

Original Research Article

A clinco epidemiological study of cutaneous markers of internal malignancy

Jyothi Sri Teki¹, Satya Sri Teki^{2*}

¹Deputy Civil Surgeon, ESI Dispensary, Devapuram, Guntur, Andhra Pradesh, India

²Department of DVL, Gandhi Medical College, Secunderabad, Telangana, India

Received: 15 November 2019

Revised: 07 January 2020

Accepted: 08 January 2020

*Correspondence:

Dr. Satya Sri Teki,

E-mail: satyadermatologist@gmail.com

Copyright: © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT

Background: The skin provides important clues to many systemic diseases. Changes in the skin can be a marker for internal malignancies. If any cutaneous disorder associated with malignancy can be recognized early, it paves way to rapid diagnosis and treatment of the underlying malignancy. we made such an attempt to recognize cutaneous disorders in 40 patients suffering with internal malignancies at government general hospital, Guntur attending dermatology and radiology departments.

Methods: Patients with internal malignancy having specific features were included in our study. Biopsy was done in every patient. The present study lasted for 21 months i.e., from January 2008 to September 2009.

Results: We found that carcinoma cervix was the most common malignancy in females and bronchogenic carcinoma in males associated with cutaneous markers. The markers observed were pruritus, acquired lymphorroids, para neoplastic pemphigus, acquired ichthyosis and disseminated granuloma annulare. Cutaneous markers were observed within 6 months from onset of internal malignancies.

Conclusions: Recognition of any para-neoplastic skin disorders should raise suspicion for an internal malignancy which helps in rapid diagnosis and treatment of underlying malignancy.

Keywords: Cutaneous markers, Internal malignancy, Carcinoma cervix, Pruritus

INTRODUCTION

It has been said that the eyes are the window to the soul and the skin to within.

Human integument mirrors many internal diseases, enabling a practitioner to make tremendous contribution to patient care and if, any cutaneous disorder associated with malignancy can be recognized early, may lead to a rapid diagnosis and treatment of underlying malignancy.

Internal malignancies give rise to many number of cutaneous disorders through their metastatic, metabolic

and immunological consequences. These changes can be divided into specific malignant infiltrates and non-specific lesions. Specific infiltrates show characteristic malignant cells on histopathologic examination and they can occur due to contiguous or non-contiguous spread.

Specific changes are broadly classified into direct tumour spread/cutaneous metastasis, geno-dermatosis, cutaneous markers on exposure to carcinogens, and paraneoplastic syndromes.

Non-specific lesions can be infective, non-infective and changes due to chemotherapy or radiotherapy. The skin

lesions may proceed, be concurrent, or follow the detection of the associated malignancy. Subtle cutaneous manifestations identified early will give primafacie evidence for internal malignancies. Recognition of these disorders is important for the practitioner, so that in the best-case scenario, he or she may aid in diagnosing a cancer in early stages of the disease. Necrolytic migratory erythema, the cutaneous manifestation of the glucagonoma syndrome, was described in 1942 by Becker et al.¹ Curth et al pointed out that an apparently high incidence of cancer, predominantly gastric carcinoma in family members.² Barne's data shows majority of patients with dermatomyositis preceding cancer, the discovery of tumour was within a year. Barnes BE dermatomyositis and malignancy Ann Intern Med 84:681. So, keeping all these historical studies as reference, the present study has been conducted.

Objective

The objective was to analyse and understand the association of specific skin lesions in relation to various malignancies. Confining to the cases only with specific cutaneous markers broadened the possibility to recognize the most common cutaneous markers and its association with internal malignancy. All patients were closely followed for a brief period during their treatment to know the association between internal malignancy and the cutaneous markers.

METHODS

It is a hospital based observational study. It was done in all malignancy cases confirmed by various investigations with specific skin changes attending dermatology and radiology OPD at Guntur Medical College, Guntur over a period of 21 months from January 2008 to September 2009.

Only 40 cases with cutaneous changes that are specific to internal malignancy were included in our study. Skin biopsy was taken from all the patients and the cutaneous marker was confirmed.

Inclusion criteria

Inclusion criteria were all patients of various age groups, the dermatoses must have developed only after development of malignant tumours, and the dermatoses and the malignant tumour should follow a parallel course i.e., result in clearing of the disease and recurrence of cancer should cause relapse of dermatoses.

Exclusion criteria

Exclusion criteria were patients with internal malignancy having non-specific lesions were not included in our study. Patients who are HIV seropositive were excluded from our study. This study was approved by ethical committee of Guntur medical college, Guntur.

Data was entered and analyzed using microsoft excel. Data was presented in percentages and proportions.

RESULTS

40 cases were included in our study. Out of these 20 cases were males and 20 females. In our study, carcinoma cervix was present in 12 cases while bronchogenic carcinoma in 8 cases. The incidence of various carcinomas was as in (Table 1).

Table 1: Incidence of carcinomas.

Type of carcinoma	No. of cases
Carcinoma cervix	12
Bronchogenic carcinoma	8
Carcinoma of breast	6
Multiple myeloma	5
Hodgkin's lymphoma	3
Leukemias (acute myeloid leukemia and chronic myeloid leukemia)	3
Carcinoma stomach	1
Sarcoma of ovary	1
Primary cutaneous T-cell lymphoma	1

Out of 20 male patients, 8 cases were found to have bronchogenic carcinoma, multiple myeloma was observed in 4 patient's leukemia and lymphomas constituted 6 patients. one patient suffered from carcinoma stomach and cutaneous T cell lymphoma was observed in a patient as shown in (Table 2).

Table 2: Incidence of carcinomas in males.

Type of carcinoma	No. of cases
Bronchogenic carcinoma	8
Multiple myeloma	4
Hodgkin's lymphoma	3
Leukemias	3
Carcinoma stomach	1
Primary cutaneous T-cell lymphoma	1

Table 3: Age distribution.

Age (in years)	No. of cases	Percentage
1-10	2	5
11-20	1	2.5
21-30	0	0
31-40	4	10
41-50	13	32.5
51-60	12	30
61 and above	8	20

In females, carcinoma cervix was most common whereas sarcoma of ovary and multiple myeloma were present in

one case. In our study of 40 cases, 32 cases were above 40 years of age, constituting 82.5% and forming the major portion of the study group. The remaining 17 cases were under 40 years constituting only 17.5%. This shows the association of malignancy and older age. All 5 cases of multiple myeloma were in the age group of 40 to 50 years indicating its common incidence in the middle age. 2 cases were under the age of 10 years. Both were male children suffering with acute myeloid leukemia. They had xeroderma pigmentosum as cutaneous marker (Figure 1). Sarcoma of ovary was observed in a female of 20 years of age. No cases were recorded in the age group between 21 to 30 years as shown in (Table 3).

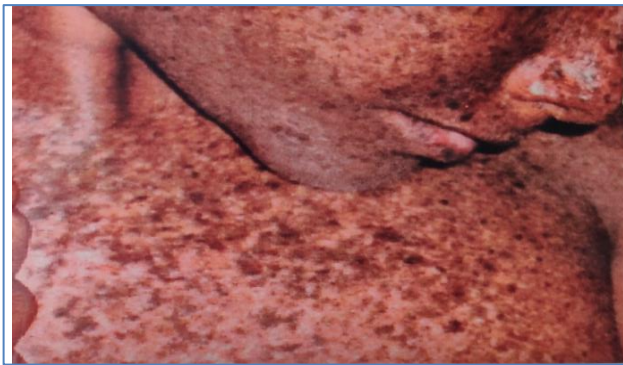


Figure 1: Xeroderma pigmentosum.

In our study, carcinoma cervix was the most common malignancy associated with cutaneous markers. And generalized itching was the most common marker in carcinoma cervix. Lymphorrhoids secondary to lymphatic obstruction was the next common marker.

One female came with generalized pruritus and blistering disorder. And the biopsy report of skin suggested paraneoplastic pemphigus. she was investigated and found to have carcinoma cervix. Disseminated granuloma annulare associated with generalized ichthyosis was observed in one case of carcinoma of cervix. This patient also had diabetes mellitus.

Bronchogenic carcinoma stood second and was observed in 8 cases. All were male patients. Secondaries in neck were the most common presentation in bronchogenic carcinoma. Other cutaneous markers observed in this malignancy were acquired ichthyosis in 3 cases, generalized pruritus in one case and hypertrophic osteoarthropathy in one case. Carcinoma breast was the third most common malignancy observed in our study. The cutaneous markers observed in this malignancy were Paget's disease (Figure 2) in 3 patients, carcinoma encurraisse (Figure 3 and 4) in one case, and generalized pruritus in 3 cases.

Multiple myeloma occupied 4th position. Out of 5 cases, one was a female patient. She was diagnosed as POEMS syndrome (Figure 5 and 6) when she presented with

multiple myeloma, hyperthyroidism, hepatosplenomegaly, hyperpigmentation and hypertrichosis. All the cases presented with primary amyloidosis.



Figure 2: Paget's disease of nipple.



Figure 3: Carcinoma encurraisse.



Figure 4: Carcinoma encurraisse.

2 out of 3 cases of Hodgkin's lymphoma presented with acquired ichthyosis and one case presented with intractable itching and acquired ichthyosis. Chronic myeloid leukemia presented with generalized pruritus and ichthyosis. Acanthosis nigricans was the presenting symptom in adenocarcinoma stomach. Both cases of acute myeloid leukemia presented with xeroderma pigmentosum.

Table 4: Cutaneous markers.

S. no.	Associated malignancy	Number	Cutaneous markers
1	Carcinoma cervix	12	Generalized pruritus-8
			Acquired lymphangiomas-4
			Granuloma annulare-1
			Paraneoplastic pemphigus-1
			Acquired ichthyosis-1
2	Bronchogenic carcinoma	8	Secondaries neck-5
			Acquired ichthyosis-3
			Generalized pruritus-1
			Hypertrophic osteoarthropathy-1
3	Carcinoma breast	6	Paget's disease of breast-3
			Encuirasse-1
			Generalized pruritus-3
4	Multiple myeloma	5	Primary amyloidosis-5
			POEMS syndrome-1
			Acquired ichthyosis-1
			Acquired ichthyosis-2
5	Hodgkin's lymphoma	3	Generalized pruritus-2
			Xeroderma pigmentosum-2
6	Acute myeloid leukemia	2	Acquired ichthyosis-1
	Chronic myeloid leukemia	1	Generalized pruritus-1
			Acquired ichthyosis-1
7	Carcinoma stomach	1	Acanthosis nigricans
8	Primary cutaneous T-cell lymphoma	1	Erythroderma-1
			Generalized pruritus -1
9	Sarcoma of ovary	1	Multiple secondaries skin-1
			Generalized pruritus-1

One case of acute myeloid leukemia presented with xeroderma pigmentosum, one case also had generalized dryness of skin.

**Figure 5: POEMS syndrome.**

Primary cutaneous T cell lymphoma presented with generalized pruritus and erythroderma. Generalized itching associated with multiple secondaries of skin were the cutaneous markers in sarcoma of ovary as shown in (Table 4).

**Figure 6: POEMS syndrome.**

DISCUSSION

Skin can provide an important clue to systemic diseases, enabling the practitioner to make a tremendous contribution to patient care.¹ If a cutaneous marker associated with internal malignancy can be identified, it may aid in diagnosing cancer at an early stage of disease. Thus, recognition of external clues is important to

facilitate both early diagnosis and prompt treatment of internal disorder.

In our study, males and females were equal in number. This indicates that cutaneous markers have no sex predilection. In men, the most common malignancy was bronchogenic carcinoma. Its increased incidence was due to widely prevailing habit of smoking. All these patients had secondaries in neck. Other associated markers like hypertrophic osteoarthropathy, generalized pruritus and generalized ichthyosis were noted. Among females, carcinoma cervix was common in our study. Increased incidence of cervical cancer may be due to early marriage, parity in developing countries and also increased incidence of human papilloma virus (HPV) infection.

The most common cutaneous marker observed was generalized pruritus. Numerous malignancies associated with pruritus as a paraneoplastic manifestation included carcinoma cervix, bronchogenic carcinoma, Hodgkin's lymphoma, chronic myeloid leukemia, primary cutaneous T-cell lymphoma, and sarcoma of ovary.^{2,3} 2 cases out of 3 cases of Hodgkin's lymphoma presented with generalized pruritus.

Acquired lymphangiomas appeared as clear fluid filled blisters around the vulva. In our study, they were observed in cases of carcinoma cervix. Paraneoplastic pemphigus was observed in association with a case of carcinoma cervix.⁴ Histopathological examination showed supra basal acantholysis and necrotic keratinocytes thus differentiating it from pemphigus vulgaris. Associated marker along with pemphigus vulgaris was pruritus. Disseminated granuloma annulare was observed in case of carcinoma cervix.⁵ Diabetes mellitus was an associated finding.

Simultaneous treatment of carcinoma cervix with radiation and anti-diabetic treatment for diabetes mellitus made the lesions subside. Carcinoma breast was observed in 6 cases. The presenting symptoms were Paget's disease in 3 cases, encruraisse and pruritus in 1 case and only generalized pruritus in 2 cases. one case of Paget's disease presented as scaling and erythema over the right nipple. There was puckering and paeu d'orange appearance.⁶ The other two cases of Paget's disease presented with oozing from nipples. The oozing was unilateral and greenish in colour in both the cases. Biopsy revealed ductal adenocarcinoma in both. Acanthosis nigricans was associated with adenocarcinoma of stomach.⁷ Hyper pigmented, velvety lesions involving neck and axillae developed over a period of 8 months in this patient. HPE revealed hyperkeratosis, acanthosis and papillomatosis.

Two cases of xeroderma pigmentosum were observed in our study. Both were male children and were 7 years old. Both presented with acute myeloid leukemia. Freckles, generalized dryness of skin were present and was evident

in both the patients since infancy.^{8,9} Photophobia, diminution of vision were associated symptoms in these two patients.

Out of 5 cases of multiple myeloma, 4 were males. All five cases presented with primary amyloidosis. POEMS syndrome was an associated finding in one patient. Polyneuritis, hyperthyroidism, hepato splenomegaly were associated.¹⁰ Skin manifestations were hypertrichosis and hyperpigmentation.

CONCLUSION

Cutaneous markers had an equal incidence in both sexes in our study. The most common internal malignancy presenting with cutaneous markers was carcinoma cervix in females and bronchogenic carcinoma in males. Taking all malignancies into consideration, the most common cutaneous was pruritus. The most common age group involved in internal malignancies was between 40-60 years. Acquired ichthyosis and generalized pruritus were the most common presenting cutaneous markers in Hodgkin's lymphoma. Cutaneous markers were observed within six months from the onset of internal malignancies.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the institutional ethics committee

REFERENCES

1. Becker SW, Kahn D, Rothman S. Cutaneous manifestations of internal malignant tumours. Arch Dermatol Syphilol. 1942;45:1069-80.
2. Curth HO, Aschner BM. Genetic studies on acanthosis nigricans. Arch Dermatol. 1959;79:55.
3. Sneddon IB. Acquired ichthyosis and related conditions. Int J Dermatology. 1984;23(7):458-61.
4. Niimi Y, Kawana S, Hashimoto T. Paraneoplastic Pemphigus Associated With Uterine Carcinoma. J Am Acad Dermatol. 2003;48(5):69-72.
5. Li A, Hogan DJ, Sansui DI, Smoller BR. Granuloma Annulare and malignant neoplasms. Am J Dermatopath. 2003;25:113-6.
6. Worth WDL, Carline V, Susser WS. Dermatologic diseases of the breast and nipple. J Am Acad Dermatol. 2000;43(5):735-51.
7. Yeh JS, Munn SE, Plunkett TA. Coexistence of acanthosis nigricans and the sign of lesar-trelat in a patient of adenocarcinoma: a case report and literature review. J Am Acad Dermatology. 2000;42:357-62.
8. Kramer KH, Lee MM, Scotto J. Xeroderma pigmentosum. Cutaneous, ocular and neurologic abnormalities in 830 published cases. Arch Dermatol. 1987;123(2):241-50.
9. Kramer KH, Lee MM, Andrews AD. the role of sunlight and DNA repair in melanoma and non-

melanoma skin cancer. The xeroderma pigmentosum paradigm. Arch Dermatol. 1994;130(8):1018-21.

10. Soubrier MJ, Jacques JD, Sauvezie BJM. POEMS Syndrome: a study of 25 cases and review of literature. Am J Med. 1994;97:543-53.

Cite this article as: Teki JS, Teki SS. A clinico epidemiological study of cutaneous markers of internal malignancy. Int J Res Dermatol 2020;6:468-73.