

FNAC of cutaneous metastatic nodules; a clinicopathologic study with review of literature

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Abstract: *Background:* Cutaneous metastasis (CM) from an underlying carcinoma is not an uncommon event. The incidence epidemiology and prognosis of these patients is poorly known. *Aims:* This study attempts to find out, the prevalence of metastasis in cutaneous nodules. The associated clinical features, the age, sex distribution of these patients, and distribution of primary lesions in patients presenting with CM are to be sought. *Methods:* In this study 381 patients with cutaneous nodules referred mostly from different OPD's underwent FNAC in our clinic. FNAC was done by standard methods using 18-22 gauze needle, and slides stained by Romanowsky, PAP, or H& E alone or in combination. All relevant clinicopathological data were collected during FNAC. *Results:* Out of 381 patients, 16 were found to be suffering from CM. Carcinoma of breast, ovary, lung, colon were the most common offenders. No definite age and sex predilection was noted in this study. CM may also be the presenting sign of the disease. It was found that CM usually implies very poor prognosis. *Conclusion:* As CM is not a very uncommon event, and it carries a poor prognosis, a high index of suspicion is to be maintained among clinicians and pathologists to diagnose this condition earliest.

Keywords: Metastases, cutaneous, nodule

Introduction

CM from an underlying carcinoma is an well known complication. The incidence of such skin involvement is about 5% in standard literature [1]. Though some data regarding incidence, prevalence, and prognosis of these patients are available for western countries similar information from our country is lacking. This study attempts to find out the distribution of CM, with reference to site, type of malignancy, and common primary site.

Material and Methods

This study was carried out in the Department of Pathology in a government hospital. The study spanned 1.5 years and the study population consisted of 381 patients who presented with

cutaneous nodules, and were referred to us for FNAC. The study included patients referred from different OPD's as well as those admitted in our own hospital. All relevant clinical data was collected from the patient's records. FNAC was done by standard procedure after taking informed consent of the patients, by 18 to 22 gauze needle attached to a 10ml syringe. The slides were stained by PAP, Romanosky, H&E, alone or in combination wherever necessary.

Results

Among the 381 patients who underwent FNAC for any cutaneous nodules, 16 (4.2%) were diagnosed to be having CM from some underlying carcinoma. The results are summarized in table 1.

Table-1: Case Summary

Age range	Sex	Site of swelling	Size range	Type of swelling	Primary tumor
4.5yrs To 80 years	Male-8 Female-8	Abdominal wall-4 Chest - 6 Back - 5 Calf -1	2x1.5 cm To 11.5x10 cm.	Painless nodule-11. Indurated erythematous lesion-3 Ulcerated lesion-2	Ovarian carcinoma- 4. Breast carcinoma-3 (all ductal) Lung carcinoma-3 (2adeno, 1scc) Unknown primary-2. (1adeno, 1scc) Colonic carcinoma- 1. Chloroma - 2. Lymphoma -1.

As seen in the present study; CM can occur in patients as young as 4.5 yrs to as old as 80 yrs; however most commonly the middle age is affected. No sex predilection was noted either, M:F -1:1 (male-8 & female-8). The onsets of these lesions were insidious and most of them occurred in the trunk, extremities were uncommon. In most of these cases the lesions presented as painless nodules (11 cases 68.75%), in some (3cases 18.75%) as indurated erythematous lesions and in some other cases (2cases 12.5%) as ulcerated lesions. In most of the cases the lesions were small, the smallest that

we found were 2X1.5cm. however, the biggest that we encountered was 11.5X10cm. In 14 out of 16 cases (87.5%) the primary lesion could be traced to ovary (25%), breast (18.75%), lung, (18.75%), colon (6.25%), lymphoma (18.75%), or chloroma. However in 2 cases (12.5%) the primary lesion could not be traced (unknown primary) and patient was lost to follow up. One of these lesions were an adenocarcinoma and the other was a squamous cell carcinoma. Detailing of the individual cases is done in table no 2.

Table-2: Clinicopathologic details of all 16 cases

Case	Year	Case history	Clinical findings	Relevant findings	Clinical presentation	FNAC from the lump
Case no 1	50 yrs, female	FU case of ovarian mucinous cystadenocarcinoma	2 X2 cm sized nodule on anterior abdominal wall	Patient had peritoneal effusion	Painless nodule.	Ovarian carcinoma (surface epithelial type)
Case no 2	38 yrs, female	FU case of ovarian serrous cystadenocarcinoma	3 X2 cm sized nodule on anterior abdominal wall	Blood showed increased CA-125 level.	Nodule with central ulceration	Ovarian carcinoma (surface epithelial type)
Case no 3	45 yrs, female	FU case of ovarian mucinous cystadenocarcinoma	3.5 X 2 cm nodule on lower abdomen	Patient had peritoneal effusion	Painless nodule.	Ovarian carcinoma (surface epithelial type)
Case no 4	44 yrs, female	FU case of ovarian serrous cystadenocarcinoma (fig -1a)	2X3 cm swelling in left lumbar region	Blood showed increased CA-125 level.	Painless nodule.	Ovarian carcinoma (surface epithelial type)
Case no 5	48 yrs, female	Known case of ductal carcinoma (Fig- 1b)	3X 3 cm sized chest wall swelling.	Patient underwent MRM and received chemotherapy.	Painless nodule.	Metastatic ductal carcinoma
Case no 6	55 yrs, female	Known case of ductal carcinoma	Huge 11.5X 10 cm swelling at axilla	Patient underwent MRM and received chemotherapy earlier.	Indurated erythematous lesion.	Metastatic ductal carcinoma
Case no 7	37 yrs, female	Known case of ductal carcinoma (Fig- 1c)	4X4 swelling on chest wall	Patient underwent MRM and received chemotherapy.	Indurated erythematous lesion.	Metastatic ductal carcinoma

Case	Year	Case history	Clinical findings	Relevant findings	Clinical presentation	FNAC from the lump
Case no8	80 yrs male	A case of disseminated lung adenocarcinoma (fig-1d)	5x4 cm swelling over the sternum.	CXR showed a tumor in left lung	Painless nodule	Metastatic lung carcinoma
Case no9	60 yrs male	A case of disseminated lung adenocarcinoma	3X2 cm Swelling on the back.	CXR showed pleural effusion, cytology showed malignant cells.	Indurated erythematous lesion.	Metastatic lung carcinoma
Case no10	59 yrs male	Admitted with subacute intestinal obstruction and was diagnosed to have colonic carcinoma	3X3 cm nodule on left flank.	He was also found to have multiple metastatic nodules in the liver.	Painless nodule	Metastatic colonic carcinoma
Case no11	45 yrs female	Primary was unknown. (fig-2a, 2b)	A 3X2.5 cm hard swelling on right scapula.	Patient lost to follow up.	Ulcerated lesion	Metastatic adeno carcinoma
Case no12	63 yrs male	Patient was having squamous cell CA lung. (fig-2c)	A 2X 4 cm on left thigh.	Patient died in hospital	Painless nodule	Metastatic squamous cell CA
Case no13	52 yrs male	Primary was unknown. (Fig-2d, 3a)	2.5X2.5 cm Calf swelling.	Patient had a 2cn cervical LN too. Patient was lost to follow up.	Painless nodule	Metastatic squamous cell CA
Case no14	4.5 yrs male	Pt was admitted for intestinal obstruction & was found to have a high grade gastrointestinal lymphoma following laporotomy.	Patient reported with multiple small (<1cm) non-tender nodules on back.	Hemogram was unremarkable.	Painless nodule.	NHL
Case no15	48 yrs male	Patient was eventually diagnosed to have AML following bone marrow examination. (fig-3b)	Patient presented with two small subcutaneous nodules (2cm) in neck & abdominal region.	Hemogram showed anemia, thrombocytopenia, & neutropenia.	Painless nodule.	chloroma
Case no16	45 yrs male	Known case of CML	Presented with 3 firm swellings (2.5X2.5cm largest) on back.	Pt showed hepatospleenomegaly, anaemia and PBS showed picture of CML.	Painless nodule.	chloroma

Fig-1a: Ovarian serrous cystadenocarcinoma showing pleomorphic cells with high N/C ratio.

Fig-1b: Ductal carcinoma breast metastasizing to chest wall (x400).

Fig-1c: Another case of Ductal carcinoma breast metastasizing to chest wall (x100).

Fig-1d: Disseminated lung adenocarcinoma, cells are arranged in aciner pattern (x400).

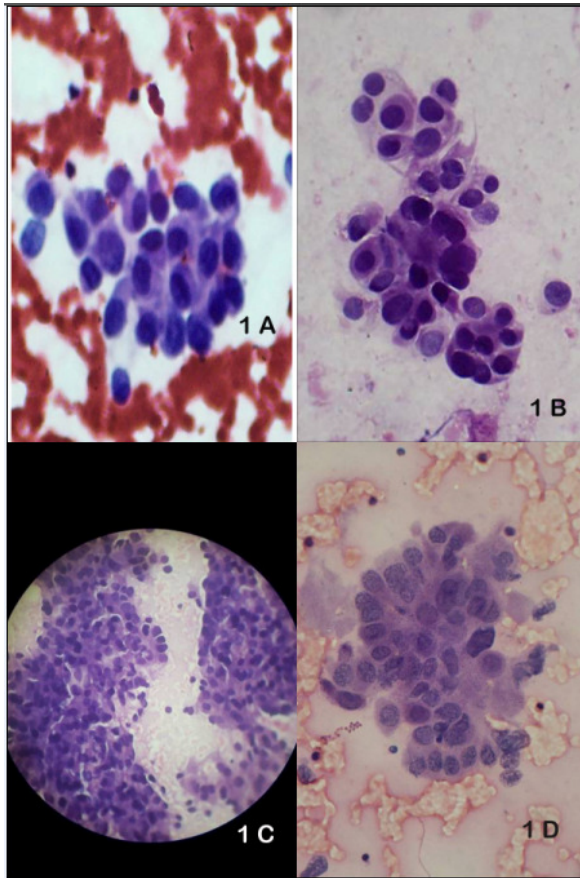


Fig-2a: Adenocarcinoma with unknown primary metastasizing to scapula (x 100)

Fig-2b: Same case as 2a, but under higher power (x400).

Fig-2c: Squamous cell carcinoma metastasizing to thigh (x100).

Fig-2d: Squamous cell carcinoma with unknown primary metastasizing to calf. (x100).

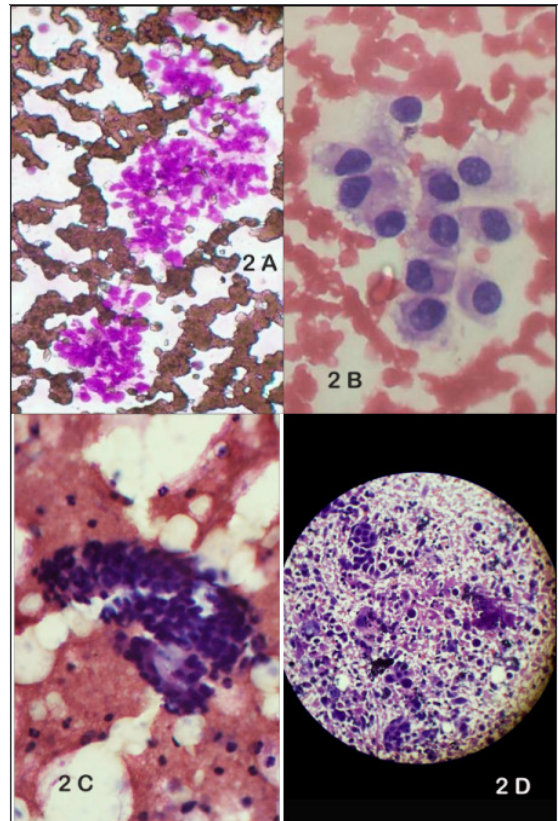
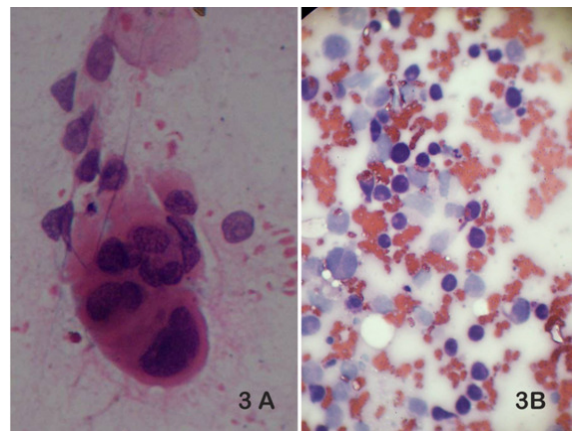


Fig-3a: Same case as 2d, under higher power (x400), to show orangophillia under PAP stain.

Fig-3b: A case of granulocytic sarcoma showing immature cells of myeloid lineage.



Discussion

Cutaneous metastasis (CM) implies spread of malignant cells from any internal malignancy to skin, or metastasis from a primary skin cancer. The metastatic cascade occurs in an

orderly stepwise process where cells from a primary malignant tumor are gradually shed off, migrate to a nearby blood vessel or lymphatic, enter it and move elsewhere to form a distant colony of malignant cells at a different site. To establish this aim, tumour cells need to secrete various growth factors, proteases, collagenases, and other enzymes. They also need to evade host anti-tumor defenses, apoptosis, and promote angiogenesis at the distant site. This is established by activation of different oncogenes, and loss of various tumor suppressor genes. Thus the transformed cell acquires selective growth advantage, and is able to grow autonomously, evade apoptosis, promote angiogenesis, and has capacity of invasion, tissue destruction and metastasis. The cell which has the exact genetic machinery to accomplish all these tasks sequentially is selected in a process analogous to Darwinian natural selection to form a metastatic clone within the primary tumor, and metastasis will ultimately occur from these group of cells.

There may be a long time lag between the diagnosis of the primary cancer and the detection of the cutaneous metastasis. Generally carcinomas, melanomas & hematolymphoid malignancies have the greatest propensity to go to skin [1]. Among 381 patients who underwent FNAC in our cytology clinic for some cutaneous nodules, 16 cases were having CM. (4.199%). This is similar to what we find in the standard literature in the classic study conducted by Lookinbil et.al who found the incidence of CM to be about 5% in his study [1]. The primary lesions usually lied in breast, ovary, lung, colon or as melanomas [1-2]. In our study, (18.75%) cases were from breast and lung, 25% from ovary, 6.25% each from colon & lymphomas. Brownstein said that breast, ovary & colon constituted the common sources of CM in women and lung, colon & oral cavity in men [2]. In our study too the results were not dissimilar. However Brownstein found melanoma as the source of CM in 15% patients (specially in men); surprisingly, we did not find any case of melanoma in our series of CM. This may be due to smaller size of our study population.

We found ovarian carcinoma in 25% of cases producing CM. All were surface epithelial tumors (2 serous & 2 mucinous). A similar study conducted by A Moussa [3] reported 36 such

cases of ovarian carcinoma causing CM. Most patients were having advanced surface epithelial tumors mostly of serous type. In our case too all four patients were in advanced disease with two having malignant cells in their peritoneal washings.

Lung was another common source of CM, in this study there were two patients having CM from lung. (one squamous & one adenocarcinoma). It is generally seen that about 50% & 80% of non-small cell & small cell lung carcinomas are metastatic at the time of diagnosis [4]. Another study by Hidaka T said that CM occurs in 2.8% of lung cancers [5]. Site of CM is usually in trunk, and prognosis was dismal with median survival about four months, they concluded [4-5]. In our case too CM was located in chest wall (trunk) and both the patients were in advanced disease. In women breast cancer is the commonest source of all CM, ductal carcinoma being the commonest culprit to produce cutaneous nodules [6]. Metastasis commonly occurs in chest wall. Breast cancer is the commonest cancer to produce CM in the western world. In our study too all three cases of CM were from ductal carcinomas with chest wall metastasis. However the incidence of CM due to breast cancer was lower in our study (18.75%), w.r.t western population

In men colonic cancer was another common primary lesion. It usually occurs in abdomen & perineum in patients of advanced colonic carcinomas but rarely may occur in the head & neck region also [1,7]. In our study however we found a solitary case of CM in the abdominal wall from a case of adenocarcinoma colon.

Regarding lymphomas NHL (B cell type) usually produce cutaneous nodules [8]. Most commonly the scalp is involved [8]. In our study two cases of NHL were found, both located at the back. About chloromas it is seen that 2 to 15% of leukemias may have chloromas [9]. Microscopically myeloid cells in different stages of maturation are found, eosinophilic metamyelocyte being the diagnostic cell. In our case the patient was a known case of CML.

Conclusion

Thus to conclude we can say that subcutaneous nodules though usually benign, but may also be malignant. CM usually denotes advanced disease with poor prognosis. The common primary sites are ovary, breast, lung, colon. Rarely CM may be the first presenting sign of an occult malignancy.

As CM indicated a poor prognosis, with advanced disease, a high index of suspicion is to be maintained in patients suffering from cancers & biopsy performed without delay for non-healing ulcers, persistent indurated erythema & unexplained skin nodules to diagnose this condition earliest.

References

1. Lookingbill DP, Spangler N, Sexton FM. Skin involvement as the presenting sign of internal carcinoma. A retrospective study of 7316 cancer patients. *J Am Acad Dermatol*, 1990;22(1):19-26
2. Brownstein MH. Metastatic tumors of the skin. *Arch Dermatol*, 1973;107: 80.
3. Adnène Moussa, Walid Denguezli, Leïla Njim, Anis Haddad, Raja Faleh, Mohamed Sakouhi, *et al.*. Skin metastases revealing a bilateral ovarian invasive micropapillary serous carcinoma. *Archives of Gynecology and Obstetrics*, 2007; 278(1):71-74.
4. Perng DW, Chen CH, Lee YC, Perng RP. Cutaneous metastasis in lung cancer; an ominous prognostic sign. *Zhonghua Yi Xue Za Zhi (Taipei)*, 1996; 57: 343.
5. Hidaka T, Ishii Y, Kitamura S. Clinical features of skin metastasis from lung cancer. *Intern Med*. 1996; 35(6):459-62.
6. Vilmer C, Trassard M. A case for diagnosis: cutaneous metastasis of breast carcinoma. *Ann Dermatol Venerol* 1993; 120: 561.
7. Stavrianos SD, McLean NR, Kelly CG, Fellows S. Cutaneous metastasis to the head & neck from colonic carcinoma. *Eur J Surj Oncol*, 2000; 26:518.
8. Wiernick PH, Serpick AA; Granulocytic sarcoma (chloroma) *Blood*. 1970; 35: 361-69.
9. Mason TE, Damree R Margolis CI; Granulocytic sarcoma 2 yrs preceding myelogenous leukemia; *Cancer*, 1973; 31:423-32.

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