Volume : 5 | Issue : 4 | April 2016 • ISSN No 2277 - 8179 | IF : 3.508 | IC Value : 69.48

Research Paper

Skin Manifestations Of Internal Malignancy - A Descriptive Study

Medical Science

KEYWORDS : Skin manifestations, malignancy, paraneoplastic dermatoses.

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ABSTRACT

Background: Most of the previous studies regarding skin manifestations of internal malignancies were about direct spread and cutaneous metastasis. Only few studies are available about paraneoplastic dermatoses.

Aims: To find out the different types of skin manifestations in internal malignancy and to determine the frequency and type of malignancies presenting with skin manifestations. Methods: A descriptive study was conducted in the departments of radiotherapy, haemato-oncology and dermatology of a tertiary care centre. Three hundred and fifty patients with internal malignancy were examined to find out the skin manifestations.

Results: Skin manifestations were seen in 119 (34 %) patients out of which 99 (28.3%) patients had paraneoplastic dermatoses, 16 (4.5%) patients had specific lesions (direct spread and cutaneous metastases) and four (1.1%) patients had both specific and paraneoplastic lesions. Common malignancies showing skin manifestations were haematological malignancies in 32 (26.9%) patients, carcinoma lung in 29 (24.4%), carcinoma breast in 12 (10%) and carcinoma oral cavity in nine (7.5%) patients. Skin manifestation was the first sign of malignancy in 27 (7.7%) patients out of which specific lesions were seen in five (1.4%) patients and paraneoplastic dermatoses in 22 (6.3%) patients. Malignancies presented with skin lesions were haematological malignancies in 12 (3.4%) patients, carcinoma lung in seven (2%), carcinoma pancreas and breast in three (0.9%) patients each and carcinoma cervix and ovary in two patients.

Conclusions: Skin manifestations can be the warning sign of malignancy. Early detection of skin signs helps in the diagnosis and treatment of malignancy.

Introduction

Skin reflects health and disease and changes in the internal organs. Various skin manifestations can occur in internal malignancy. They can occur before, during or after the diagnosis of malignancy. Sometimes skin manifestation can be the only clue to the diagnosis of malignancy or its recurrence. [1]

Though there are many studies about cutaneous metastasis, most of them were conducted retrospectively. Some studies derived their conclusions from autopsy findings. These studies also varied in inclusion criteria adopted, making it difficult to compare the findings in various population groups. [2,3,4,5] Only few studies are available about paraneoplastic dermatoses. Data about malignancies presenting with skin lesions are also rare.

In this scenario, we carried out a cross sectional study among newly diagnosed patients with internal malignancy aimed at finding out the different types of skin lesions.

Materials & Methods

A two year descriptive study was conducted in recently diagnosed patients with internal malignancy attending the departments of radiotherapy and haemato-oncology of our tertiary care institution after getting approval from Institutional Ethics Committee. Patients presented with skin lesions in the dermatology department and found to have internal malignancy on evaluation were also included in the study.

Exclusion criteria: Patients with long duration of malignancy, patients receiving treatment for malignancy and primary skin cancers were excluded from the study.

A preset proforma was used to collect data regarding patient characteristics, underlying malignancy, skin manifestations and the temporal relationship between the latter two. Each patient was evaluated for mucocutaneous manifestations. The skin lesions were assessed clinically and using skin biopsy. Tissue scrapings and Tzanck smear were done in selected patients. Skin lesions were classified into direct tumor spread, cutaneous metastases, and paraneoplastic dermatoses.

Data was analysed to find out the relation between the type of malignancy and the type and site of skin lesions and the time interval between the onset of malignancy and the appearance of skin lesions. The frequency and type of malignancies presenting with skin manifestations were also noted.

Results

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During the study period, 350 patients with malignancy including 174 males (49.7%) and 176 females (50.3%) were examined for skin manifestations. The common malignancies observed were carcinoma lung and haematological malignancies in 61 (17.4%) patients each, carcinoma breast in 43 (12.3%) and carcinoma cervix in 29 (8.3%) patients. The other common malignancies were carcinoma oral cavity in 23(6.6%) patients, carcinoma oesophagus in 21 (6%), carcinoma colorectum in 15 (4.3%), carcinoma hypopharynx in 13 (3.7%), carcinoma stomach in 12 (3.4%) and carcinoma ovary in 10 (2.9%) patients. The haematological malignancies observed were acute myeloid leukemia (AML) in 15 (24.6%) patients, non Hodgkin's lymphoma (NHL) in 14 (23%) patients, multiple myeloma (MM) and acute lymphocytic leukemia (ALL) in 10 (16.4%) patients each, chronic lymphocytic leukemia (CLL) in four patients, chronic myeloid leukemia (CML) in three patients, Hodgkin's lymphoma (HL) and myelofibrosis in two patients each and polycythemia rubra vera (PRV) in one patient.

The common malignancies seen in males were carcinoma lung in 54 (15.4%) patients, haematological malignancies in 31(8.9%) patients and colorectal cancer in 14 (4%) patients. Carcinoma breast was the commonest malignancy in females {43 (12.3%) patients} followed by haematological malignancies {30 (8.6%) patients} and carcinoma cervix {29 (8.3%) patients}.

Skin manifestations were seen in 119 (34%) patients, out of which 66 (55.5%) were males and 53 (44.5%) were females. Male to female ratio was 1:0.82. Age of the study population ranged from two to eighty two years with majority belonging to the age group of 51-70 years. Age distribution of patients with malignancy and skin manifestations are shown in Table 1. Common malignancies showing skin manifestations were haematological malignancies in 32 (26.9%) patients, carcinoma lung in 29 (24.4%), carcinoma breast in 12 (10%), carcinoma oral cavity in nine (7.5%), carcinoma thyroid in six (5%) and carcinoma cervix in four (3.4%) patients. Out of the 61 patients with haematological malignancies, skin manifestations were seen in AML (14 patients), NHL (6 patients), CLL (4 patients), ALL (2 patients), CML (2 patients), MM, HL, myelofibrosis and PRV (1 patient each).

Out of 119 patients with skin manifestations, 99 had paraneoplastic lesions, 16 had specific lesions (direct spread and cutaneous metastasis), and four patients had both specific and paraneoplastic lesions. Thus out of 119 patients, 20 (5.7%) had direct spread/metastasis and 103 (29.4%) had paraneoplastic dermatoses. Skin manifestations were the first sign of malignancy in 27 (7.7%) patients out of which 12 (3.4%) had haematological malignancy, seven (2%) had carcinoma lung, three (0.9%) had carcinoma pancreas, another three had carcinoma breast and the other two had carcinoma cervix and ovary. Specific lesions were the presenting sign of malignancy in 5 (1.4%) and paraneoplastic dermatoses were the first sign of malignancy in 22 (6.3%) patients. A total of 141 paraneoplastic dermatoses were observed in 103 patients as more than one skin lesions were present in 26 patients.

Out of 20 (5.7%) patients with specific lesions, eight (2.3%) had direct spread and 12 (3.4%) had distant metastases. Among the 12 patients with distant metastases, five patients had leukemia cutis.

Out of the eight patients with direct spread, four patients had well differentiated squamous cell carcinoma oral cavity, three patients had adenocarcinoma breast and one patient had poorly differentiated squamous cell carcinoma lung. Among the eight patients, six patients were females and two patients were males. Patients with carcinoma oral cavity had erythematous, indurated nodules and plaques on face and neck. One patient with carcinoma oral cavity showed central ulceration of the nodule (Figure 1). Two patients with carcinoma breast had erythematous, oedematous plaque on anterior chest wall and one patient had Paget's disease. One patient with carcinoma lung presented with erythematous, oedematous plaque with ulceration on chest wall. Out of eight patients with direct spread two patients (0.6%) presented with skin lesions which were Paget's disease of the breast and erythematous ulcerated plaque of carcinoma lung. Direct spread appeared three weeks to five months after the diagnosis of malignancy in the other six patients.

Out of the twelve patients with cutaneous metastases, six patients were males and six were females. Four patients had acute myeloid leukemia, two patients had carcinoma lung and others had carcinoma breast, thyroid, pancreas, oesophagus, chronic lymphocytic leukemia and neuroblastoma. Cutaneous metastasis was the first sign of malignancy in three (0.9%) patients and the underlying neoplasms were lobular carcinoma of breast, carcinoma pancreas and chronic lymphocytic leukemia. In the remaining nine patients skin metastasis appeared two weeks to seven months after the diagnosis of malignancy. Face, anterior chest wall, abdomen, arms and back of trunk were the sites of predilection. In eleven out of twelve patients the skin lesions were multiple, skin coloured or erythematous, firm papules and nodules. One patient with carcinoma pancreas presented with single umbilical nodule and skin biopsy showed features of papillary cystadenocarcinoma. Multiple, bright red, soft, fluctuant swellings on scalp were seen in a patient with follicular carcinoma thyroid (Figure 2).

Four patients with acute myeloid leukemia and one patient with chronic lymphocytic leukemia had asymptomatic, multiple papules and nodules of leukemia cutis distributed over face, trunk and extremities (Figures 3 and 4). These lesions were skin coloured in the beginning, but within few days changed the colour to erythematous, purpuric and violaceous with few of them showing an erythematous halo. Number of lesions ranged from ten to more than hundred.

In the present study 103 (29.4%) patients had paraneoplastic dermatoses. Common malignancies causing paraneoplastic dermatoses were haematological malignancy (30 patients), carcinoma lung (27 patients) and carcinoma breast (eight patients). The common paraneoplastic dermatoses were clubbing in 26 (7.4%) patients, acquired ichthyosis in 22 (6.3%), pruritus in 13 (3.7%) and exaggerated insect bite reaction in 11 (3.1%) patients. The sex distribution and frequency of different paraneoplastic dermatoses and associated malignancies are shown in Table 2. Paraneoplastic dermatoses were the presenting sign of malignancy in 22 (6.3%) patients. All the patients with exfoliative dermatitis, Leser-Tre'lat sign, necrolytic migratory erythema and paraneoplastic pemphigus presented with skin lesions and the underlying malignancies were diagnosed after detailed evaluation. The other paraneoplastic dermatoses that preceded the diagnosis of malignancy were pruritus in seven (54%) patients, Sweet's syndrome in two (40%) patients, acanthosis nigricans in one (20%) patient and acquired ichthyosis in three (13.6%) patients. Exfoliative dermatitis was seen in two patients and it preceded the diagnosis of malignancy by two and four months. Pruritus preceded the malignancy in seven patients and the interval between the two varied from six months to two years. Paraneoplastic dermatoses as the first sign of malignancy were commonly seen in haematological malignancies {12 (3%) patients}, carcinoma lung {six (1.7%) patients} and carcinoma pancreas (two patients). Urticaria and vasculitis when present succeeded the malignancy.

Leser-Tre'lat sign, exfoliative dermatitis, palmoplantar keratoderma and clubbing were common in males while pruritus, urticaria, insect bite reaction and xerosis were common in females. No sex predilection was noted for other paraneoplastic dermatoses.

Three patients (60%) with acanthosis nigricans also had acquired ichthyosis and one patient had coexisting palmoplantar keratoderma.

Four patients (1.1%) had both specific and paraneoplastic dermatoses in our study. Malignancies showing both specific and nonspecific lesions were acute myeloid leukemia (two patients), carcinoma lung and carcinoma oral cavity.

Various skin infections were observed in 46 (13%) patients. The infections observed were extensive tinea versicolor, tinea corporis, candidiasis, chronic paronychia, herpes zoster, molluscum contagiosum, extensive verruca vulgaris, Kaposi's varicelliform eruption, impetigo, folliculitis, furuncle and cellulitis. Two out of seven patients with herpes zoster had multidermatomal involvement. Infections were common in haematological malignancy followed by carcinoma lung and carcinoma oral cavity.

Discussion

Skin is the largest and the most accessible organ of our body. Skin signs are the window to internal malignancy. Skin manifestations were much higher in our study compared with previous studies. [6,7] This may be due to the inclusion of patients presenting with skin lesions in the dermatology department in addition to those attending the oncology departments. Skin manifestations were more common in males. Although malignancies and skin manifestations were common in the age group 51-70 years, the chance of getting skin lesions were more in the younger age group (11-30yrs).

The percentage of specific lesions in our study was in concordance with some previous studies, [2,5,6,8] whereas others noted a lower rate. [7,9] There was a slight increase in patients presenting with specific lesions as the first sign of malignancy in the present study. [2,6] Cutaneous metastases outnumbered direct tumour spread as reported earlier, though certain studies noted a higher number of patients presenting with direct spread. [6,7] The common malignancies producing direct spread in our study were carcinoma oral cavity and carcinoma breast similar to earlier reports. [6,7]

Prevalence of cutaneous metastasis in different studies vary between 0.7 and 12% with most Indian studies showing 1.5 - 2%. Carcinoma lung, breast, kidney, oral cavity and colon were the underlying neoplasms on most occasions, but two studies conducted in India also showed lymphoma and leukemia as common cause of skin metastasis. [2,3,5,6,7,8,9,10]

Our finding of multiple asymptomatic nodules as the common manifestation of cutaneous metastasis was in concordance with the existing literature. Face was the most common site of cutaneous metastasis in our patients, whereas anterior chest wall was the most common site in the previous studies. [5,6,7,9] Unlike previous reports lower extremities were not found to be a common site for metastasis in our study. [6,7]

Paraneoplastic dermatoses were more common in the present study compared with previous reports. [6,7] One patient with acute myeloid leukemia (AML) presented with Sweet's syndrome which subsided with systemic steroids and treatment of AML (Figure 5).

Exfoliative dermatitis, necrolytic migratory erythema, paraneoplastic pemphigus and pruritus assumed significance as they preceded malignancy in all patients by a couple of months to few years. We would like to highlight the importance of thorough work up to rule out underlying neoplasm, whenever patients present with unexplained and intractable pruritus and exfoliative dermatitis. Even when no underlying cause is found, patients may be kept under regular follow up for early detection of malignancy.

The major limitation of our study was the small sample size. Number of cases of each malignancy was not enough to arrive at any conclusion regarding the risk of developing one particular manifestation in one specific neoplasm. Since this was a cross sectional study we were not able to arrive at any conclusion regarding the prognostic significance of individual skin manifestations. Still we were able to study the different skin manifestations seen in many malignancies as the study was conducted in a tertiary referral centre. By restricting the study to patients not on any treatment, we were able to assess the effects of neoplasms on the skin. In many previous studies, it was difficult to differentiate whether a particular manifestation was due to the underlying disease or due to the treatment given for the disease.

Conclusion

Skin involvement can be the presenting sign of underlying neoplasm. With the advent of newer treatment options, several malignancies can be cured by early diagnosis and treatment. Every dermatologist should have a thorough knowledge about skin manifestations of malignancy so that we can help in the early diagnosis of this dreadful disease.

Acknowledgment if any: We would like to thank Jamal P, Executive Engineer, Kerala Water Authoriy and teachers of Dept of Dermatology & Pathology, Govt. Medical College, Kozhikode for their invaluable help in the preparation of this article.

Table 1: Age distribution of patients with malignancy and skin manifestations

Age group	No of patients with skin manifestations	Total no of patients with internal malignancy	% of patients with skin manifestations
1-10	2	10	20
11 – 20	6	12	50
21 – 30	7	11	63.63
31 – 40	9	37	24.32
41 – 50	16	62	25.81
51 – 60	35	94	37.23
61 – 70	32	82	39.00
71 – 80	11	37	29.73
81 – 90	1	5	20.00
TOTAL	119	350	34.00

Table 2: Sex distribution and frequency of paraneoplastic dermatoses and associated malignancies

Paraneoplastic dermatoses	**Male**	**Female**	Total patients	% in total patients	Associated malignancy
Acanthosis nigricans	3	2	5	1.43	Lung,breast
Acquired ichthyosis	11	11	22	6.29	Haematological, lung
Clubbing	24	2	26	7.43	Lung
Erythema multiforme	0	1	1	0.29	Thyroid
Exfoliative dermatitis	2	0	2	0.57	Lung,CLL*
Gum hypertrophy	4	3	7	2	Acute Myeloid Leukemia
Exaggerated insect bite reaction	4	7	11	3.14	Breast,thyroid, haematological
Necrolytic migratory erythema	1	0	1	0.29	Pancreas

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Koilo-nychia	1	3	4	1.14	GIT
Leser-Tre'lat sign	3	1	4	1.14	Lung,haematological
Para-neoplastic pemphi-gus	0	2	2	0.57	Non Hodgkin's Lymphoma,Lung
Palmo-plantar kerato-derma	2	1	3	0.86	Stomach,lung, haematological
Pruritus	3	10	13	3.71	Haematological
Purpura	2	2	4	1.14	Haematological
Sub-corneal pustular derma-toses	0	1	1	0.29	Non Hodgkin's Lym-phoma
Sweet's syndrome	3	2	5	1.43	Acute Myeloid Leu-kemia
Urticaria	0	2	2	0.57	Thyroid,oral cavity
Vasculitis	1	1	2	0.57	AML†,lung,thyroid

CLL: Chronic Lymphocytic Leukemia †AML: Acute Myeloid Leukemia

Legends for figures

Figure 1: Direct spread from carcinoma oral cavity showing single ulcerated nodule.

Figure 2: Distant metastases from follicular carcinoma thyroid showing soft fluctuant swellings on scalp.

Figure 3: Multiple skin coloured and erythematous papules and nodules of leukemia cutis in acute myeloid leukemia.

Figure 4: Histopathology of leukemia cutis showing diffuse infiltration of atypical mononuclear cells (H and E, X 100).

Figure 5: Erythematous oedematous plaque of Sweet's syndrome in a patient with acute myeloid leukemia.

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