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OPEN ACCESS JOURNALS

Archives of Clinical & Experimental Dermatology

Research | Vol 5 Iss 2
ISSN: 2583-6374
https://dx.doi.org/10.46527/2583-6374.146

Dermatological Manifestations in Patients with Malignancy Attending a Tertiary Care Hospital in North-East India

Anita Marak[1], Mary Zothanpuii Chhangte[2*], Shakeel Abdul Jabbar[1], Zahbi H Fatima[1], Shikha Verma[1], Caleb Harris[3] and Vikas Kantilal Jagtap[4]

[1]Department of Dermatology & STD, North Eastern Indira Gandhi Regional Institute of Health & Medical Sciences, India
[2]Department of Dermatology, Venereology & Leprosy, All India Institute of Medical Sciences, Guwahati, Assam, India
[3]Department of Surgical Oncology, North Eastern Indira Gandhi Regional Institute of Health & Medical Sciences, India
[4]Department of Radiotherpay & Oncology, North Eastern Indira Gandhi Regional Institute of Health & Medical Sciences, India

[*]**Corresponding author:** Mary Zothanpuii Chhangte, Assistant Professor, Department of Dermatology, Venereology & Leprosy, All India Institute of Medical Sciences, Guwahati, Assam, India, Tel: 91 9862579601; E-mail: mchhangte@ymail.com

Received: August 30, 2023; **Accepted:** September 13, 2023; **Published:** September 20, 2023

Abstract

Background: Dermatological manifestations in patients with malignancy can provide essential diagnostic and prognostic information. However, limited research has been conducted in North-East India to comprehensively study these cutaneous changes in patients with proven malignancies. This study aims to investigate the frequency and types of dermatological manifestations in patients with proven malignancies attending various departments of a Tertiary Care Hospital over the course of one year.

Methods: A prospective study was conducted on consecutive patients of all ages and both sexes with proven malignancies with dermatological manifestations attending a Tertiary Care Hospital for one year. Detailed histories and thorough examinations of mucocutaneous, hair, and nail conditions were conducted using a prestructured proforma after obtaining informed consent. Relevant investigations, including KOH for fungal elements, Gram's stain for bacterial infections, and dermoscopy, were performed when needed. Clinical photographs were taken for documentation and record-keeping purposes.

Results: Among 872 proven malignancy cases, 27 patients (3.09%) exhibited dermatological involvement, with a male-to-female ratio of 4.4:1. The most affected age group was 61-80 years, comprising 37% of patients, followed by the 41-60 years group (33.3%). Skin cancer was the most common malignancy observed in this study, affecting 33.3% of patients, followed by gastrointestinal malignancy in 22.2%. The most frequent dermatological site of presentation was the skin (81.48%), followed by hair (18.5%) and nails (14.8%). Plaques were the most common morphological presentation (29.6%), and the scalp was the

Citation: Marak A, Chhangte MZ, Jabbar SA, et al. Dermatological Manifestations in Patients with Malignancy Attending a Tertiary Care Hospital in North-East India. Arc Clin Exp Dermatol. 2023;5(2):146.

most involved site (29.6%). Specific dermatological manifestations were seen in 33% of cases, non-specific manifestations in 55.5%, and treatment-related manifestations in 40.7%.

Conclusion: This study sheds light on the prevalence and diverse types of dermatological manifestations associated with malignancy in North-East India. The data obtained from this study will contribute to enhancing the understanding of cutaneous changes in cancer patients in this region, thereby aiding early diagnosis, appropriate management, and potentially improved patient outcomes.

Keywords: ***Dermatological manifestations; Malignancy; North-East India; Mucocutaneous; Hair; Nails; Skin cancer***

1. Background

Skin, the largest organ of our body, reflects the changes in the internal organs. Skin manifestations in internal malignancies are diverse and may be specific or non-specific.

Curth proposed criteria for the causal relationship between skin manifestations and internal malignancy.

a. Both conditions should begin simultaneously.
b. Development of a parallel course.
c. The dermatoses are not a part of any genetic syndrome.
d. The dermatoses are uncommon in general population.
e. There is a high frequency of association between both conditions.

- The underlying malignancy may produce cutaneous manifestations either by direct invasion of skin or spread through lymphatics or blood, producing metastasis in skin.
- Carcinogen exposure and certain inherited disorders with internal malignancies may be associated with skin lesions.
- Radiotherapy and chemotherapy instituted for treating malignancies may lead to cutaneous manifestations.
- Identification of cutaneous lesions in patients with internal malignancies may be helpful in assessing the extent of disease, disease progress, and its response to treatment [1].

The manifestations of skin lesions in patients with malignancy may be of greatest importance in the detection and management of cancer because of easy accessibility of the skin to examination in cancer patients and as such can provide important insights into underlying cancer processes or possible complications from cancer chemotherapy or opportunistic infection.

No studies have been done on cutaneous manifestations of cancer patients in this part of the country and considering the high prevalence of cancer in North-east India, a study was conducted.

2. Methodology

A prospective study was conducted on consecutive patients of all ages and both sexes with proven malignancies attending different departments of a Tertiary Care Hospital for one year from 1st January 2022 – 31st December 2022. Skin all ages and

both sexes who were diagnosed as having Malignancies and having Skin, hair or nail manifestations were included in the study. Patients who were not willing to give Informed Consent were excluded from the study. Detailed histories and thorough examinations of mucocutaneous, hair, and nail conditions were conducted using a prestructured proforma after obtaining informed consent. Relevant investigations, including KOH for fungal elements, Gram's stain for bacterial infections, and dermoscopy, were performed when needed. Clinical photographs were taken for documentation and record-keeping purposes.

3. Results

At the end of one year, we observed that 27/872 (3.09%) proven malignancy cases had either skin, hair or nail involvement. Males (22) outnumbered females with a male: female ratio of 4.4:1. The age group of 61-80 years, with 10 patients (37%) followed by 41-60 years (33.3%) were the two most common age groups affected in our study. The mean age of presentation was 53.9 years. There were no patients who were less than 20 years (TABLE 1).

TABLE 1. **Age group distribution.**

Age group	Frequency (n)	Percentage (%)
<20	0	0
21-40	7	25.9
41-60	9	33.3
61-80	10	37
>80	1	3.7

Patients with rural background were seen in 55.6% (15 patients) while the rest 44.4% (12) were from the urban areas. Patients hailed from different regions of North East India with majority of the patients came from Meghalaya (62.9%) (TABLE 2).

TABLE 2. **Statewise distribution of patients.**

Name of State	Name of tribe	Number of patients	Percentage
Meghalaya	Khasi - 11 Jaintia - 2 Garo - 1 Mizo – 2 Others -1	17	62.9
Mizoram	Mizo -1	1	3.7
Assam	Assamese - 5	4	18.5
Nagaland	Ao - 1 Sema - 1	2	7.4
Arunachal Pradesh	Nyishi - 1	1	3.7
Manipur	Meitei - 1	1	3.7

3.1 Clinical characteristics

The most common malignancy seen in our study was Skin cancer, which was found in 9 (33.3%) patients. This was followed by Gastrointestinal malignancy in 6 patients (22.2 %). Leukaemias, Thymic neoplasms, Urogenital and Lung cancers comprised 2 (7.4%) each of the malignancy. Lymphomas, Germ cell mediastinal tumour, Adrenal tumours and Ewing's sarcoma and Ca

breast comprised 1 each (3.7%) of all the malignancy presented to us. TABLE 3 shows the frequency of different malignancies noted in our patients who had dermatological manifestations.

TABLE 3. **Distribution of patients by type of malignancies.**

Type of Malignancy	Frequency (N)	Percentage (%)
Skin cancers	9	33.3
Gastrointestinal cancers	6	22.2
Leukemias	2	7.4
Ca Lung	2	7.4
Thymic neoplasms	2	7.4
Urogenital cancers	2	7.4
Lymphomas	1	3.7
Adrenal tumours	1	3.7
Germ cell mediastinal tumours	1	3.7
Ewings sarcoma	1	3.7
Breast Ca	1	3.7

3.2 Dermatological manifestations of the study population

Distribution of various dermatological manifestations were seen as follows; Skin was the most common site of presentation in 22 (81.48%) patients, followed by hair in 5(18.5%) patients while nails were involved in only 4 (14.8%) and oral mucosa in 1 (2.7%) of the study population.

Morphologically the most common presentation was plaques (29.6%) followed by nodules and papules in 18.5% each, nodular ulcers, and pustules (14.8%) each, abscess, ulcers, wheals, petechiae and hyperpigmented macules in 3.7% each.

Most common site involved was the Scalp seen in 29.6%, followed by face in 25.9%, extremities in 22.2% and trunk in 11.1% whole body involvement was seen in 7.4% and Lip involvement in 2 (7.4%) individuals.

A total of 9 (33.3) patients presented within 1- 6 months of developing the skin lesions while 8 (29.6%) individuals presented after one year of onset of cutaneous lesions. 7 individuals (25.9%) exhibited cutaneous manifestations for a duration of less than a month while in 3(11.1%) individuals the lesions persisted for 6 to 12 months With respect to cutaneous manifestations, three categories were included- Specific, Non specific manifestation and Treatment related manifestations as shown in TABLE 4. A total of 35 manifestations were presented to us in the form of skin, hair, or nails. Few patients (8) had more than one manifestation.

TABLE 4. **Type of Cutaneous manifestation.**

Type of cutaneous manifestation	**Frequency (n)**	**Percentage (%)**
• **Specific**	**9**	**33.3**
1. Basal cell carcinoma	3	11.11
2. Squamous cell carcinoma	2	7.4
3. Malignant melanoma	2	7.4
4. Sebaceous carcinoma	1	3.7
5. Epithelioid Sarcoma	1	3.7
• **Non specific**	**15**	**55.5**
1. Acanthosis Nigricans	1	3.7
2. Lichen planus with oral involvement	1	3.7
3. Bacterial infections	3	11.11

4. Eczema	3	11.11
5. Psoriasis	1	3.7
6. Purpura	1	3.7
7. Xerosis	1	3.7
8. Molluscum contagiosum	1	3.7
9. Neurofibromatosis	1	3.7
10. Nevus sebaceous	1	3.7
11. Longitudinal melanonychia	1	
• **Treatment related**	**11**	**40.7**
1. Melanonychia	2	11.11
2. Anagen effluvium	5	18.5
3. Pruritus	1	3.7
4. Skin hyperpigmentation	2	7.4
5. cellulitis lip	1	3.7

Specific manifestations included dermatological manifestations which were specific to the malignancy and this category was represented by Skin cancers, which was seen in 9 patients (33%) (FIG. 1-5). Non-specific manifestations included those presentations that were not specifically related to the underlying malignancy (FIG. 6-11 seen in 15 patients (55.5%) (TABLE

4). Dermatological manifestations which were treatment related were seen in 11 patients (40.7%) (FIG. 12-14). Various chemotherapeutic agents related with different cutaneous manifestations are shown in TABLE 5.

FIG. 1. **Epithelioid Sarcoma.**

FIG. 2. **Sebaceous Carcinoma.**

FIG. 3. **Fibroma of lip.**

FIG. 4. **Malignant Melanoma.**

FIG. 5. **Noduloulcerative BCC.**

FIG. 6. **Nevus Sebaceous in a patient with Bladder Carcinoma.**

FIG. 7. **Longitudinal Melanonychia in a treatment-naïve patient of Bladder carcinoma.**

FIG. 8. **Furunculosis in a patient with Gastric Carcinoma.**

FIG. 9. **Neurofibromas in a patient with Adrenal Cancer.**

FIG. 10. **Oral Lichen planus in a patient with Thymoma.**

FIG. 11. **Purpura in a patient with Leukaemia.**

FIG. 12. **Flagellate Hyperpigmentation in a patient who received Cisplatin, Bleomycin & Etoposide**

FIG. 13. **Proximal Melanonychia in a patient who received Bleomycin, Cisplatin, Etoposide and G-CSF.**

FIG. 14. **Anagen Effluvium in a patient who had received Carboplatin and Paclitaxel.**

TABLE 5. **Chemotherapeutic agents associated with Cutaneous manifestations.**

Presentation	Frequency	Percentage	Treatment taken
Anagen effluvium	5	18.5	Carboplatin GCSF Peg GCSF Paclitaxel Pemetrexed Bleomycin Etoposide
Melanonychia	2	7.4	Bleomycin Cisplatin Etoposide

			G-CSF
Skin hyperpigmentation	2	7.4	Carboplatin Cisplatin GCSF Pemetrexed Bleomycin Etoposide
Cellulitis lip	1	3.7	Carboplatin trastuzumab

4. Discussions

Our study highlights the distribution of cutaneous involvement in patients with malignancy in North east India and compares with other parts of India. The percentage of cutaneous manifestations in malignancy ranged from 11.5% to 27.3% as reported by various studies [2,3]. However, our study reported a lower percentage of cutaneous manifestations.

Our study found a higher preponderance of malignancies with cutaneous manifestations in males 85%. Ayyamperumal A, R. Rajagopal, and Hasan et al also reported similar sex distribution of various malignancies [4,2,3]. Few other studies demonstrated a higher prevalence in female patients [5,6].

When considering the age group of the patients with cutaneous involvement, our study noted that 61-80 years was most commonly affected as compared to other age groups. Tandel J et al reported 41-60 years as the most commonly affected age group [5]. Hasan I et al, and Ayyamperumal A, also reported its occurrence more in the 5^{th} followed by 6^{th} decade [3,4].

4.1 Clinical characteristics of various malignancies

Depending on the origin of malignancies, the most common malignancy seen in our study was Skin cancer which was found in 9(33.3%) patients while Gastrointestinal origin was the most common internal malignancy seen in 22.2% of the subjects out of which Oesophageal carcinoma was seen in 3(11.1%) patients, Gall bladder, Cholangiocarcinoma and Pancreatic cancer were seen in 1 (3.7%) each. Similarly, Wani et al reported oesophageal cancer as the most common site followed by Lung, Stomach and Colorectal cancer [7]. Hassan et al also found GI alignancies (colorectal) to be the most common. However, Ayyamperumal A, reported Leukemia and Lymphomas as the most common malignancies (19.2%), followed by Carcinoma breast (13.46%), Carcinoma stomach (11.5%), Carcinoma cervix (5.76%), Carcinoma of the prostate (5.76%) and Carcinoma of the buccal mucosa (5.76%). GI cancer was the most common malignancy seen in males (5/22) while all five females had different type of carcinoma in our study. Similarly, the leading sites of cancer in males reported by Wani et al were oesophagus and gastroesophageal (GE) junction (19.95%), lung (16.54%), stomach (11.60%) and colorectal (7.36%). While Rajagopal et al. reported lymphomas as the most common malignancy in males in 8.6%, and breast carcinoma in females. Thus, there are variations according to the region regarding the most common malignancy in different populations. The higher prevalence of GI malignancy from this part of India can be related to the different genetic makeup or the dietary habits in our population as

beetle nut and leaf consumption is popular and almost universal in Meghalaya. Five most common causes of cancer in Meghalaya according to gender reported are Oesophageal cancer in both genders, followed by Hypoparynx, Stomach, Lung and Tongue in males while in females Cervix and Uteri, Mouth, Breast and Stomach [8].

4.2 Dermatological manifestations of the study population

Skin involvement either by direct or distant spread is a rare phenomenon. Contrary to some studies that found direct extension to the skin, our study did not find any contagious cutaneous metastasis as reported by other studies. One patient of Ewing's sarcoma had a lesion on the scalp which turned out to be a Sebaceous Carcinoma on histopathology. The reported involvement of skin as a direct spread of internal malignancy was as low as 0.8% by Lookingbill DP et al, 5.04% by Simon et al. [9,10] and 6% by Rajagopal R et al [2]. Whether this occurrence is actually rare as seen in our study as majority of the patients presented within a year of onset of the symptoms or could this be because the sample size was less is debatable.

Our study noted 9/27 patients had primary skin cancer without any internal malignancy, so we categorised them as specific skin changes. Basal cell carcinoma was seen in 3 patients all of them involving the face, Squamous cell carcinoma in 2 patients (one on lip and one on genitals) and Malignant melanoma in 2 patients both affecting the soles, and Epitheloid sarcoma and Sebaceous carcinoma, one in each patient. All these patients were presented to the oncosurgical department.

When comparing the non specific dermatosis, we noted that 14/26 patients had the following; Infections were the most common manifestations in 18.5%, followed by Eczema in 11.1%. Lichen planus with oral involvement, Psoriasis, Purpura, Xerosis were seen in one patient each. Additionally, there was a patient of carcinoma of the bladder who had Nevus Sebaceous and another patient of adrenal carcinoma who had Neurofibromatosis. One treatment naive patient had longitudinal melanonychia with squamous cell carcinoma of lung.

Other studies reported the occurrence of non specific category of skin involvement in 4.62% by Ayyamperumal A, 15.6% by Hasan I et al and 80.66% by Tandel J et al. Ayyamperumal A et al noted Herpes zoster as the most common manifestation where as our study noted bacterial infections as the most common seen in 4 patients out of which one had lip cellulitis and remaining had folliculitis. The other infection noted was molluscum contagiosum in 1 patient. No patients of herpes zoster was seen in our study.

All the patients with infections did not receive any treatment at time of diagnosis. Tandel et al reported dermatitis as the most common nonspecific dermatosis, followed by infections in which herpes zoster was the most common infection seen. Our study noted dermatitis as the second most common manifestation in non specific category where 2 patients had discoid eczema and 1 had seborrheic dermatitis.

The malignancies associated with bacterial infections in our study were GI malignancies and Lymphoma. The most common non-specific cutaneous manifestation noted by Simon Net al were generalized pruritis, observed in 17.88% of the patients, followed by acquired ichthyosis in 12.38% of the patients, and herpes zoster in 11.46% of the patients.

4.3 Treatment related dermatosis

A total 11 (40.7%) out of 16 patients received some form of chemotherapy with or without radiotherapy. Manifestations in treatment related cutaneous group were as follows; Anagen effluvium observed in 5/11 (45.45%) patients while Skin hyperpigmentation and Melanonychia was seen in 2 /11 (18.8%) each and 1 patient had cellulitis of lip. Thus, hair involvement was seen only in patients who received treatment while nail involvement was seen in one treatment naive patient too.

Two out of five patients with anagen effluvium received carboplatin therapy. While the remaining 3 individuals did not have any common chemotherapeutic agents causing the hair fall. Both the patients of longitudinal melanonychia received bleomycin. The most common chemotherapeutic agents that were received by patients with nail involvement in a study by Hassan et al were cisplatin, cyclophosphamide, epirubicin, 5-fluorouracil, doxorubicin and docetaxel.[3]

Patients with skin pigmentation received different drugs for their management. Details of the drugs have been given in table 6. Three most common drugs implicated in the treatment associated dermatosis included carboplatin cispaltin and paclitaxel given in 2/11 each (18.18%). The most common chemotherapeutic agents attributed to drug reaction were capecitabine, sorafenib, cisplatin, and 5-fluorouracil according to Simon et al [10].

While overall paclitaxel and carboplatin were the most common drugs received as treatment in our study, Hassen et al reported 5-Fluoro uracil, Cisplatin, Oxaliplatin and Carboplatin as the most common drugs received [3].

Anagen effluvium was the most common hair condition seen in 19.33% patients in the study conducted by Tandel et al while Hassan *et al*. noted telogen effluvium as the most common cause of hair involvement (12.8%). Reported nail changes were observed in as low as 12.8% by Hassan et al to as high as 85.84% by Naveed et al [11].

In contrast to our study that noted only nail pigmentation as a sole manifestation of treatment associated nail changes, other studies have reported different changes such as pigmentary disturbances, nail dystrophy, leukonychia and onycholysis [12,13].

5. Conclusion

The pattern of Cutaneous manifestations in patients with malignancy may differ according to the region as the type of Cancers may vary. Even though many similar studies have been done, this is the first study done in North-east India where the profile of patients is different. The data obtained from this study will contribute to enhancing the understanding of cutaneous changes in cancer patients in this region, thereby aiding early diagnosis, appropriate management, and potentially improved patient outcomes.

6. Limitations

1. Small sample size.
2. There was no Radiotherapy facility at our hospital hence we could not study the mucocutaneous effects of radiation.

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