper CVAD – 8 (4.6%)
		EWALL - 2 (1.2%)
		Dasatinib - 1 (0.6%)
	T Cell ALL - 19 (11%)	Hyper CVAD – 12 (7%)
		ALL IC-BFM 2009 (modified) protocol – 7 (4%)
NHL - 29 (16.9%)	DLBCL - 24 (14%)	R-CHOP - 15 (8.7%)
		R-DA-EPOCH - 4 (2.3%)
		B+R regimen – 2 (1.2%)
		CPR - 1 (0.6%)
		R-CODOX-M – 1 (0.6%)
		Lenalidomide – 1 (0.6%)
	BL - 2 (1.2%)	R-IVAC - 2 (1.2%)
	FL - 1 (0.6%)	B+R regimen – 1 (0.6%)
	Anaplastic large cell lymphoma - 1 (0.6%)	Mini-CHOP - 1 (0.6%)
	MZL - 1 (0.6%)	B+R regimen – 1 (0.6%)
Plasma cell dyscrasias - 24 (14%)	Multiple myeloma - 23 (13.4%)	CyBorD - 12 (7.0%)
		RVD - 8 (4.7%)
		BorD - 2 (1.2%)
		KRd - 1 (0.6%)
	Waldenstrom Macroglobulinemia - 1 (0.6%)	BDR - 1 (0.6%)
MPN & MDS/ MPN - 22 (12.8%)	CML - 17 (9.9%)	Imatinib - 10 (5.8%)
		Nilotinib - 4 (2.3%)
		Dasatinib – 2 (1.2%)
		EWALL – 1 (0.6%)
	MDS - 2 (1.2%)	Hypomethylating agent (Decitabine) – 2 (1.2%)
	CMML - 1 (0.6%)	Hydroxyurea - 1 (0.6%)
	MPN unclassified - 1 (0.6%)	Hydroxyurea - 1 (0.6%)
	Polycythemia Vera - 1 (0.6%)	Hydroxyurea - 1 (0.6%)
AML - 17 (9.9%)	AML M5-3 (1.7%)	AML BFM 2004 protocol (7+3 induction) – 2 (1.2%)
		Hypomethylating agent (Decitabine) – 1 (0.6%)
	APML - 2 (1.2%)	Arsenic trioxide+ATRA - 2 (1.2%)
	MPAL - 1 (0.6%)	Hyper CVAD – 1 (0.6%)
	AML unclassified – 11 (6.4%)	AML BFM 2004 protocol (7+3 induction) – 8 (4.7%)
		HiDAC consolidation – 3 (1.7%)
Hodgkin's lymphoma (HL) - 8 (4.7%)	HL unclassified – 8 (4.7%)	ABVD - 7 (4.1%)
		BEACOPP - 1 (0.6%)
Chronic lymphoproliferative disorders - 3 (1.7%)	CLL - 3 (1.7%)	B+R regimen – 3 (1.7%)

ALL - Acute lymphoblastic leukemia; NHL – Non-Hodgkin lymphoma; DLBCL – Diffuse large B cell lymphoma; BL - Burkitt's lymphoma; FL – Follicular lymphoma; MZL – Marginal zone lymphoma; MPN – Myeloproliferative neoplasm; MDS – Myelodysplastic syndrome; CML – Chronic myeloid leukemia; CMML - Chronic myelomonocytic leukemia; AML – Acute myeloid leukemia; APML – Acute promyelocytic leukemia; MPAL – Mixed phenotype acute leukemia; CLL – Chronic lymphocytic leukemia; ALL IC-BFM 2009 (modified) protocol - Vincristine, Dexamethasone, Methotrexate, Prednisolone, L-Asparaginase, Daunorubicin, Doxorubicin, Cyclophosphamide, Cytarabine, 6-Mercaptopurine; CVAD - cyclophosphamide, vincristine, doxorubicin (adriamycin), and dexamethasone; EWALL - European Working Group for Adult ALL (dexamethasone, vincristine, and idarubicin in phase 1 and cyclophosphamide and cytarabine in phase 2); R-CHOP - Rituximab, cyclophosphamide, doxorubicin (hydroxydaunorubicin), vincristine (oncovin), and prednisone; R-DA-EPOCH – Dose adjusted etoposide, prednisone, vincristine (oncovin), cyclophosphamide, doxorubicin (hydroxydaunorubicin), and rituximab; B+R regimen - Bendamustine+Rituximab; CPR - Cyclophosphamide, prednisone, and lenalidomide (Revlimid®); R-CODOX-M - Rituximab, cyclophosphamide, vincristine, doxorubicin, methotrexate; R-IVAC – Rituximab, ifosfamide, etopside, cytarabine; CyBorD - Cyclophosphamide, bortezomib and dexamethasone; RVD - Lenalidomide, Bortezomib, Dexamethasone; KRd – Carfilzomib, Revlimid®, Dexamethasone; BDR - Bortezomib, low-dose dexamethasone, rituximab; AML BFM 2004 protocol (7+3 induction) - Cytarabine for 7 days, anthracycline for 3 days; ATRA - All trans-retinoic acid; HiDAC - High-dose cytarabine; ABVD - Doxorubicin (adriamycin), bleomycin, vinblastine, dacarbazine; BEACOPP - Bleomycin, etoposide, doxorubicin (adriamycin), cyclophosphamide, vincristine (oncovin), procarbazine, prednisone

Table 2: Hematological malignancy and chemotherapy-related mucocutaneous manifestations

Hematological malignancy-related mucocutaneous manifestations – 27 (15.6%)				Chemotherapy-related mucocutaneous manifestations	
Direct infiltration – 8 (4.6%)		**Paraneoplastic conditions – 19 (11%)**			
Leukemia cutis	4 (2.3%)	Leukocytoclastic vasculitis	5 (2.9%)	Nail findings	81 (47.1%)
Lymphomatous infiltrates	2 (1.2%)	Acquired ichthyosis	5 (2.9%)	Hair findings	80 (46.5%)
Extramedullary blast crisis	1 (0.6%)	Exaggerated insect bite-like reactions	3 (1.7%)	Mucocutaneous infections	76 (44.2%)
Plasma cell infiltrates	1 (0.6%)	Acanthosis nigricans	2 (1.2%)	Cutaneous hyperpigmentation	54 (31.4%)
		Pruritus without skin lesions	2 (1.2%)	Oral findings	42 (24.4%)
		Acquired perforating dermatosis	1 (0.6%)	Xerosis/Dry skin	32 (18.6%)
		Sweet's syndrome	1 (0.6%)	Cutaneous hypopigmentation	10 (5.8%)
				Papulopustular eruptions/acneiform eruption	8 (4.7%)
				Melasma-like pigmentation	3 (1.7%)
				Drug-induced urticaria	3 (1.7%)
				Toxic erythema of chemotherapy/ palmoplantar erythrodysesthesia	2 (1.2%)
				Maculopapular drug rash	2 (1.2%)
				Bullous drug eruption	1 (0.6%)
				Neutrophilic eccrine hidradenitis	1 (0.6%)
				L-Asparaginase allergic reaction – flushing	1 (0.6%)
				Localized blistering secondary to G-CSF	1 (0.6%)
				Perifollicular eruption secondary to G-CSF	1 (0.6%)

Table 3: Association between individual chemotherapeutic drugs and mucocutaneous manifestations secondary to chemotherapy

Drug	Mucocutaneous manifestation	Significance value (*P*)*
6-Mercaptopurine	Transverse melanonychia	*P*=0.046
Cyclophosphamide	Distal melanonychia	*P*=0.008
	Longitudinal melanonychia	*P*=0.011
Cytarabine	Cutaneous hyperpigmentation	*P*=0.039
	Transverse melanonychia	*P*=0.002
	Chemotherapy-induced alopecia	*P*=<0.001
Daunorubicin	Chemotherapy-induced alopecia	*P*=0.030
Doxorubicin	Cutaneous hyperpigmentation	*P*=0.004
	Distal melanonychia	*P*=0.034
	Chemotherapy-induced alopecia	*P*=0.023
Methotrexate	Transverse melanonychia	*P*=0.007
	Mucositis	*P*=0.011
	Chemotherapy-induced alopecia	*P*=<0.001
Vincristine	Cutaneous hyperpigmentation	*P*=0.028
	Transverse melanonychia	*P*=0.030
	Chemotherapy-induced alopecia	*P*=<0.001

**P*<0.05 was considered significant

Distal melanonychia was significantly associated with cyclophosphamide ($P = 0.008$) and doxorubicin ($P = 0.034$). Longitudinal melanonychia was significantly associated with cyclophosphamide ($P = 0.01$). Mucositis was significantly associated with methotrexate ($P = 0.01$). Chemotherapy-induced alopecia was significantly associated with cytarabine ($P = <0.001$), daunorubicin ($P = 0.03$), doxorubicin ($P = 0.02$), methotrexate ($P =<0.001$), and vincristine ($P =<0.001$).

Discussion

The spectrum of mucocutaneous presentation in hemato-oncology patients is large and heterogeneous. The present study was done with the aim to observe mucocutaneous manifestations in patients with hematolymphoid neoplasms and those due to chemotherapy. The commonest hematological malignancy encountered was B cell acute lymphoblastic leukemia (ALL) [29.1%], which is in corroboration with the existing literature.[3,4]

Hematological malignancy-related mucocutaneous manifestations encountered, namely malignant cell infiltration (n = 8, 4.6%) and paraneoplastic features (n = 19, 11%), were in concordance with Merlo *et al*.[4] Leukemia cutis (LC) was seen in four (2.3%) patients as diffuse, coalescing, purpuric to hemorrhagic [Figure 2a] nodules/plaques. Differentials of LC include lymphoma, pseudolymphoma, erythema nodosum, erythema multiforme, pyoderma gangrenosum, urticaria, viral exanthems, drug rashes, vasculitis, graft-versus-host disease (GVHD), etc.[5] LC is seen in patients already diagnosed with leukemia (55% to 77%) or may appear at the presentation of systemic leukemia (23% to 44%), or even precede the development of leukemia (2% to 3%).[6] LC is accompanied by the infiltration of malignant cells into liver, spleen, and lymph nodes and marks rapid disease progression and early mortality. The mean interval between diagnosis of LC and death is 3.8 months to 1 year.[7] Cutaneous lymphomatous infiltrates were noted in one patient of diffuse large B-cell lymphoma (DLBCL) and one case of precursor B lymphoblastic lymphoma. Malignant skin involvement in Hodgkin's lymphoma is uncommon (0.5 – 7.5%)[8] and indicates stage IV disease and early mortality.[9] One patient of chronic myeloid leukemia (CML) had an extramedullary blast crisis, with skin being the commonest site of extramedullary involvement (22 – 36%).[8] In this study, a single patient of cutaneous plasmacytoma [Figure 2b] who presented with red to violaceous, non-tender dermal and subcutaneous nodules was diagnosed as IgA lambda multiple myeloma (MM) and succumbed to his disease in 4 months. Cutaneous presentation of MM is seen in 3% of new cases and in about 5% of relapsed cases that represent extensive tumor burden, risk of plasma cell leukemia, and a poor prognosis.[10,11]

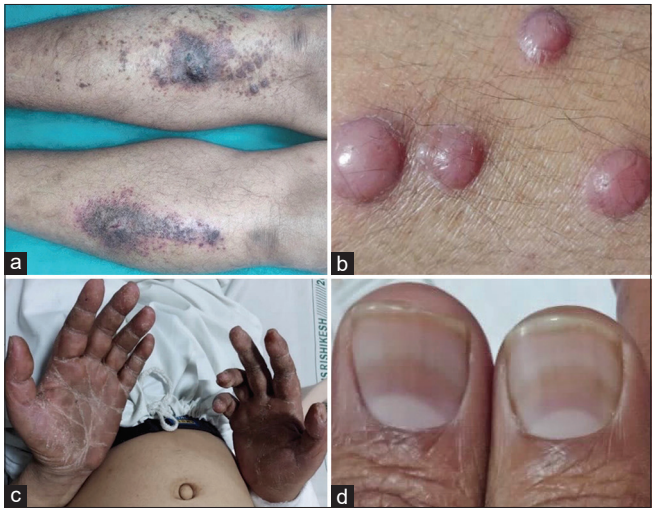

Figure 2: (a) Leukemia cutis presenting as hemorrhagic nodulo-plaques in a patient with chronic myelomonocytic leukemia. (b) Cutaneous plasmacytomas in an IgA lambda multiple myeloma patient. (c) Palmoplantar erythrodysesthesia in a multiple myeloma patient on CyBorD protocol (d) Transverse melanonychia in a patient on acute lymphocytic leukemia BFM protocol

The commonest paraneoplastic manifestation encountered was leukocytoclastic vasculitis (2.9% cases). Prevalence of vasculitis in malignancies ranges between 3% and 8% and can predate the diagnosis by 2 to 4 years.[12] We noted acquired ichthyosis in 5 (2.9%) cases, while Haque *et al*.[13] reported the same in 14.96% of patients. In our study, DLBCL was the predominant malignancy associated with acquired ichthyosis. Exaggerated insect bite-like reactions were encountered in 3 (1.7%) cases, the pathogenesis of which is hypothesized to be immune dysregulation associated with underlying malignancy, the commonest of which are chronic lymphocytic leukemia, mantle cell lymphoma, ALL, acute myeloid leukemia, Burkitt's lymphoma, and myelodysplastic syndrome.[1] Malignant acral acanthosis nigricans (AN), in the form of velvety plaques over knuckles, was seen in only 2 (1.2%) cases similar to Song *et al*.[14]; other causes of AN, such as diabetes, obesity, drugs, etc., were ruled out. Pruritus without any skin eruption was noted in only two (1.2%) patients of leukemia, while existing literature reports it frequently with Hodgkin's disease (>25% cases).[15] Malignancy associated with Sweet's syndrome (SS) was found in one patient with anaplastic large cell lymphoma (ALCL). Malignancy-related SS has reported a prevalence of 7%–35%, commonly with acute myeloid leukemia and less commonly with Hodgkin's disease, non-Hodgkin's lymphoma, myelodysplastic syndrome, myeloproliferative disease, and CML.[16] Progression of lesions to bullae/ulceration and mucosal involvement are strongly correlated with underlying malignancy in SS.[15] A single patient of acquired perforating dermatosis had Hodgkin's disease, also reported by Eigentler *et al*.[17]

In this study, maximum number (26.6%) of participants were on ALL IC-BFM 2009 (modified) induction chemotherapy protocol. The commonest chemotherapeutic agents used were vincristine (50.6%), methotrexate (41.3%), and cyclophosphamide (38.4%), while Garg *et al*.[3] reported methotrexate (72%) and vincristine (68%) as the commonest. The commonest steroids used were dexamethasone (52.9%) and prednisolone (30.8%), similar to the previous study.[3] The commonest chemotherapy-associated mucocutaneous manifestations noted were nail findings (n = 81, 47.1%), followed by hair findings (n = 80, 46.5%) and cutaneous infections (n = 76, 44.2%). Melanonychia constituted 38.3% of cases, of which 20.9% were transverse melanonychia [Figure 2d], a prevalence similar to existing literature.[18-20] 6-Mercaptopurine, cytarabine, methotrexate, and vincristine were found to be significantly associated with transverse melanonychia. On the other hand, cyclophosphamide was significantly associated with distal and longitudinal melanonychia. Stimulation of matricial melanocytes and drug accumulation in nail plates both can lead to discoloration.[21] Three patients had Muehrcke's lines [2 - Hyper CVAD, 1 - ALL IC-BFM

2009 (modified) induction protocol] and one patient on hyper CVAD had Mee's lines, similar to a study by Pavey *et al*.[19] While Torres *et al*.[22] reported Beau's lines in 20.5% of patients, we noted it in only 0.6%. CIA was noted in 46.5% of patients, similar to previous studies.[3,19,20,22] Statistically significant association of CIA was noted with cytarabine, daunorubicin, doxorubicin, methotrexate, and vincristine. Anagen effluvium was commoner than telogen effluvium, as confirmed by hair examination under light microscopy; anagen hair shows long indented roots with pigmented bulb.[23] It usually begins 1–2 weeks after starting the drug, with spontaneous recovery by 6 months.[24] CIA has a significant impact on patient's quality of life and has been reported to be the most difficult to cope with, more than the loss of a breast, by breast cancer patients.[24]

Range of cutaneous infections noted was similar to previous studies.[3,4,13,22] Higher prevalence of fungal infections in this study reflects the ongoing epidemic of superficial fungal infections in India. Diagnosis of bacterial folliculitis in 6.4% (11/172) was made based on clinical morphology, Gram's stain, and culture. Combined cutaneous herpes infection and mucosal candidiasis were seen in 5.2% (9/172), whereas Haque *et al*.[13] reported the same in 25.19% of patients. Low prevalence of herpes virus infection is reported in patients with acute leukemia on acyclovir prophylaxis compared to those who were not (2.7% vs. 16.7%).[5] Acyclovir prophylaxis is routinely given in our institute to patients with lymphoid malignancies and neutropenic leukemia.

Prevalence of cutaneous hyperpigmentation (31.4%) was similar to other studies.[13,19,20,22] The mechanism is postulated to be due to the accumulation of drugs in the skin or a direct toxic effect on melanocytes stimulating increased melanin production or elevated adrenocorticotropic hormone and melanocyte-stimulating hormone.[19] Out of 54 patients with cutaneous hyperpigmentation, 14 and 11 were on ALL IC-BFM 2009 (modified) protocol and hyper CVAD protocol, respectively. Vincristine, doxorubicin, and cytarabine were found to be significantly associated with cutaneous hyperpigmentation. We also noted three cases with melasma-like pigmentation, of which two were on imatinib, similar to a report by Ghunawat *et al*.[25] Three patients each on ABVD, R-CHOP, and B+R regimens, respectively, developed hyperpigmentation of the tongue, as also reported by Blaya *et al*.[26] and Pavey *et al*.[19]

About 18.6% of patients had xerosis similar to previous studies.[19,20,22] Xerosis may be related to the presence of antiproliferative and cytostatic drugs in the epidermis, particularly in the basal layer, basal lamina, and microfibrils of the papillary dermis. Malignancy or chemotherapy-associated malnutrition, anemia, and hypoproteinemia may contribute.[22] Two (1.2%) patients each on CyBorD and ALL IC-BFM 2009 (modified) induction protocols, respectively, developed palmoplantar erythrodysesthesia, while Saini *et al*.[18] reported the same in 20%.[18] Palmoplantar erythrodysesthesia [Figure 2c] presents as painful, swollen, erythematous palmoplantar patches that evolve into bullae and later desquamate and resolve. Recurrence with increasing severity in subsequent cycles of chemotherapy is common. Pathogenesis is the direct toxicity of chemotherapeutic agents excreted through an eccrine duct, the acrosyringium, and into the epidermis.[27] Eight (4.7%) of our patients had papulopustular eruptions, much less than the existing literature.[19] It presents as erythematous, pruritic, painful papules and sterile pustules. Gram-negative folliculitis, pityrosporum folliculitis, steroid acne, and acute generalized exanthematous pustulosis are to be excluded. Bacterial culture from a pustule helps in diagnosis. Neutrophilic eccrine hidradenitis (NEH) was noted in one patient on ALL IC-BFM 2009 (modified) protocol. Commonest causative agents are cytarabine, decitabine, vincristine, imatinib, and G-CSF.[1] NEH presents as edematous, erythematous plaques or nodules on the trunk, face, and ears; histologically, vacuolar degeneration and necrosis of the eccrine glands with surrounding neutrophils on biopsy helps to rule out other differentials like cellulitis, GVHD, erythema multiforme, leukemia cutis, etc.[28]

Lenalidomide-induced maculopapular drug exanthem was noted in two patients; viral exanthem was ruled out in all cases by temporal association with the drug, presence of severe itching, and absence of prodrome. Sviggum *et al*.[29] reported morbilliform and urticarial rashes with lenalidomide. Oral drug provocation revealed nilotinib as the culprit drug in two patients developing urticaria, as also reported earlier.[4] We did not encounter other severe drug rashes like erythroderma, Stevens-Johnson syndrome, or toxic epidermal necrolysis.

Mucositis was the commonest (11.0%) oral finding and was significantly associated with methotrexate. Chemotherapy-induced oral mucositis ranges from 14.16% to 38.4%.[20,22] Oral ulcers typically develop within 3 to 4 days of starting therapy and heal without scarring 2 to 3 weeks after discontinuation.[21] Severe grade mucositis may warrant discontinuation of chemotherapy as was seen in one case of methotrexate-induced grade 4 mucositis. Palifermin, a recombinant human keratinocyte growth factor 1 (KGF-1), is the only drug approved by the FDA for oral mucositis.[30] Four (2.3%) patients had oral lichenoid drug reaction (OLDR) – two were on decitabine, one each on Hyper-CVAD and dasatinib. Imatinib is associated with OLDR in the literature.[31]

Limitations

Limitations of this study include the inability to make histopathological confirmation of all skin lesions. Also, as most patients were on multiple drugs, no single drug could be solely associated with various chemotherapy-related mucocutaneous manifestations.

Conclusion

Our study is different from the existing literature[5,32] as an attempt was made to better categorize mucocutaneous lesions into malignancy-associated and chemotherapy-associated lesions. Mucocutaneous manifestations during chemotherapy are common but not well known among oncologists. Early recognition and appropriate management facilitate symptom control and continuation of chemotherapy with less morbidity. A multidisciplinary approach based on close collaboration between the hemato-oncologist and the dermatologist is crucial to achieving this target.

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Conflicts of interest

There are no conflicts of interest.

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