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ORIGINAL ARTICLE

Fine Needle Aspiration Cytology of Cutaneous Metastatic Nodules: An Institution Based Study

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Abstract

Background: Cutaneous metastases are quite rare and represent growth of malignant cells in skin from an internal malignancy and indicate poor prognosis. Fine needle aspiration cytology (FNAC) is an important technique in the early diagnosis of such lesions. **Objective:**To evaluate the cytomorphological features of cutaneous metastatic nodules on FNAC. **Material and Methods:** This retrospective diagnostic analytical study was carried out in the department of pathology from January 2016 to December 2020. Forty Four patients diagnosed as cutaneous metastasis on FNAC were included in the study. FNAC slides along with record of the patients were retrieved and findings recorded. The smears were examined in detail for cytomorphological evaluation.**Results:** 26 patients were males and 18 were females with M:F ratio of 1.4:1. The site of primary malignancy was known in 32 cases only. Chest wall was the commonest site of cutaneous metastasis, with solitary palpable skin nodule being the commonest clinical presentation. In patients with known primary, lung carcinoma and breast carcinoma were the commonest primary malignancy in males and females respectively. Metastatic adenocarcinoma was the commonest cytomorphological type of malignancy (31.8%) followed by squamous cell carcinoma (SCC). FNAC diagnosis helped in detecting the primary site in 5 (41.6%) out of 12 cases with unknown primary malignancy. **Conclusions:** FNAC is an easy, rapid and minimally invasive procedure in the diagnosis of cutaneous metastases.

Key Words

Skin, Metastases, Nodules, Fine Needle Aspiration Cytology, Cytomorphology

Introduction

Cutaneous metastases refer to the spread of tumour to the skin from the site of its primary origin [1] and indicate adverse prognosis for the patients. Vascular or lymphatic spread of primary tumour is responsible for cutaneous metastasis. In some cases, it may be the presenting feature of an underlying asymptomatic malignancy.[2] The prevalence of cutaneous metastasis increases with advancing age.[2] Breast, lung and gastrointestinal malignancies are the commonest primary malignancies which can cause cutaneous metastasis.[3,4] The incidence of cutaneous metastasis varies from 0.8 to 5%.[5] Skin

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biopsy is the commonest and most reliable method in the diagnosis of skin lesions. Fine Needle Aspiration Cytology (FNAC) of skin lesions is a relatively newer technique and has less popularity as compared to cytology at other sites.[6] There is limited application of FNAC in tumours of skin and subcutis presumably because of ease of surgical excision.[7] However FNAC is a rapid and easy technique in hands of experienced cytologists and is quite useful in differentiating benign and malignant tumours.[6] FNAC offers early and accurate diagnosis of cutaneous metastases in patients having known or unknown primary malignancies. So the study was undertaken to evaluate the cytomorphological features of cutaneous metastatic nodules on FNAC.

Material and Methods

This retrospective diagnostic analytical study was conducted in department of pathology in a tertiary care institute in north India. Approval from institutional ethics committee (Approval number: IEC/GMC/2021/598) was obtained before conducting the study. Forty Four patients diagnosed as cutaneous/subcutaneous metastasis on FNAC between January 2016 and December 2020 was included in the study. Patients with recurrent tumours and primary skin adnexal tumours were excluded from the study. The socio-demographic data pertaining to patient's age, sex and anatomical site were recorded from the requisition forms and data registers. Routine protocol followed in the Department for FNACs was adopted for the present study. Informed consent was obtained from all patients before undergoing FNAC. FNAC was performed using a 22-gauge needle and a 10-mL plastic syringe with a detachable syringe holder (Franzen Handle). Air-dried smears were stained with MGG stain and PAP smears were fixed in 95% ethyl alcohol. Special stains like periodic acid Schiff (PAS) were used whenever required. However, immunocytochemistry could not be performed due to financial constraints. The slides were examined by trained cytopathologists for cytomorphological findings and type of tumour. In case of any discrepancy, the diagnosis of senior cytopathologist was considered. In patients with known primary tumour, the sites of primary tumour were assessed. The data was analysed using standard analytic techniques. The quantitative variables were expressed as mean and qualitative variables were expressed as percentages.

Results

Forty Four patients with diagnosis of cutaneous metastasis formed the material of the study with age range of 12-72 years. Majority of the cases were seen in 51-60 years age group. Twenty six patients were males & 18 were females with male to female ratio of 1.4:1. Majority of the lesions were seen in the chest wall (36.3%) cases, followed by the abdominal wall (31.8%) and scalp (18.2%). Three lesions were seen in extremities while two cases were seen in neck. Solitary nodule was seen in 34 cases while multiple nodules were seen in 10 cases. Out of 44 cases, 32 (72.7 %) patients had a diagnosed primary malignancy while 12 (27.3 %) had no known primary malignancy. In patients with known primary malignancy, lung and breast cancer were the commonest tumour observed in our study (6 cases each). Lung cancer was the most common primary site in males (5 cases) while in females, the most common cancer with cutaneous metastasis was breast carcinoma (6 cases). Four cases each of colonic carcinoma [*Fig 1B*], Gall Bladder carcinoma and renal cell carcinoma (RCC) were seen. Two cases each of esophageal carcinoma and malignant melanoma [*Fig 2D*] and solitary case of urothelial carcinoma and rhabdomyosarcoma (RMS) [*Fig 1D*] were also seen (*Table 1*). On FNAC of cutaneous deposits, the commonest morphologic patterns were adenocarcinoma (11 cases) [*Fig 2A*] followed by poorly

Table 1. Distribution of Cases with known Primary (n=32)

Site of Primary	Sex M	Sex F	Site of the Lesion	FNAC Diagnosis
1. Breast	0	6	Chest wall (4), Scalp (2)	Adenocarcinoma (4), PD (2)
2. Lung	5	1	Chest wall (4), Scalp (1), Abdominal wall (1)	Adenocarcinoma (2), SCC (3), PD (1)
3. Gall Bladder	1	3	Abdominal wall (4)	Adenocarcinoma (2), PD (2)
4. Colon	3	1	Abdominal wall (4)	Adenocarcinoma (3), PD (1)
5. Kidney	3	1	Scalp (2), Chest wall (1), Abdominal wall (1)	RCC (4)
6. Urinary Bladder	1	0	Abdominal Wall (1)	PD (1)
7. Esophagus	1	1	Chest wall (2)	SCC (2)
8. Adrenal (NB)	1	1	Face (1), Scalp (1)	Small round cell tumour
9. Thigh (RMS)	0	1	Lower Limb (1)	Small round cell tumour
10. Skin	2	0	Lower Limb (2)	Melanoma

Table 2. Distribution of Cases with unknown Primary (n=12)

Cytological Diagnosis	Sex M	Sex F	Site of the Lesion	Detected Primary Site
1. Adenocarcinoma (5)	4	1	Chest wall (3), Abdominal Wall (1), Scalp (1)	Lung (1), Breast (1), Unknown (3)
2. SCC (3)	2	1	Chest Wall (1), Neck (2)	Lung (1), Unknown (2)
3. PD (2)	2	0	Abdominal Wall (2)	Unknown (2)
4. Medullary Carcinoma (1)	0	1	Chest wall (1)	Thyroid (1)
5. RCC (1)	1	0	Scalp (1)	Kidney (1)

Figure 1. A) Cutaneous metastasis in poorly differentiated carcinoma showing clusters of pleomorphic tumour cells (MGG stain; x100). B) FNAC smears in cutaneous metastasis from colonic adenocarcinoma showing individually scattered tumor cells with eccentric nuclei and abundant vacuolated cytoplasm (PAP stain; x400). C) FNAC smear in cutaneous metastasis of neuroblastoma showing clusters and individually dispersed round to oval cells with high nuclear: cytoplasmic ratio (PAP stain; x100). D) Aspirate from metastatic rhabdomyosarcoma showing fragments of oval to spindle tumor cells in a syncytium (PAP stain; x100).

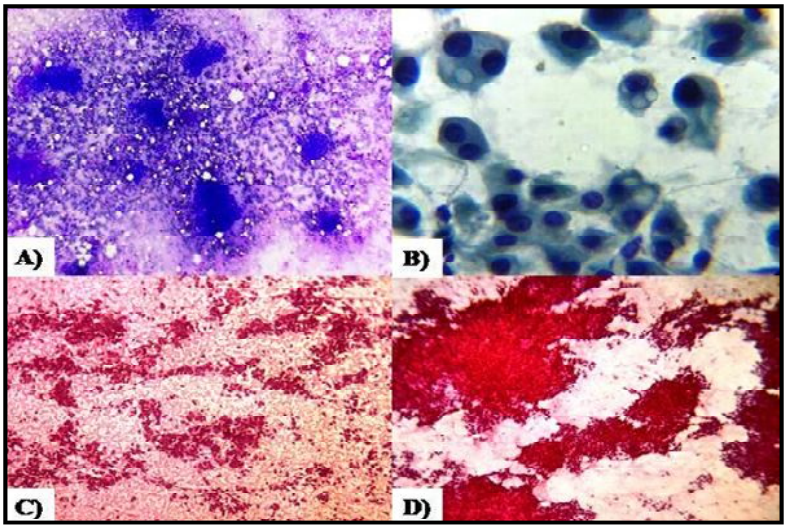
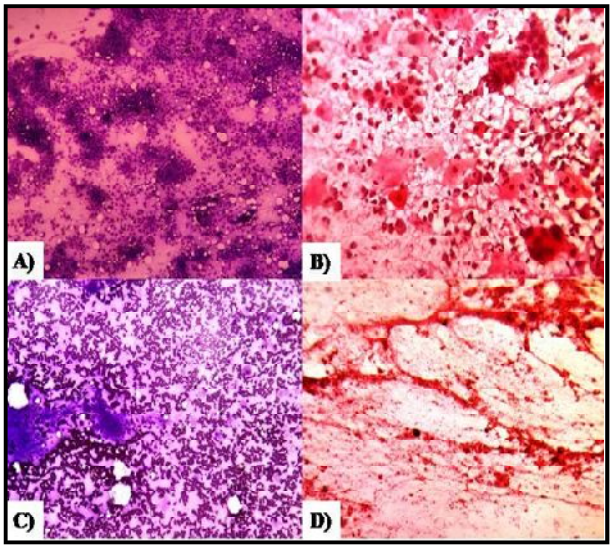


Fig 2. A) Cutaneous metastasis in the chest wall from Breast Carcinoma showing hypercellular smears with poorly cohesive clusters of malignant cells (MGG stain; x100). B) Cutaneous Metastasis to the chest wall from lung carcinoma showing features of SCC (PAP stain; x400). C) Cutaneous metastasis from RCC showing tumour cells with round nuclei and abundant clear to granular cytoplasm along with endothelial clinging of tumour cells (MGG stain; x100). D) Cutaneous metastasis from melanoma showing clusters and dispersed tumor cells, many containing cytoplasmic blackish-brown pigment (PAP stain; x100).



differentiated (PD) carcinoma (7 cases) [*Fig1A*] and squamous cell carcinoma (SCC) (5 cases) [*Fig 2B*]. On FNAC, three cases of small round cell tumour on FNAC were seen with primary sites being neuroblastoma [Figure 1C] and RMS (*Table 1*).

In 12 cases, primary site of malignant cancer was unknown (Table 2). In this group, chest wall was the most common site for cutaneous metastasis (5 cases) followed by abdominal wall (3 cases). Among these 12 cases, the cytomorphologic diagnoses on FNAC included adenocarcinoma (5 cases), SCC (3 cases) and two cases of PD carcinoma. Solitary case each of RCC [*Fig 2C*] and medullary carcinoma of thyroid were also seen. Following the FNAC diagnosis, the definite primary site could be identified with the help of imaging modalities (Magnetic Resonance Imaging/Computed Tomography) in 5 cases only. In rest 7 cases, the primary site of malignancy remained undetected as the patients did not underwent further investigations or were lost to follow up (*Table 2*).

Discussion

Numerous skin lesions manifest as nodular lesions including benign and malignant tumours. Cutaneous metastasis from internal malignancies represents diffuse metastatic disease and indicates poor prognosis.[6] Early detection of cutaneous metastasis is essential to initiate specific treatment with increased survival.[7] FNAC is a rapid, convenient and less invasive modality in suspected cases of cutaneous metastasis and obviates the need for other invasive diagnostic procedures.[8]

Cutaneous metastasis may result from direct extension, local spread through lymphatic channels or distant spread via the hematogenous or lymphatic route.[9,10] The molecular mechanisms responsible for cutaneous spread of metastasis are still not completely understood. It is believed that interactions between dermal/epidermal factors and tumor cells have a plausible role in the development of cutaneous metastasis homing mechanism of neoplastic cells.[10] Maximum cases in our study were seen in the 51-60 years age group followed by 31-40

years age group. Majority of patients were males with Male to female ratio of 1.4:1. Similar results were obtained by Gupta B *et al* [11] in their study.

Cutaneous Metastasis primarily appear as solitary or multiple, variable sized flesh-colored dermal or subcutaneous nodules which are usually painless.[12,13] However certain malignancies may have peculiar cutaneous deposits such as pulsatile red/purple-colored nodules in renal cell carcinoma.[14] All the cases in the current study presented as nodular lesions, similar to results of Gupta B *et al*.[11] The plausible explanation is that nodular lesions are easily amenable to FNAC and don't require surgical biopsies in majority of cases.[11]

In our study, chest wall and abdomen were the commonest site of cutaneous metastasis, similar to previous studies.[6] The abdominal wall is the preferred site for the primary from the gastrointestinal tract[15] while malignant lung and breast cancer show preference for the chest wall. Renal tumours have a predilection for the back.[16] The pattern of spread of cutaneous metastasis depends upon the mode of spread and the anatomic proximity of the primary tumour.[16,17]

In our study, the site of primary tumour was known in 72.7% cases while it was unknown in 27.3% cases. Adenocarcinoma was the commonest morphological pattern observed in our study. The results were similar to previously published studies in literature.[18] PD was the second commonest type of pattern observed in our study (21.9%) cases followed by SCC (15.7%). In patients with unknown primary, adenocarcinoma was the predominant type seen in 41.7% cases, similar to previous studies.[19]

In patients with cutaneous metastasis from an unknown primary site, the aim of FNAC is to provide appropriate cytological diagnosis to identify the site of primary tumour. This can guide the clinician to order appropriate investigations for diagnosing primary tumour. Signet ring cells with intracellular mucin points towards stomach as the primary site while cell balls or cells arranged as single file may be seen in invasive carcinoma of breast.[19] In suspected thyroid malignancies, microfollicular pattern is seen while malignant melanoma shows prominent nucleoli, spindle cells or plasmacytoid cells. Simultaneously, immunocytochemistry may also be used to suggest the possible primary site in these cases. Although majority of cutaneous metastasis can be reliably diagnosed on FNAC, in some cases differentiation from primary skin Adnexal tumour is quite challenging. Sebaceous neoplasms or clear cell hidradenoma can mimic metastatic renal cell carcinoma or a clear cell variant of SCC.[20] PAS-positive diastase-sensitive reaction points towards renal origin while orangeophilia on PAP stain and a negative fat stain using oil red O indicate SCC.[21]

Our study had few limitations. First it was a retrospective study. Second limitation of the study was that approximately 1/4rd of the subjects had unknown primary tumour and the confirmed site of primary tumour in majority of these patients could not obtained due to lack of immunocytochemistry in the institution.

Conclusion

Thus we conclude that FNAC is a quick, minimally invasive and reliable technique in the diagnosis of cutaneous metastases. Cutaneous metastatic lesions have significant therapeutic and prognostic implications and FNAC is the primary investigation in the confirmation of these lesions. Cytomorphology on FNAC along with relevant investigations helped in diagnosing an unknown primary in few cases and provides a reliable alternative to histopathology in a low resource setting

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Conflicts of Interest
There are no conflicts of interest.

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