

## Malignant Cutaneous Infiltration and Metastasis in Baghdad, a Prospective Study

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### ABSTRACT:

#### BACKGROUND:

Cutaneous metastases and malignant infiltrations occur in 1% to 10% of patients with metastatic disease (to any organ). Their recognition is important because they have profound prognostic implications.

#### OBJECTIVE:

To evaluate cutaneous metastases and infiltrations in a population of Iraqi patients.

#### PATIENTS AND METHODS:

Cutaneous malignant infiltrations were diagnosed in (30) patients (23 F, 7 M) attending the dermatology clinic at Baghdad Teaching Hospital during a period of 21 months. All patients were evaluated clinically; a biopsy was obtained for routine H/E examination and special stains when indicated. Patients were evaluated for presence of internal malignancy by proper investigations including U/S, CT when indicated.

#### RESULTS:

The age of patients ranged from 37 to 75 years with a mean  $\pm$ SD (52.66 $\pm$  10.08) years. The most common primary cancer was breast cancer followed by malignant melanoma. The most common site for cutaneous infiltrations was chest followed by back then abdomen. Regarding the clinical presentation, the most common presentation was dermal and subcutaneous nodules, followed by carcinoma erysipeloides. Nine patients presented with cutaneous infiltration without a history of previous cancer, in the rest of patients the mean duration between the discovery of primary and secondary tumors  $\pm$ SD (26.9  $\pm$ 19.2) months. The most common histopathological findings were dermal nodules, Indian filing, and signet ring cells. Intravascular invasion was detected in 7 patients.

#### CONCLUSION:

Cutaneous malignant infiltration is a common problem facing dermatologist with variable presentations. It can be the presenting sign of internal malignancy or follows the discovery of tumor by many months.

**KEY WORDS:** Cutaneous malignant infiltration, breast cancer, malignant melanoma.

### INTRODUCTION:

Cutaneous metastases and malignant infiltrations represent an important dermatologic entity. From 5% to 10% of patients with cancer develop skin metastases.<sup>(1)</sup> Their recognition is important because they can be the presenting sign of an internal malignancy (<1% of all new cancer diagnoses)<sup>(2,3)</sup> and, as a result, have profound prognostic implications.

In general, cutaneous metastases develop an average of 36 months<sup>(4)</sup> (range 1 to 177 months)<sup>(5)</sup> after the initial diagnosis of the primary malignancy. Metastasis to the skin occurs as a result of lymphatic or haematogenous

dissemination of tumour; direct infiltration of the skin by an underlying tumour and, rarely, iatrogenic implantation.<sup>(1,6)</sup>

Cutaneous metastases generally present as solitary or multiple nodules, erysipeloid-like carcinoma, carcinoma en cuirasse, telangiectatic metastatic carcinoma, alopecia neoplastica.<sup>(1,4)</sup> Breast carcinoma cutaneous metastasis rarely presents as dermatitis-like lesion.<sup>(7)</sup> Less common patterns of direct tumour invasion include breast carcinoma presenting as an inframammary intertrigo-like pattern.<sup>(8)</sup> Certain metastases can have a more unique clinical appearance, e.g. both Paget's disease and extramammary Paget's disease may resemble dermatitis.

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### PATIENTS AND METHODS:

This observational study was conducted at Baghdad Teaching Hospital/ Medical City during the period between November 2014 and August 2016 (21 months). All patients consulting the dermatology outpatient clinic who were proved to have cutaneous malignant infiltrations were enrolled in this study. Total of (30) patients were included, thirteen patients were referred from other departments of the hospital, while seventeen patients consulted as outpatient.

Full history was taken from every patient regarding age, occupation, residence, chief complaint and its duration, the duration of diagnosis of primary malignancy, duration of skin lesions, symptoms, family history and drug history. Then physical examination was done concentrating on the site of skin lesions, morphology, color, size and number of lesions and any associated features.

Biopsy was done at dermatology clinic for 27 patients while the other patients were diagnosed previously with cutaneous infiltration at oncology department. Biopsies were sent for routine H/E stain and immunohistochemical study was performed to eight patients (CK7, CK20, LMW and HMW CK, vimentin, Her2/neu, CD10, EMA, Melan-A, HMB 45, GCDFP-15 ,RCC marker, CA 125, ER, PR, TIF-1 and E-cadherin). Patients were evaluated for internal malignancy by proper investigations including X-Ray, ultrasound and CT scan when indicated.

### RESULTS:

Total of 30 patients were included in this study; 7 male patients and 23 female patients. Male to female ratio was 1:3.3. The age of the patients ranged from 37 to 75 years with a mean  $\pm$  standard deviation (SD) ( $52.66 \pm 10.08$ ) years, and median of 50 years. Table (1) shows the number of patients in age groups.

Twenty one patients had history of previous primary malignancy, while in 9 patients the cutaneous infiltrations were the initial clinical presentation. The primary neoplasms in patients without previous history of malignancy were as follows; 3 patients with mammary Paget's disease, 2 patients with extramammary Paget's disease, 2 patients with renal carcinoma and 1 patient with local invasion of breast cancer at presentation and in 1 patient no primary malignancy could be detected even after investigations.

The time period between diagnosis of primary malignancy and the appearance of cutaneous malignant infiltrate ranged from 3 months to 64

months, and the mean  $\pm$  SD was ( $26.89 \pm 19.2$ ) months, and the median was 22 months. Table (2) shows the time period between diagnosis of primary malignancy and the appearance of cutaneous malignancy in 19 patients in whom there was a time lag between the diagnosis of primary malignancy and appearance of secondaries. The time period was not known in 2 patients.

Regarding the origin of primary malignancy; breast cancer was diagnosed in 20 patients (66.66%), malignant melanoma (figure 1) in 3 patients (10%), renal cell carcinoma in 2 patients (6.66%), extramammary Paget's disease in 2 patients (6.66%), gastric carcinoma in 1 patient (3.33%) and parotid cancer in 1 patient (3.33%) and cutaneous metastases from unknown primary origin in 1 patient (3.33%). Table (3) shows the primary malignancies in male and female patients and their percentages.

The most common affected site was the chest, followed by the back Table (4) shows the localization.

The most common morphological appearance was dermal and subcutaneous nodules (figure 2) in 20 patients, carcinoma erysipeloides in 5 patients, carcinoma en cuirasse in 4 patients, carcinoma telangiectoides in 3 patients, Paget's disease in 5 patients, alopecia neoplastica (figure 3) in 1 patient and pyogenic granuloma-like vascular mass in 1 patient. Table (5) shows total number and percentage of the clinical morphologies as well as the origin of cutaneous infiltrations.

Regarding histopathological findings, different patterns were seen; dermal nodules were detected in 8 specimens (36.36%), intravascular tumors (figure 4) were seen in 7 specimens (31.81%), Indian filing were evident in 7 specimens (31.81%), clear cell differentiation seen in 7 specimens (31.81%), signet ring cells were found in 6 specimens (27.27%), tumor cells forming glandular structures (acini) were seen in 8 specimens (36.36%), dermal fibrosis seen in 19 specimens (86.36%), involvement of panniculus were detected in 19 specimens (86.36%), necrosis in 4 specimens (18.18%), hemorrhage in 4 specimens (18.18%), Grenz zone in 12 specimens (54.54%), and epidermotropism in 10 specimens (45.45%). Regarding the degree of atypia; 5 specimens were well differentiated, 6 were moderately differentiated and 9 were poor differentiated. Table (6) shows the histopathological findings in specimens.

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Internal organs metastases were detected in 10 patients (lung metastases in 5 patients, liver metastases in 5 patients and bone metastases in 3 patients).

**Table 1: Age of patients.**

Age of patients (years)	No. of patients	Percentage (%)
(31-40)	3	10
(41-50)	15	50
(51-60)	6	20
(61-70)	3	10
(71-80)	3	10
Total	30	100

**Table 2: Time period between the diagnosis of primary malignancy and secondary cutaneous malignancy in 19 patients, the time period cannot be calculated in 2 patients.**

Time Period (months)	No. of patients
(2-12)	8
(13-24)	2
(25-36)	4
(37-48)	3
(49-60)	1
(61-64)	1
Total	19

**Table 3: The primary malignancy in males and females with cutaneous infiltration. (EMPD: Extramammary Paget's disease).**

Primary Malignancy	Male	Female	Total	Percentage (%)
Breast	1	19	20	66.66
Renal	2		2	6.66
Gastric	1		1	3.33
Face & Neck (Parotid)		1	1	3.33
EMPD	1	1	2	6.66
Malignant melanoma	2	1	3	10
Unknown		1	1	3.33
TOTAL	7	23	30	100

## MALIGNANT CUTANEOUS INFILTRATION AND METASTASIS

**Table 4: Localization of skin infiltration. (EMPD:Extramammary Paget's disease).**

Anatomic Site	Primary Malignancy (Men)	Primary Malignancy (Women)	No. Of Patients	Percent-age (%)
Scalp	1Renal cell carcinoma	1Breast cancer 1Unknown	3	4.84
Face&Neck	1Gastric cancer 1Breast cancer 1Renal cell carcinoma	2Breast cancer 1Parotid cancer	6	9.68
Upper Limb	1Gastric cancer 1Breast cancer 1Renal cell carcinoma	5Breast cancer 1Unknown	9	14.52
Lower Limb	1Renal cell cancer 1Malignant melanoma		2	3.23
Chest	1Malignant melanoma 1Breast cancer 1Renal cell carcinoma	17Breast cancer	20	32.26
Abdomen	1Gastric cancer 1Breast cancer 1Renal cell carcinoma	5Breast cancer 1Malignant melanoma	9	14.52
Back	1Gastric cancer 1Breast cancer 1Malignant melanoma 1Renal cell carcinoma	5Breast cancer 1Malignant melanoma 1Unknown	11	17.74
Perianal &Groin	1EMPD	1EMPD	2	3.23
Total			62	100

**Table 5: Clinical morphology of cutaneous infiltration. (EMPD: Extramammary Paget's disease, Ca: cancer).**

	Morphology of cutaneous infiltration	Associated primary malignancy	Total no. of patients	Percentage of total no. of patients (%)
1	Dermal or subcutaneous nodules	13 Breast Ca 3 Malignant melanoma 1 Gastric Ca 1 Renal cell carcinoma 1parotid gland Ca 1Unknown	20	51.28
2	Inflammatory carcinoma (carcinoma erysipeloïdes)	Breast Ca	5	12.82
3	En cuirasse	Breast Ca	4	10.26
4	Carcinoma telangiectodes	Breast Ca	3	7.69
5	Paget's disease	3 Breast Ca 2 EMPD	5	12.82
6	Alopecia neoplastica	Breast Ca	1	2.56
7	Pyogenic granuloma –like Vascular mass	Renal cell carcinoma	1	2.56
	Total		39	100

**Table 6: Histopathological findings in specimens.**

	Histological findings	No. of specimens
1	Dermal nodule	8
2	Intravascular	7
3	Indian filing	7
4	Signet ring	6
5	Clear cell deff	7
6	Acini	8
7	Involving the panniculus	19
8	Fibrosis	19
9	Necrosis	4
10	Hemorrhage	4
11	Grenz zone	12
12	Epidermotropisim	10
13	Degree of atypia	5 well differentiated 6 moderate differentiated 9 poor differentiated



**Figure 1: In-transit metastasis of malignant melanoma, primary tumor in the right big toe of 60 years old male.**



**Figure 2: Metastatic multiple subcutaneous nodules and mucosal nodule in 49 years old male with history of gastric carcinoma.**



**Figure 3: Alopecia neoplastica in 47 years old female with history of breast cancer.**

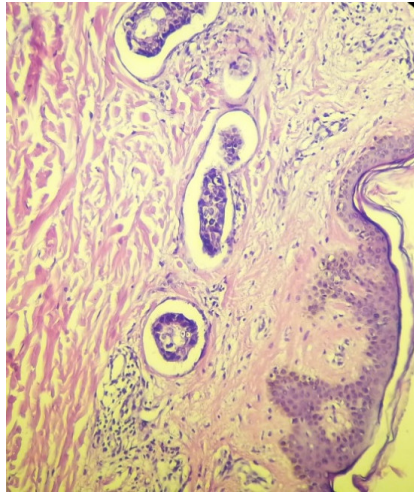


Figure 4 : H&E stained skin section of 50 years old female with breast cancer showing intravascular invasion of tumor cells in metastatic breast cancer.

#### DISCUSSION:

The importance of detecting cutaneous metastases or malignant infiltrations in a patient with a known primary malignancy cannot be overestimated, because it greatly affects the prognosis and will direct the management. Sometimes the cutaneous metastasis is detected before the primary malignancy and it is the first clue to the diagnosis. Despite these facts, there is no published report concerning cutaneous metastases in Iraq.

The most common primary malignancy in our patients was breast cancer. This may be related to the high prevalence in the population studied. Breast cancer is the most common malignancy in Iraqi women. According to the "Iraqi cancer registry center" publications,<sup>(9)</sup> it constituted 36.1% in 2009 and 34.44% in 2011 of all cancer cases. Iraq is the fifth country in the incidence of breast cancer all over the world<sup>(10)</sup>. The high percentage of cutaneous breast cancer metastasis may be also related to its propensity to metastasize to the skin (lymphatic, hematogenous and direct extension).<sup>(11,12,13)</sup>

The second most common primary malignancy was malignant melanoma which reflects the great ability of malignant melanoma to metastasize to skin, 45% of all cases of malignant melanoma metastasize to the skin which is the highest among all malignancies.<sup>(12)</sup>

Females constitute 76.7% of our patients with an M: F ratio of 1:3.3. This may be due to great number of breast metastases.

However in recent years, there was an increasing in percentage of new cancer patients among females compared to males. In 1991 females constituted 45.3% of Iraqi cancer patients, in 2009 they constituted 52.78% and in 2011 they constituted 53.88%.<sup>(14)</sup>

In the present study, the median age was 50 years. This may be due to the fact that the highest incidence of breast cancer in Iraqi women is at their 40s followed by 50s.<sup>(9)</sup> Also this may be related to the age of Iraqi population as young people constitute a higher percent of the population than old age.<sup>(10)</sup>

The most common locations for cutaneous infiltration were the chest and back. This is probably related to the high percentage of breast cancer which metastasizes to the chest wall. In addition, the surface area of the trunk constitutes 36% of total body surface area.

The median time period between the diagnosis of primary malignancy and secondary was 22 months and the mean  $\pm$  SD was  $26.9 \pm 19.2$  months which reflects the importance of cutaneous examination at each visit on the follow up of patients with cancer.

In 9 patients, the cutaneous infiltration was detected before the primary and was biopsied which led to the diagnosis of primary. This stresses the importance of skin biopsy for any suspicious skin lesion.

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