

Case Report

Cutaneous metastasis as presenting feature of internal malignancy - report of two cases

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Abstract Cutaneous metastasis (CM) from internal malignancy is usually seen in advanced stage and hence is associated with bad prognosis. Sometimes, CM alone is a presenting feature without any obvious feature of internal malignancy. High index of suspicion and histopathology can establish the diagnosis of CM. Identification of underlying malignancy is based on clinical features, histopathology, immunohistochemistry and other investigations. CM was the presenting feature in our cases and identification of CM led to search for underlying malignancy and then initiation of therapy.

Key words

Cutaneous metastasis, internal malignancy.

Introduction

Cutaneous metastasis (CM) from internal malignancy is relatively uncommon (5.3%)¹ and is historically associated with advanced disease and hence bad prognosis; 50% of patients have evidence of secondaries at other internal sites.² CM at presentation 1.3% and as presenting feature 0.8% is even rare.³ CM as presenting feature is of particular importance to dermatologists as they are in best position to suspect CM and initiate search for internal malignancy. We, here, report two cases presenting with CM, with primary in gallbladder in one case and in liver in the other.

Case 1

A 65-year-old male presented with multiple skin-colored to erythematous nodules of variable size over forehead, trunk and extremities for last

2 months. It was first noticed over the left knee as pea-sized painful lesion. It gradually increased in size to 4cm and became ulcerated. Over time new lesions appeared on face, trunk and extremities. They kept increasing in size but did not ulcerate. There was history of weakness and occasional upper abdominal pain for the last one year and he has significant weight loss in this period. He used to take alcohol once or twice a week for last 20 years. Rest of the history was unremarkable. On examination multiple skin-colored subcutaneous nontender nodules were found on face, trunk (**Figure 1**) and extremities (**Figure 2**).

The nodules were of variable size from 6mm to 5cm and were nontender, hard and fixed to overlying skin but not underlying structures. Only the lesion over left knee was having ulcer and was covered with crust and necrotic material. Rest of the mucocutaneous examination was unremarkable. Systemic examination revealed nothing but pallor. Our differential diagnosis included leukemia cutis, lymphoma, multiple lipoma and cutaneous

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Figure 1: Subcutaneous nodules on face and trunk.

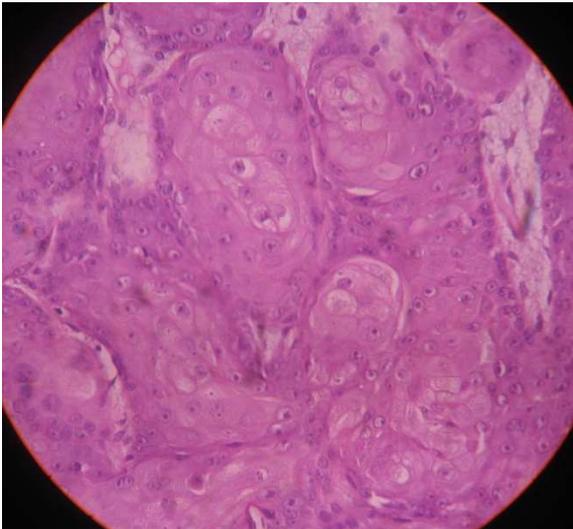


Figure 3 Squamous cells with tendency towards keratinization.



Figure 5 Multiple erythematous nodules on chest. Large one is ulcerated.



Figure 2 Erythematous nodule on forearm.



Figure 4 Computed tomography of abdomen.

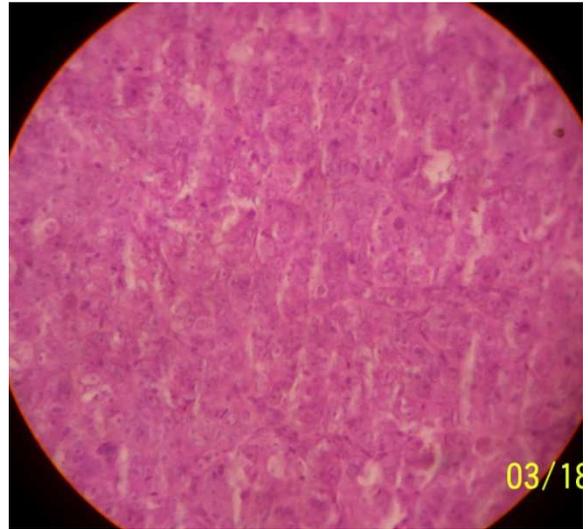


Figure 6 Strands of squamous cells with numerous mitotic figures (H&E X 400).

metastasis from internal malignancy. Routine investigations showed hemoglobin 7.8 mg/dl, increased liver enzymes and increased cholesterol and triglycerides. Histopathology of the nodule showed thinned epidermis with dermis full of irregular masses of 'foreign' tumor cells. These masses had squamous cells

with ample cytoplasm and anisocytosis and numerous mitotic figures. Some tendency towards keratinization was noted (**Figure 3**). These findings were consistent with the diagnosis of CM. However, histopathology did not prove to be useful for identification of focus of internal malignancy.

Ultrasonography (USG) of abdomen provided the much needed help. It showed irregular mass of heterogeneous echogenicity in gall bladder fossa with enlarged lymph nodes and dilated portal vein. There were foci of hyperechoic mass in surrounding liver tissue. USG features were suggestive of gall bladder carcinoma with liver metastasis. Computed tomography (CT) scan of abdomen was done and confirmed malignancy of gall bladder with liver metastasis (**Figure 4**).

Patient was diagnosed with gall bladder carcinoma with liver and cutaneous metastasis and was referred to Medical Oncology department of our institution for further evaluation and management. He was found to be inoperable and was started on radiotherapy.

Case 2

A 70-year-old female presented with multiple painful erythematous nodules over trunk and extremities for 3 months. It first appeared over chest as small painful nodule and increased in size. Soon few satellite lesions developed around the chest lesion and merged with it. Over time new similar lesions developed on trunk, genitalia and head and neck including scalp. All lesions were painful and gradually increased in size. Few of them developed central ulcer. She gave history of weakness, anorexia, intermittent fever and mild intermittent discomfort in upper abdomen for last 1 year. She had not lost

significant weight in recent past. Rest of history was unremarkable.

On examination, multiple erythematous tender nodules were found on scalp, neck, trunk (**Figure 5**) and genitalia, distributed randomly. Nodules were of variable size ranging from 5 mm to 3 cm and were tender. They were firm and fixed to skin but not to underlying structure. Chest and genitalia lesions were ulcerated and were covered with necrotic debris. Rest of the mucocutaneous examination was unremarkable. Systemic examination revealed pallor and cervical lymphadenopathy. Cervical lymph nodes were enlarged (1.5-2 cm), firm to hard, non tender and were fixed to surrounding tissue.

Primary B cell lymphoma, leukemia cutis and cutaneous metastasis were considered as differential diagnosis. Routine examination revealed anemia (microcytic hypochromic), increased liver enzymes and increased serum lactate dehydrogenase (LDH). Fine needle aspiration cytology (FNAC) from chest lesion showed features of malignant epithelial tumor. Biopsy was taken from chest lesion and it showed thinned epidermis with dermal masses with 'foreign' tumor cells. Dermis had strands of squamous cells with ample cytoplasm and numerous mitotic figures (**Figure 6**). However, there was no tendency towards keratinization. Again, histopathology was unhelpful in locating internal malignancy.

USG of whole abdomen revealed a large space occupying lesion (SOL) of 12.5 cm X 5.2 cm in right lobe of liver. It was irregular in shape and of heterogeneous echogenicity with foci of reduced echogenicity (necrotic areas). A small stone (1.7cm) was found in gallbladder. USG features were suggestive of malignant lesion in liver. Patient was advised USG guided FNAC from liver SOL and CT of abdomen and was

referred to Medical Oncology department of our institution.

Discussion

Cutaneous metastases (CM) from internal carcinomas are relatively rare (5.3%)¹ and may present in three different settings: patient with a known malignancy developing CM, patient presenting with CM along with obvious systemic features of malignancy and those presenting with CM without any obvious malignancy. It is the later group where dermatologists can play a significant role in raising suspicion and initiating the search for underlying malignancy. Clinical examination, histopathological examination of CM and immunohistochemistry in doubtful cases can establish the primary malignancy in patients presenting with CM.

CM from one organ may be indistinguishable from that arising from another, making the diagnosis of primary malignancy quite difficult. CM usually presents as firm to hard, painless, mobile, skin-colored or erythematous, dermal or subcutaneous nodule, which may ulcerate.⁴ The nodules may be single or multiple; and when multiple, they may be localized or scattered diffusely.⁴ However, some metastases do have a distinct clinical appearance and whenever present, they are an important diagnostic clue. For example, carcinoma erysipeloides (sharply demarcated, elevated, red plaque mimicking erysipelas), carcinoma telangiectoides (red papules and telangiectasia) and carcinoma *en cuirasse* (dusky indurated skin with an orange peel appearance) are not specific to, but most commonly seen in, breast carcinoma.⁵ Whereas blue to black CM is usually indicative of melanoma; a prominent vascular appearance and granuloma pyogenicum like lesion have been described for CM from renal cell carcinoma.^{4,5}

Zosteriform CM is commonly seen in breast and prostate cancer while blueberry muffin-like lesions are seen in neuroblastoma.⁵ Cutaneous metastases are generally in the anatomic vicinity of the primary cancer and this could serve as a clue to location of primary.^{4,5} Evidently CM mostly localized to abdomen are from GI tract, uterus, cervix and ovary tumors and those localized to anterior chest are usually from breast and lung cancers. Involvement of upper and lower extremities is quite rare and when present, is usually from melanoma. However, distant metastases, too, are known. For example, subungual metastasis has been seen from lung, kidney and breast cancers and carry extremely poor prognosis.^{5,6}

Apart from clinical examination, histopathology of cutaneous lesions is of paramount importance in localizing primary malignancy. In most of the situations, CM has histological features either identical to or very similar to those of primary malignancy, thereby allowing diagnosis of primary malignancy.⁴ In general, tumor cells appear 'foreign' and have some of the features of primary malignancy, which help dermatopathologists in identifying primary malignancy e.g. goblet cells may be seen in CM of colonic origin.⁷ A 'commonsense approach' to the histological diagnosis of the CM deserves mention.⁴ The most common oncologic patterns of CM are adenocarcinoma, squamous cell carcinoma and melanoma. Adenocarcinoma CM has been most commonly associated with breast, colon and lung cancer. Squamous CM are typically from oropharynx and lung. CM melanoma is most commonly from skin.⁴ However, histopathology was not useful enough in locating primary malignancy in our cases.

Immunohistochemistry is another important tool in establishing organ of origin when histology is not conclusive^{4,7} e.g. CK-7 and CK-20

immunostaining will allow differentiation between colorectal and pulmonary adenocarcinoma. Most colorectal adenocarcinoma show CK7/CK20⁺ pattern while pulmonary adenocarcinoma show reverse pattern.⁷ So, immunostaining for organ specific molecules will help in establishing primary malignancy in doubtful cases.

Primary carcinoma of the gallbladder spreads by extension and metastases, the former occurring earlier and more often. The liver is most frequently involved by direct extension, with an incidence ranging from 60% to 90%.⁸ Metastases occur most frequently to the liver (76%-86%), while regional lymph nodes are involved in about 60% of cases.⁸ CM is seen in 5.5% cases.⁴ The most common histological type of malignancy of the gallbladder is adenocarcinoma.⁷ The occurrence of metastatic adenocarcinoma from the gallbladder to the skin is rare, with only nine reported cases.⁹ Cutaneous metastases were located on the preauricular area, upper lip, umbilicus, scalp, neck, upper arms, and back. The lesions were described as nodular, smooth, and red-brown (as in our case).⁹ Only one case showed epidermal invasion with ulceration.¹⁰ The presence of cutaneous metastases is a grave prognostic indicator, with an average survival time of 7.5 months.⁹ CM from gallbladder as presenting feature is well known and has been reported by Kronic *et al.*¹¹ and Pandey *et al.*¹² All such cases are gallbladder adenocarcinoma. Our case is unique as it is first reported case of squamous CM from gallbladder malignancy. Cardiac metastasis is a rare known entity in such cases. Total of four cases have been reported, two from squamous carcinoma of gall bladder.¹¹

Most common site of hepatocellular carcinoma (HCC) metastases are the lungs, followed by the periportal lymph nodes and the bones.¹³ Skin

metastases from HCC are very rare (5%).¹⁴ Iatrogenic CM too has been described.¹⁵ CM has been described as rapidly growing nodules found mostly on the face, scalp, chest and shoulders (as in our case). The lesions appear singly or in multiples as firm, painless, non-ulcerative, reddish nodules which are approximately 1 cm to 2.5 cm in diameter. Other lesions are larger and have been described resembling pyogenic granuloma or hemangioma, both of which bleed easily and grow rapidly.^{16,17} CM can present as the first clinical sign of HCC.² Our case was unique as she developed ulceration of lesions.

Our cases were unique in the sense that CM was the only presenting feature with no obvious symptoms suggestive of underlying malignancy. The high index of suspicion and histopathology led to diagnosis of CM. However, histopathology was unhelpful in locating primary malignancy, contrary to popular opinion in literature.⁴ USG came to rescue in both cases and led to identification of primary malignancy. We recommend routine USG in suspected cases of CM. We believe dermatologists should have a high index of suspicion while dealing with multiple subcutaneous nodules even when there are no obvious features of malignancy.

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