

**Clinicopathological Profile of Cutaneous** Metastasis from Internal Malignancies: A Five Year Retrospective Study

NUPUR GOYAL<sup>1</sup>, KANTHILATHA PAI<sup>2</sup>, SATHISH B PAI<sup>3</sup>, PADMA PRIYA JAIPRAKASH<sup>4</sup>

# **ABSTRACT**

Introduction: Cutaneous metastasis is the infiltration of skin by malignant cells from an underlying internal malignancy.

Aim: To analyse clinicopathological profile of patients with cutaneous metastasis from internal malignancies.

Materials and Methods: This was a five year retrospective study that included patients diagnosed with cutaneous metastasis from internal malignancies during the period January 2010 to December 2014. Information pertaining to patient demographics and disease details including site and type of previously diagnosed malignancy were noted.

Results: Eighteen patients with cutaneous metastasis were identified. Cutaneous metastasis was the presenting feature in six patients, in others it occurred in previously diagnosed

cases of malignancy after a mean duration of 25 months. Patients presented with painless cutaneous nodules in 10 (55.56%), ulcerated nodules in six (33.33%), painful nodules and indurated plaques in one (5.56%) each. Most common site of involvement was anterior abdominal wall. Most common histological subtype of metastatic carcinoma was adenocarcinoma, followed by squamous cell carcinoma.

Conclusion: Cutaneous metastases are relatively uncommon, but it is important to recognise them. They may occasionally be the first manifestation of an underlying malignancy. The prognosis is usually poor in patients with cutaneous metastases, although early recognition offers some chance of survival

## INTRODUCTION

Cutaneous metastasis is a relatively rare complication of internal malignancies with a reported incidence of 0.7-9%. Ten percent of the patients with metastatic cancer have cutaneous metastases [1,2]. Clinically, cutaneous metastases can sometimes mimic common dermatoses like cellulitis, epidermal inclusion cysts, ulcers; thus making the diagnosis difficult [3]. The most common sources of cutaneous metastases are breast, lung, colon, stomach, upper aerodigestive tract, uterus and kidney; the most common skin metastases from a previously unknown primary tumour originate from the kidney, lung, thyroid or ovary [4-6]. Cutaneous metastases are usually indicative of disseminated disease and indicate a correspondingly poor prognosis; survival is typically only about three months in patients with disseminated skin metastases [7]. Their recognition is important as they can be the first sign of extranodal metastatic disease and hence, can have profound prognostic implications. This study was conducted to understand the relative proportion of different internal malignancies metastasising to the skin and study the clinicopathological features in a tertiary care hospital in India.

# MATERIALS AND METHODS

This was a five year retrospective study that analysed patients with a proven diagnosis of metastatic carcinoma to skin on histopathology, conducted in the Department of Pathology, after obtaining Institutional Ethical Committee clearance during the period January 2010 to December 2014. Eighteen cases with a diagnosis of metastastic carcinoma to skin were retrieved from Pathology database in the Department of Pathology. Only cases with a diagnosis of solid internal malignancy recorded consecutively from 2010 to 2014 in the archives were included, and cases of haematolymphoid neoplasms were excluded from the study. Also, cases with direct extension of primary malignancy into the overlying skin were excluded. Information pertaining to patient demographics,

duration of skin lesions, clinical presentation and site of lesions, details of previous internal malignancy, response to treatment and prognosis were noted from patients medical records and histopathological features were obtained from pathology reports.

# RESULTS

Keywords: Carcinoma, Metastatic, Skin

Eighteen patients with cutaneous metastasis were identified. There were 10 males (55.56%) and eight females (44.44%). Mean age was 52.33 years (range 30 to 73 years).

In 12 (66.67%) patients, cutaneous metastases appeared in patients with history of known malignancy after a mean duration of 25.75



months (range two months-20 years). Cutaneous metastasis was the presenting feature in six (33.33%) patients. The most common internal malignancy was from upper aerodigestive tract, followed by breast as shown in [Table/Fig-1].

S. No.	Age (years) and Sex (M/F)	Primary malignancy	Time interval*	Clinical presentation	Site	Туре	Outcome, following diagnosis of cutaneous metastasis
1.	40, F	Infiltrating duct carcinoma of breast	Eight months	Painless nodules	Chest, scar back	Contiguous	Lost to follow up
2.	42, M	Adenocarcinoma of colon	22 months	Ulcerated nodules	Abdominal wall	Contiguous	Succumbed within one month
3.	50, F	Squamous cell carcinoma of tongue	Four years	Ulcerated nodules	Face	Contiguous	Lost to follow up
4.	58, M	Squamous cell carcinoma of tongue	Two years	Painless nodules	Neck	Non- contiguous	Lost to follow up
5.	55, F	Adenocarcinoma of endometrium	Two months	Ulcerated nodules	Abdominal wall	Contiguous	Lost to follow up
6.	73, F	Adenocarcinoma of colon	Presenting feature	Painless nodules	Abdominal wall	Contiguous	Improved with treatment
7.	49, M	Squamous cell carcinoma of soft palate	Four months	Painless nodules	Neck shoulder	Non- contiguous	Improved with treatment
8.	70, M	Adenocarcinoma of colon	Presenting feature	Painless nodules	Abdominal wall, scar	Contiguous	Improved with treatment
9.	58, M	Renal cell carcinoma	Presenting feature	Ulcerated nodules	Groins	Non- contiguous	Improved with treatment
10.	30, M	Adenocarcinoma of lung	Presenting feature	Painless nodules	Abdominal wall	Non- contiguous	Lost to follow up
11.	47, F	Infiltrating ductal carcinoma of breast	Two years	Painless nodules	Chest, scar thighs	Contiguous and Non- contiguous	Lost to follow up
12.	69, F	Serous cystadenocarcinoma of ovary	Presenting feature	Indurated plaques [Table/Fig-3]	Abdominal wall	Contiguous	Improved with treatment
13.	41, M	Renal cell carcinoma	Two years	Painful nodules	Abdominal wall, back	Contiguous and Non- contiguous	Lost to follow up
14.	52, M	Leiomyosarcoma alveolus and hard palate	20 months	Painless nodules	Abdominal wall axilla groins	Non- contiguous	Lost to follow up
15.	61, M	Squamous cell carcinoma of tongue	Three months	Ulcerated nodules [Table/Fig-4]	Chest, scalp	Non- contiguous	Succumbed within one month
16.	50, F	Infiltrating duct carcinoma of breast	Presenting feature	Painless nodules [Table/Fig-5]	Abdominal wall, chest axilla	Non- contiguous	Succumbed after 16 months
17.	43, F	Infiltrating duct carcinoma of breast	20 years	Painless nodules	Chest	Contiguous	Lost to follow up
18.	54, M	Squamous cell carcinoma of pharynx	Eight months	Ulcerated nodules	Neck	Non- contiguous	Improved with treatment

[Table/Fig-2]: Clinicopathological data of patients with cutaneous metastasis. \*Time interval between diagnosis of primary malignancy and development of cutaneous metastases

M=Male, F=Female



[Table/Fig-3]: Indurated lesions over the thigh skin in a patient with serous cystadenocarcinoma of ovary.

[Table/Fig-4]: Ulcerated lesions on the neck in a patient with squamous cell carcinoma of tongue.

[Table/Fig-5]: Nodular lesions over the abdominal wall in a patient with carcinoma breast. (Images from left to right)

The lesions were multiple in all cases and the clinical presentation was painless, firm to hard cutaneous nodules in 10 (55.56%) patients, ulcerated nodules in six (33.33%), painful nodules in one (5.56%) patient and indurated plaques in one (5.56%) patient [Table/Fig-2].

Cutaneous metastases were associated with fatal outcome in three (16.67%) patients. Two patients, one with adenocarcinoma colon and other with carcinoma tongue succumbed in about a month after developing cutaneous metastasis. Another patient with carcinoma breast died 16 months after being diagnosed with cutaneous metastasis. Six patients improved following treatment. Nine patients were lost to follow up.

## DISCUSSION

The single most basic biologic process that characterises a malignant tumour is the ability to produce secondary deposits (metastases) at distant sites [8]. Cutaneous metastasis is defined as the spread of malignant cells from a primary malignancy to the skin. This may occur from spread of tumour cells from an internal malignancy or from a primary skin cancer [9]. Skin is not a common site for distant metastasis, and is reported to be involved in about 0.7-9% of all patients with cancer [1,2].

The most common internal malignancies giving rise to cutaneous metastases are lung and colon cancers in males and breast, colon and ovary cancers in females [2,10]. In our study, the most common internal malignancies with skin metastasis were breast carcinoma in females and colon, kidney and tongue cancers in males. In a study from Taiwan, the highest rates of skin metastases were found to occur from carcinoma of the breast, followed by the lung, oral mucosa, colon rectum, stomach and oesophagus [11].

Cutaneous metastases are generally detected during the advanced stages of malignancy, they can occasionally be the presenting feature of an internal malignancy [4]. Cutaneous metastases is reported as initial manifestation of underlying cancer in 34% patients in a study [12]. Most common primary site of cutaneous metastasis in females was reported from breast carcinoma followed by carcinoma of large intestine, lungs and ovaries, while

in males in decreasing order were from lungs, large intestine, oral cavity, kidney and stomach [13]. Brownstein MH and Helwing EB, reported that lung, kidney and ovary cancers are the most common type of cancers with skin involvement as the presenting sign [10]. In our study, cutaneous metastasis was the presenting feature in 33.33% patients. Cancers of the breast, ovary, kidney, lung, colon and palate showed skin involvement as the presenting sign in our study. On the other hand, one patient with carcinoma breast developed cutaneous metastasis 20 years after being diagnosed with the breast cancer. Others developed skin metastatic deposits after a period ranging from two months to four years after being diagnosed with primary malignancy.

Clinically, cutaneous metastases have a varied presentation. The lesions may present as dermal papules, subcutaneous nodules, inflammatory patches, fixed, indurated lesions, ulcerated lesions or rarely as bullous lesions, cutaneous cysts, alopecia neoplastica, sclerodermoid or zosteriform lesions. The most common presentation is as multiple nodular lesions [2,9,14]. In our study, the most common presentation was multiple painless nodules in 10 patients followed by ulcerated lesions in six patients. One of our patients presented with painful nodules (renal cell carcinoma) and another patient with ovarian malignancy presented with diffuse cutaneous infiltration.

Cutaneous metastases show predilection for certain regions. Breast and lung cancers frequently metastasise to the chest wall, whereas cancers of the bowel, ovary, and bladder most often metastasise to the abdomen [12]. In our study, cutaneous metastasis was seen over the anterior chest wall in five patients, four of whom had breast cancer. Nine patients had abdominal wall metastasis, three of whom had bowel cancer and one each had ovarian cancer, endometrial cancer and renal carcinoma. Cutaneous metastasis was seen at the site of previous surgery scar in two patients with carcinoma breast and one patient with adenocarcinoma colon. Metastatic deposits over the skin were seen at contiguous sites in eight patients and non-contiguous sites in eight patients. Two patients showed skin metastases at both contiguous as well as non-contiguous sites.

Generally, cutaneous metastases herald a poor prognosis. They are usually indicative of disseminated, progressive disease or rarely recurrence of the primary tumour. The average survival time of patients with skin metastases is a few months [14]. The patients survived for an average of three months in one study [7]. In our study, two patients, one with adenocarcinoma colon and another with squamous cell carcinoma tongue succumbed to their illness in a month after being diagnosed with cutaneous metastasis. Two patients with carcinoma breast had a survival time of 10 and 16 months after developing cutaneous metatstatic deposits. On follow up, one patient with adenocarcinoma lung was surviving after a period of four years and a patient with carcinoma breast was surviving at seven years follow up.

### CONCLUSION

Cutaneous metastases are uncommon but early recognition of cutaneous metastasis is very important as they may be the first presentation of an internal malignancy. Cutaneous metastases are highly variable in presentation and a high-index of suspicion, especially in patients with a history of cancer, is a must for prompt diagnosis. Only with prompt recognition comes the opportunity to treat the systemic spread of the cancer in early stage and thus improve the prognosis. Inspite of a low-risk of cutaneous metastasis, skin nodules of an unknown cause should be biopsied to rule out cutaneous metastasis.

#### REFERENCES

- [1] Rolz-Cruz G, Kim CC. Tumor invasion of the skin. Dermatol Clin. 2008;26(1):89-102.
- [2] Oualla K, Arifi S, Mellas N, El Mesbahi O. Cutaneous metastases of internal cancers: A retrospective study about 12 cases. J Cancer Sci Ther. 2012;4:155-57.
- [3] Saeed S, Keehn CA, Morgan MB. Cutaneous metastasis: a clinical, pathological, and immunohistochemical appraisal. J Cutan Pathol. 2004;31(6):419-30.
- [4] Benmously R, Souissi A, Badri T, Jennet SB, Marrak H, Mokhtar I, et al. Cutaneous metastases from internal cancers. Acta Dermatovenerol Alp Pannonica Adriat. 2008;17(4):167-70.
- [5] Marcoval J, Moreno A, Peyri J. Cutaneous infiltration by cancer. J Am Acad Dermatol. 2007;57(4):577-80.
- [6] Weedon D. Skin Pathology, 2<sup>nd</sup> edn. London: Churchill Livingstone, 2002:1045-56.
- [7] Reingold IM. Cutaneous metastasis from internal carcinoma. Cancer. 1966;19(2):162-08.
- [8] Rajagopal R, Arora PN, Ramasastry CV, Kar PK. Skin changes in internal malignancy. Indian J Dermatol Venereol Leprol. 2004;70(4):221-25.
- [9] Hussein MR. Skin metastasis: a pathologist's perspective. J Cutan Pathol. 2010;37(9):e1-20.
- [10] Brownstein MH, Helwing EB. Patterns of cutaneous metastasis. Arch Dermatol. 1972;105(6):862-68.
- [11] Hu SC, Chen GS, Wu CS, Chai CY, Chen WT, Lan CC. Rates of cutaneous metastases from different internal malignancies: experience from a Taiwanese medical centre. J Am Acad Dermatol. 2009;60(3):379-87.
- [12] Gan EY, Chio MT, Tan WP. A retrospective review of cutaneous metastases at the National Skin Centre Singapore. Australas J Dermatol. 2015;56(1):01-06.
- [13] Abdel-Naser MB, Zaki MS, Brunner M, Wollina U, Zouboulis CC. Cutaneous Metastases in Internal Malignancies. Egyptian Dermatology Online Journal. 2007;3(1):4.
- [14] Alcaraz I, Cerroni L, Rütten A, Kutzner H, Requena L. Cutaneous metastases from internal malignancies: a clinicopathologic and immunohistochemical review. Am J Dermatopathol. 2012;34(4):347-93.

#### PARTICULARS OF CONTRIBUTORS:

- 1. Postgraduate, Department of Dermatology, Kasturba Medical College, Manipal Academy of Higher Education, Manipal, Karnataka, India.
- 2. Professor, Department of Dermatology, Kasturba Medical College, Manipal Academy of Higher Education, Manipal, Karnataka, India.
- 3. Professor and Head, Department of Pathology, Kasturba Medical College, Manipal Academy of Higher Education, Manipal, Karnataka, India.
- 4. Associate Professor, Department of Pathology, Kasturba Medical College, Manipal Academy of Higher Education, Manipal, Karnataka, India.

#### NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Kanthilatha Pai,

Professor, Department of Pathology, Kasturba Medical College, Manipal Academy of Higher Education, Manipal-576104, Karnataka, India. E-mail: klpai@yahoo.com

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