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Pathology

EXPERIENCE OF CUTANEOUS METASTASIS AT A TERTIARY CARE CENTRE – A VERY RARE DERMATO HISTOPATHOLOGICAL STUDY

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ABSTRACT

Cutaneous metastases are rare sites of metastasis, with an incidence of 2% of all cases. The incidence of various tumors that are metastatic to the skin correlates well with the frequency of occurrence of the primary malignant tumor in each gender. This retrospective study was conducted at a Tertiary Care Hospital, to analyze the clinical and histopathologic characteristics of skin metastases. Out of 910 skin punch biopsies, 16 cases of Cutaneous metastases were diagnosed in which, primary sites were breast (5 cases - 31.25%), ovary (3 cases - 18.75%), haemato-lymphoid origin (3 cases – 18.75%), and 1 case (6.25%) each for stomach, colon, kidney, lung and skin adnexa as primary site. Special stains were performed in all cases. Metastases is seen mainly in dermis and extend to subcutaneous tissue. Overlying epidermis may be normal or hyperplastic.

KEYWORDS : Cutaneous metastases, Primary malignancy, Histopathology, Breast, Ovary

INTRODUCTION:

Metastases represents end-stage of a complex series of interreactions between tumor cells and host tissue. In the past, concept of favorable soil and unfavourable soil was proposed. Tumor cells may reach the skin by direct invasion from an underlying tumor, by accidental implantation during surgical or diagnostic procedure (as in abdominal, perineal, mastectomy, colostomy sites), by lymphatics and hematogenous spread.¹ Cutaneous metastases are rare sites of metastasis, with an incidence of 2% of all cases.^{1,2} The incidence of various tumors that are metastatic to the skin correlates well with the frequency of occurrence of the primary malignant tumor in each gender. Cutaneous metastases are common from breast in women followed by colon, ovary, melanoma and from lungs and colon in males. Due to relative rarity of carcinoma of thyroid, pancreas, liver, gall bladder, urinary bladder, endometrium, prostate, testes and neuroendocrine system, cutaneous metastases of these tumors are relatively rare. Cutaneous metastases are of diagnostic importance as they may be the first manifestation of an undiscovered internal malignancy or the first indication of metastasis of a supposedly adequately treated malignancy.³ Biopsy of a cutaneous tumor from an otherwise asymptomatic patient may disclose metastatic cancer when primary lesion is clinically inapparent.4 The presence of cutaneous metastases is a poor prognostic factor, often associated with advanced underlying disease and late diagnosis.⁵ Cutaneous metastases are more likely to be found in older individuals. In children they are found from neuroblastoma or rhabdomyosarcoma.6

Cutaneous metastases usually appear as multiple, discrete, painless, freely movable papules or nodules of sudden onset. They occur in 10% of cases of metastases.7 Nodules are

usually 1 to 3 cm in diameter, but much larger are also reported.⁸ A zosteriform pattern of cutaneous metastases to chest wall and abdominal wall is known and most common site of primary is breast, ovary, lung, prostate, bladder and stomach.³ Trunk, scalp and umbilicus are common sites for metastases. Cutaneous metastases from soft tissue sarcomas are rare.⁹ Penis is a rare site of metastases from bladder and prostate, they are multiple and associated with priapism. Other rare sites are thigh, nail bed, thumb, finger, big toe, scrotum, eyelid, eyebrows, nasal tip and ear.¹

Metastases tend to occur on cutaneous surfaces near primary tumor, but exception is scalp that may be as frequent as 5% of all cutaneous metastases. Metastases to umbilicus is relatively common and underlying primary tumor is usually an adenocarcinoma of stomach, kidney, lung, thyroid, ovaries, endometrium and breast. 'Metachronous metastases' are those which develop some months or years after primary malignancy has been diagnosed. In 7% of cases, this interval exceeds 5 years. 'Synchromous metastases' are those where cutaneous metastases and the primary tumor are diagnosed simultaneously. e.g. Breast and oral cavity.¹Average survival time after diagnosis of cutaneous metastases is only 3 to 6 months.¹ The shortest survival time reported is 2 weeks in a case of carcinoma testis.¹⁰ Tumors of breast, kidney and malignant melanoma give rise to delayed metastases.

AIMS AND OBJECTIVE:

This retrospective study was conducted at a Tertiary Care Hospital over 3 years from January 2017 to December 2019, to analyze the clinical and histopathologic characteristics of

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skin metastases and to evaluate the occurrence of the cutaneous metastases of occult or known primary tumors.

METHODS AND MATERIAL:

Present study was a retrospective study conducted at a Tertiary Care Hospital over 3 years from January 2017 to December 2019. A total of 910 skin punch biopsies were obtained from the Department of Dermatology, out of which 16 (1.75%) were found to be of cutaneous metastases. Their age, sex, clinical findings, site of lesion, family history and other relevant investigations were properly tabulated and correlated. Punch biopsy was fixed in 10% formalin for 24 hours. Paraffin sections were studied with Haematoxylene and Eosin (H and E) stain. Special stains like Alcian blue, Periodic acid-Schiff (PAS), Reticulin, Masson's Trichrome, Congo red were performed in all cases. Deeper sections were also studied wherever required. Immunohistochemistry (IHC) was done in few cases.

RESULTS:

Primary site

Punch biopsies were studied in detailed and when needed deeper sections were studied and special stains were performed. Out of 910 skin punch biopsies, 16 cases of Cutaneous metastases were diagnosed in which, primary sites were breast (5 cases – 31.25%), ovary (3 cases – 18.75%), haemato-lymphoid origin (3 cases – 18.75%), and 1 case (6.25%) each for stomach, colon, kidney, lung and skin adnexa as primary site as shown in table no.1.

Table 1: Sex-distribution of cases according to primary tumor site (n = 16)

Female

Total

Male

Ovary	00	03	03
Haemato-lymphoid	02	01	03
Stomach	00	01	01
Colon	01	00	01
Kidney	01	00	01
Lung	01	00	01
Skin Adnexa	00	01	01
Total	05	11	16

Out of total 16 cases, 11(68.75%) were female and 05 (31.25%) were males, with female to male ratio of 2.2:1. Maximum (5 cases – 31.25%) were females with breast malignancy, followed by ovary and haemato-lymphoid malignancies (3 cases each). 1 case each were of stomach, colon, kidney, lung and skin adnexal malignancy (Table 2)

Table 2: Age-wise sex distribution of cases (n = 16)

Age Group (in years)	Males	Females	Total
41-50	00	02	02
51-60	03	04	07
61-70	01	05	06
71-80	01	00	01
Total	05	11	16

Maximum number of cases belonged to 51-60 years of age group (43.75%). Only 1 case was reported in 71-80 years of age group (75 years male), with cutaneous metastases in scalp and primary tumor in kidney (Renal Cell Carcinoma - RCC). Minimum age found was 45 years female suffering from Primary lobular carcinoma of breast and presented with cutaneous metastases to trunk and eyelid. (Table 2,3)

Breast	00	05	05					
Table 3: Cutaneous	metastases s	ite distributi	on with respect	to the prime	ary tumor (n	= 16)		
Primary tumor	Umbilicus	Chest wall	Perianal, vulva	Back	Upper limb	Scalp	Eyelid	Total
Breast	-	03	-	-	-	01	01	05
Ovary	03	-	-	-	-	-	-	03
Haemato-lymphoid	-	-	-	01	02	-	-	03
Stomach	01	-	-	-	-	-	-	01
Colon	01	-	-	-	-	-	-	01
Kidney	-	-	-	-	-	01	-	01
Lung	-	01	-	-	-	-	-	01
Skin Adnexa	-	-	01	-	-	-	-	01
Total	05	04	01	01	02	02	01	16

As shown in table 3 and 4, carcinoma breast (n = 05) metastasized to chest wall, scalp and eyelid (Fig A,B,C) and presented as nodules. All the cases of carcinoma of ovary (n = 03), also showed metastases in the form of nodules and all at umbilicus (Sister Mary Joseph Nodules). 03 cases of haemato-lymphoid malignancy showed patches over upper limb and back (Fig D,E,F). Stomach and colon malignancies (1 case each) presented as nodule over umbilicus. Kidney (RCC) tumor case showed a pulsatile nodule over scalp, which is a rare presented with cutaneous metastases to chest wall. A case of Syringoid eccrine carcinoma with extramammary pagetoid spread to vulva and perineum (Fig G,H,I) was also found in the present study.

Table 4: Site-wise presentation of cases (n = 16)

Site	Nodules	Patch	Total
Umbilicus	05	00	05
Chest wall	04	00	04
Perianal skin	01	00	01
Scalp	02	00	02
Back	00	01	01
Upper Arm	01	01	02
Eyelid	01	00	01
Total	14	02	16

Skin biopsies prove to be more diagnostic for the occult primary malignancies especially those which present as a patch. Whereas, FNAC (cytology) is more helpful for diagnosis in nodular lesions. Carcinomas may be known or they may be occult. Both the modalities of skin biopsy and FNAC are very useful to diagnosis. IHC confirms specific lesions (table 5).

Table 5: Distribution of cases according to mode of diagnosis (n = 16)

Primary tumor	Skin Biopsy	FNAC	Both	Total
Breast	01	04	-	05
Ovary	02	01	-	03
Haemato-lymphoid	03	00	-	03
Stomach	01	00	-	01
Colon	01	00	-	01
Kidney	00	01	-	01
Lung	01	00	-	01
Skin Adnexa	00	00	01	01
Total	09	06	01	16

On histopathological examination, 5 cases carcinoma of breast were diagnosed as infiltrating ductal carcinoma (IDC) (3 cases) and 1 each of lobular (Fig C) and colloid carcinoma. 3 ovarian malignancies turned to be mucinous (2 cases) and serous adenocarcinoma (1 case). All 3 haemato-lymphoid malignancies belonged to chronic myeloid leukemia (Fig F). All cases turned out to adenocarcinoma, with primary lesion in stomach, colon and kidney. 1 primary lung lesion was diagnosed as SCC.

Thus, out of total 16 cases of cutaneous malignancies, 12 cases (75%) were adenocarcinoma, 1 case (6.25%) was squamous cell carcinoma and 3 (18.75%) belonged to leukemia.

Adenocarcinoma and squamous cell carcinoma together constituted 81.25% (13 cases).

DISCUSSION:

On histopathological study, more than 60% are adenocarcinoma from colon, lung or breast. 15% are SCC from oral cavity, lung and esophagus. 25% are cutaneous metastases of melanoma and anaplastic tumor.¹⁰ Thus, in present study, out of total 16 cases of cutaneous malignancies, 12 cases (75%) were adenocarcinoma from breast, ovary, stomach, colon and kidney, 1 case (6.25%) was SCC from lung and 3 (18.75%) belonged to leukemia from haemato-lymphoid.

In present study, breast was the most common primary site in 05 females showing cutaneous metastases to anterior chest wall (18.75%), scalp and eyelid (6.25% each). Histopathology is that of adenocarcinoma or 'Indian file pattern'.¹ Alopecia neoplastica occurs as oval plaques or patches on scalp.3 We also had 3 cases of IDC, 1 of colloid carcinoma and 1 of lobular carcinoma breast. 45 year female had multiple red popular lesions over bilateral eyes (Fig A) and red nodules over neck (Fig B). Skin punch biopsies from both these sites showed cutaneous metastases with 'Indian file pattern' in favor of lobular carcinoma breast (Fig C). FNAC from bilateral breast confirmed bilateral lobular carcinoma of breast with multiple cutaneous metastases. Ali Arab Kheradmand¹¹ reported one such case of 61 year female with 2 malignancies - lobular carcinoma of breast and signet ring carcinoma of stomach with multiple skin metastases. Mohsen Samy Barsoum¹² also reported 54 year female with lobular carcinoma od breast with multiple cutaneous metastases. Similar to our study, Sadhana Mahore¹³ reported one such case of 50 years female with anterior chest wall cutaneous metastases and ductal carcinoma of breast (Carcinoma en Cuirasse).

Most preferred sites for cutaneous metastases of ovarian malignancy are umbilicus, vulva and back. Psammoma bodies may also be seen.³ We had 3 cases of ovarian malignancies – 2 of mucinous and 1 of serous adenocarcinoma, showing nodules at umbilicus (Sister Mary Joseph Nodules). Also one case each of adenocarcinoma stomach (signet ring type) and colon presented as nodule over umbilicus. Colon is the second most common malignancy to give cutaneous matastases, after lung. They are multiple, metachronous seen on abdominal wall, perineum and umbilicus. It indicates poor prognosis.¹



Fig A: Cutaneous metastasis of lobular carcinoma breast: Erythematous rash over bilateral periorbital region.

Fig B: Cutaneous metastasis of lobular carcinoma breast: Nodule over the nape of the neck

Fig C: Cutaneous metastasis of lobular carcinoma breast: Microscopy showing arrangement of lobular carcinoma in Indian file pattern. (H&E 400X)

Fig D: Cutaneous manifestation of CML: Multiple Hypopigmented macules over the back.

Fig E: Cutaneous manifestation of CML: Multiple Hypopigmented macules over the trunk.

Fig F: Cutaneous manifestation of CML: Microscopy showing Epidermotrophism and leukemic infiltration in upper dermis. (H&E 400X)

Fig G: Syringoid Eccrine Carcinoma with Extramammary Pagets disease: Malignant ulcer over the perineum with multiple metastatic nodules.

Fig H: Syringoid Eccrine Carcinoma with Extramammary Pagets disease: Multiple malignant nodules over vulva spread from perineum.

Fig I: Syringoid Eccrine Carcinoma with Extramammary Pagets disease: Sheets of malignant eccrine glands encroaching epidermis with pagetoid pattern. (H&E 100X)

CML showed infiltrations in form of multiple patches over back (Fig D) and abdomen (Fig E). Skin punch biopsies from both the sites showed Epidermotropism with pagetoid cells in epidermis with diffuse infiltrate of CML cells in dermis (Fig F). A 56 year female presented with multiple nodules over vulva (Fig H) which gradually spread to perineum and ulcerated (Fig G). On FNAC and skin biopsy (Fig I) and IHC, Syringoid Eccrine Carcinoma with Extramammary Paget's disease was confirmed. This case had a contiguous spread of vulval carcinoma to perineum in the form of nodules. Derek Isrow¹⁴ also reported one such case of advanced Extramammary Paget's Disease of groin, penis and scrotum in a 50 years male. 2.8% to 6.3% cutaneous metastases are seen in RCC, with scalp been preferred site and rarely to nephrectomy scars and external genitalia.1 RCC metastases are almost always seen in men.³ Similarly, we had a case of RCC with nodular metastases to scalp. Lung is the first most common primary tumor in men to give cutaneous metastases (in 4% or less patients with carcinoma lung). Chest wall and abdomen metastases sites are common with SCC and adenocarcinoma of lung and back for oat cell carcinoma.¹ Lesions appear as papule or nodule. SCC is of moderate or poorly differentiated type.³ Present study had a single case of SCC lung with metastatic nodules at anterior chest wall.

CONCLUSION:

Histopathology is the gold standard to diagnose cutaneous metastases in occult as well as known primary malignancies. Biopsy is of utmost importance for patchy macules or papules or nodules. Common pitfalls involve confusing staining patterns with native cutaneous adnexa and distinguishing primary adnexal malignancies. Though cutaneous metastases can have an extremely wide clinical presentation, most share common features on low magnification of a nodular, dermal-based infiltrate with a foreign appearance. Metastases is seen mainly in dermis and extend to subcutaneous tissue. Overlying epidermis may be normal or hyperplastic. Hence, selection of exact site and depth of biopsy is crucial on Dermatologist part. FNAC is very fast and accurate diagnostic modality for all nodular lesions. Metastases resembles primary tumor, except in RCC which

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appears benign. Cutaneous metastases can rarely be the presenting sign of internal malignancy. IHC is most reliable tool to confirm primary site, but may not always be available in resources poor centers. Thus high index of suspicion and perfect clinical correlation is mandatory between Dermatologist and Pathologist. Follow-up of patients is also needed in cases of metachronous metastases.

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