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Metastases to the breast from extramammary malignancies: a clinicopathologic study of 12 cases

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Along with a brief review of the literature, we report the clinicopathologic features of 12 cases of extramammary malignancies metastatic to the breast. Histological diagnoses of the primary tumor were as follows: non-Hodgkin diffuse large B-cell lymphoma (3 patients), acute myeloid leukemia (3 patients), serous papillary adenocarcinoma, well-differentiated adenocarcinoma, squamous cell carcinoma, undifferentiated neoplasm, mesothelioma, and melanoma. The most common mammographic finding was a well-circumscribed mass with increased density but without speculation, calcifications or other signs that characterize the majority of primary carcinomas. Ultrasound revealed well-circumscribed masses without retrotumor acoustic shadowing. The interval between diagnosis of primary cancer and the appearance of breast metastasis ranged from 0 to 108 months (mean: 17, median: 1). Survival after the detection of the breast metastases ranged from 0.2 to 144 months (mean: 23, median: 9.5). In conclusion, metastasis can mimic either benign disease or primary malignancy and is often an unexpected diagnosis in a patient presenting with a breast mass. Thus, an accurate diagnosis is important to avoid unnecessary mutilating surgery. These masses generally indicate disseminated metastatic disease, with a very poor survival rate.

Introduction

Breast cancer is the most common malignancy in women. However, metastatic involvement of the breast from extramammary malignancies is relatively rare, representing only 0.4 to 1.2% of tumors diagnosed in the breast [8, 9, 11, 12]. Thus, metastasis is often an unexpected diagnosis in a female patient presenting with a breast mass [1].

Although virtually all malignancies may metastasize to the breast, the most common primary tumors in decreasing order of frequency are: lymphomas (17%), melanomas (15%), rhabdomyosarcomas (12%), lung tumors (8%), ovarian tumors (8%), renal cell tumors (5%), leukemia (4%), thyroid/cervical tumors (4%), intestinal carcinoid tumors (3%), squamous cell carcinomas of head and neck (3%), and leiomyosarcomas (2%) [3,17].

Most patients have a known diagnosis of extramammary malignancy at the time of the presentation with breast metastases, but a breast lump may be the first manifestation of malignancy in up to 25 to 32% of cases [2, 12]. In these cases, metastases to the breast can mimic benign disease or primary malignancy [10]. Thus, the prompt recognition of such tumors is an important step in the management of these patients for the search of the primary tumor and to avoid unnecessary mutilating breast surgery [8, 14].

Along with a brief review of the literature we report the clinicopathologic features of 12 cases of extramammary malignancies that metastasized to the breast.

Materials and Methods

The study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki and was approved by the local Ethics Committee. Twelve cases of nonmammary malignancy metastatic to the breast were retrieved from the files of the university hospital of Ribeirão Preto Medical School, Brazil, from 1980 to 2005. The clinical data were retrieved from the medical files. Mammography and ultrasound was performed in 5 and 2 patients, respectively. Fine needle aspiration (FNA) cytology was performed in 3 patients. Tissue from the breast for histological study was obtained with an incisional biopsy.

Results

A total of 12 cases were included in this study (Table 1). Eleven patients were women, and one was a man. Patient age ranged from 12 to 68 years, with a mean age of 35 years (median: 28 years). Histological diagnoses of the primary tumor were as follows: non-Hodgkin diffuse large B-cell lymphoma (3 patients), acute myeloid leukemia (3 patients), serous papillary adenocarcinoma, poorly-differentiated carcinoma with neuroendocrine differentiation, squamous cell carcinoma, undifferentiated neoplasm, mesothelioma, and melanoma. The primary sites of the malignancies were: lymph nodes (4 patients), blood and bone marrow (3 patients), ovary, rectum, pyriform sinus, pleura, and skin. The patient with melanoma was the only one who had metastases to axillary lymph nodes (4 positive lymph nodes). In the three cases in which FNA was performed the findings matched the histological diagnosis (squamous cell carcinoma and acute myeloid leukemia). The radiological findings of the breast metastases are specified in Table 1 (Fig. 1).

The interval between diagnosis of primary cancer and the appearance of breast metastasis ranged from 0 to 108 months (mean: 17 months, median: 1 month). Five of the 12 patients exhibited breast metastasis as the first clinical presentation. All metastatic breast lumps were detected by the patients themselves and confirmed by the physician. The time between the notice of the lump by the patient and the search for medical assistance ranged from 20 to 96 days (mean: 56 days, median: 40 days). The diameter ranged from 0.9 to 8 cm (mean: 3.2, median: 2). Five of twelve patients complained of pain.

Survival after the detection of the breast metastases ranged from 0.2 to 144 months (mean: 23 months, median: 9.5 months). One patient remains alive after 5 months of follow-up. The treatment of each patient is specified in Table 1. Patients 2 and 11 (adenocarcinoma of the rectum and melanoma), underwent mastectomy and lumpectomy, respectively, due to the large dimensions of the metastases.

Discussion

The breast is an uncommon site for metastatic disease because it contains large areas of fibrous tissue with a relatively poor blood supply [2, 18]. The lymphomas and other neoplasms of hematological origin are the most common extramammary malignancies that metastasize to the breast [9]. Indeed, in our series, 6 of the 12 patients had lymphoma or leukemia. It is worth commenting on the age of the patients. Six of the 12 female patients were younger than 30. The most common metastasis in men is from prostatic carci-

noma [15]. The only man in our study had metastasis from a non-Hodgkin diffuse large B-cell lymphoma. In children, rhabdomyosarcoma is the tumor most commonly associated with breast metastases [5].

The majority of metastases to the breast present as rapidly growing, painless, palpable, and firm breast masses [2]. They are usually mobile, but occasionally are adherent to the skin [5]. Skin changes are generally absent unless the mass is quite large [4]. Rarely, involvement of dermal lymphatics may simulate the inflammatory carcinoma of the breast [16]. They can be bilateral or multiple, and are slightly more frequent in the left breast [13]. In our study, 7 of the 12 patients had metastases to the left breast. None of them had bilateral metastases. Axillary lymph nodes are infrequently involved but can occur, particularly in hematological malignancies [9]. Curiously, in the present study a patient with melanoma was the only one presenting lymph node involvement.

Metastases to the breast may occur several years after the diagnosis of a primary cancer [6]. In the present study a serous papillary adenocarcinoma of the ovary metastasized to the breast 108 months after the initial diagnosis. However, the median time of metastasis was very short (1 month).

It has been advocated that metastases to the breast can be differentiated from primary malignancy on gross examination because they have a round pattern of infiltration and a bulging cut surface [11]. This criterion, however, is debatable because the breast metastasis may present as an irregular mass with speculated edges and flat cut surface, just as the primary malignancies [8]. Although metastases are usually smaller than primary tumors, this cannot be used as a diagnostic criterion because metastases can reach huge dimensions [15].

As expected, the histological findings are extremely varied. The main differential diagnostic concern is metastatic adenocarcinoma because it can mimic primary breast malignancy.

The mammographic appearance is varied and ranges from normal to patterns that mimic primary breast carcinoma. The most common mammographic findings, however, are of one or more well-circumscribed masses with increases density but without speculation, calcifications or other signs that characterize the majority of primary carcinomas [2]. Microcalcifications are unusual and are mostly associated with metastatic carcinoma of the ovary, in which psammoma bodies may be abundant [5]. Interestingly, in our study the only case that presented with microcalcifications was a lymphoma, while the case of metastases from an ovarian adenocarcinoma did not show this feature. Contrary to primary carcinomas, there is a close correlation

TABLE 1
Clinicopathologic features

Case	Age/gender	Primary site	Diagnosis	BM as the initial sign	Time until BM	Side	Histology of BM	Radiographic features of BM	Treatment for BM	Survival from BM
1	68/F	ovary	mucinous papillary adenocarcinoma	No	108 m	R	Large cells arranged in nests with a papillary configuration floating in lakes of mucus	Ma: well-circumscribed mass with high density	ChT Radiotherapy	Dead, 144 m
2	55/F	rectum	Poorly-differentiated carcinoma with neuroendocrine differentiation	No	48 m	L	Nests of undifferentiated cells showing numerous atypical mitoses and extensive areas of necrosis	NP	ChT mastectomy	Dead, 12 m
3	46/F	pyriform sinus	Well-differentiated Squamous cell carcinoma	Yes	-	L	Large nests of atypical squamous cells with prominent keratinization	NP	ChT	Alive, 5 m
4	38/M	lymph node	non-Hodgkin diffuse large B-cell lymphoma	No	21 m	R	Diffuse pattern of infiltration by large and uniform cells resembling immunoblasts	NP	ChT	Dead, 9 m
5	67/F	lymph node	non-Hodgkin diffuse large B-cell lymphoma	Yes	-	L	Same as 4	Ma: Irregular nodule with calcifications	ChT	Dead, 17 m
6	30/F	blood	acute myeloid leukemia	No	-	L	Diffuse and non cohesive proliferation of round to oval cells with eccentrically placed nuclei, some of them resembling myeloblasts	Ma: asymmetric density	ChT	Dead, 13 m
7	21/F	lymph node	non-Hodgkin diffuse large B-cell lymphoma	Yes	-	R	Same as 4	US: round hypoechoic lesion with irregular margins and heterogeneous internal echo pattern without acoustic shadowing	ChT	Dead, 0.2 m
8	15/F	lymph node	Undifferentiated neoplasm	Yes	-	L	Highly non-cohesive pleomorphic cells with extensive areas of necrosis	NP	ChT	Dead, 4 m
9	26/F	blood	acute myeloid leukemia	Yes	-	R	Same as 6	NP	ChT	Dead, 5 m
10	20/F	pleura	Mesothelioma	No	2 m	L	Poorly differentiated sheets of plump or polygonal cells with nuclear pleomorphism	Ma: same as 1	ChT	Dead, 10 m
11	21/F	skin	Melanoma	No	19 m	R	Nests of pleomorphic epithelioid cells with vesicular nuclei and conspicuous nucleoli	Ma: well-circumscribed mass with variable density	ChT lumpectomy	Dead, 48 m
12	12/F	blood	acute myeloid leukemia	No	6 m	L	Same as 6	US: round hypoechoic lesion with smooth margin and heterogeneous internal echo pattern without acoustic shadowing	ChT	Dead, 8 m

BM: breast metastases, F: female, M: male, m: month, R: right, L: left, Ma: mammography, NP: not performed, US: ultrasound, ChT: chemotherapy

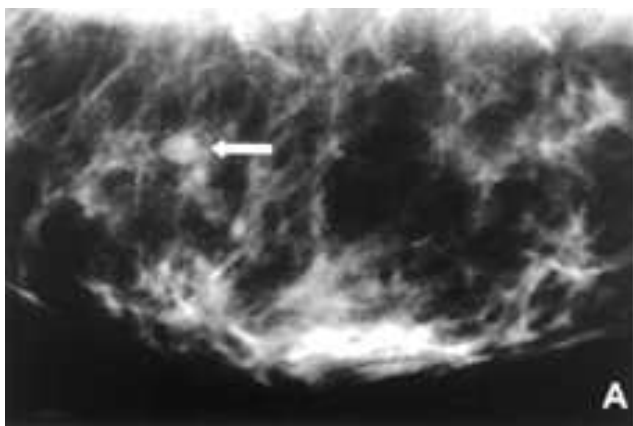


Fig. 1A. Mammographic findings of patient 11 (Table 1, melanoma). Well-defined lump with variable density (arrow).



Fig. 1B. Ultrasonographic findings of patient 12 (Table 1, acute myeloid leukemia). Well-circumscribed lump without acoustic shadowing (arrow). Both pictures suggest benignity.

between the palpable size of the mass and its mammographic size because the metastasis usually does not cause a surrounding desmoplastic reaction in adjacent normal breast [6].

A variety of ultrasound findings have been reported [2]. The most common pattern, however, is hypoechoogenicity in a well-circumscribed mass without retrotumor acoustic shadowing [18]. Our findings are in accordance with these data. A differential diagnosis from fibroadenoma by breast ultrasound may be difficult. The main clue is a posterior acoustic enhancement that is normally present in fibroadenomas, but not in metastases.

Metastases of solid tumors are treated by local excision. The treatment for hematological malignancies is non-surgical and includes chemotherapy and, in some cases, radiotherapy [12]. In the present study only two patients were submitted to a surgical resection of the breast metastasis (1 mastectomy and 1 lumpectomy). Mastectomy should be avoided but it is sometimes required when the tumor is bulky, deep-seated or painful [5].

Many studies have proved that fine-needle aspiration cytology is the best initial approach to these cases and may provide a definitive diagnosis, thus avoiding unnecessary surgery [1, 6, 9]. Unfortunately, FNA was performed in only three patients however, in all of them the cytological diagnosis was accurate.

The prognosis is very poor. Up to 92% of patients died within one year after the metastasis [12]. These data are in accordance with our findings. The median survival after the breast metastasis was only 9.5 months.

In summary, although breast metastases from extramammary malignancies are infrequent, they generally indicate disseminated metastatic disease and carry a very poor survival rate. An accurate diagnosis is important to avoid unnecessary mutilating surgery.

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