

Metastatic disease in the breast from nonmammary neoplasms

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Summary

Breast cancer is the leading cause of death from cancer in women. The metastatic involvement of the breast from nonmammary neoplasms is a relatively rare condition. Female patients are affected five to six times more frequently than male patients. We present seven patients with metastasis in the breast from extramammary tumors. Females seemed to be more frequently affected (6 women and 1 man) and included a wide range of ages (17-70 years old). All female patients had suspicious-looking abnormalities (BI-RADS 4) or lesions highly suspicious of malignancy (BI-RADS 5) in the mammography, without a confirmative fine needle aspiration cytology. The primary malignancies were equally distributed between non-hematological (1 renal adenocarcinoma, 1 melanoma, 1 leiomyosarcoma) and hematological (1 non-Hodgkin's, 2 Hodgkin's lymphomas and 1 leukemia). Treatment is therefore modified, taking into consideration the treatment and prognosis of the primary disease.

Key words: Metastases to the breast; Extramammary neoplasms.

Introduction

Breast cancer is the commonest malignancy in women and accounts for 32% of all female cancers [1]. However, metastatic involvement of the breast is relatively rare. Autopsy reports indicate an incidence of 1.7-6.6% for nonprimary breast malignancy [2]. In contrast, the clinically observed ranges are only 0.5-1.3% [3, 4]. Female patients are affected five to six times more frequently than male patients [5]. The commonest cause is spread from a contralateral breast carcinoma, with a relative risk of 5-15%. The most common tumors to metastasize to the breast from extramammary sites are, in declining order of frequency, malignant melanoma, lymphoma, lung cancer, ovarian carcinoma, soft tissue sarcoma, gastrointestinal and genitourinary tumors, followed by sporadically reported tumors, e.g. osteosarcoma, thyroid neoplasms and cervical, vaginal and endometrial carcinomas [6]. Virtually any malignancy can metastasize to the breast and it usually indicates disseminated metastatic disease and a poor prognosis [7]. The aim of our study is to present seven cases of metastases to the breast from nonmammary neoplasms and to correlate them with a review of the literature.

Material and Methods

During the past 17 years (1988-2004), 2,500 patients were admitted to the breast department of our clinic for surgical treatment of breast cancer. Analyzing the data obtained from the patients' records and the histology reports of the excised breast lesions, we retrospectively found that seven patients had metas-

tasis to the breast from nonmammary neoplasms (Table 1). In addition, we reviewed the literature (using PubMed) of the past 30 years and present the most interesting and representative series published (Table 2).

Results

Seven patients (0.28%) presented with metastasis of the breast from extramammary tumors. Females seemed to be more frequently affected (6 women and 1 man) and included a wide range of ages (17-70 years old, median 50,6 years). In three patients (cases 2, 5, 6) there was a known history of primary or systemic disease three to ten years before, with appropriate treatment adjusted for each of them. In cases 2 and 5 (Hodgkin's lymphoma and CLL) systemic therapy had taken place in the past, while surgical treatment was applied in case 6 (intestine leiomyosarcoma and duodenum neuroendocrine tumor). For the remaining four patients, the metastasis in the breast revealed a coexisting (not previously known) primary or systemic disease: case 1 and 3 were lymphomas (non-Hodgkin's and Hodgkin's, respectively), case 4 revealed a melanoma and case 7 a renal adenocarcinoma. In case 4, the diagnosis of the primary lesion was not found. All female patients had suspicious-looking abnormalities (BI-RADS 4) or lesions highly suspicious of malignancy (BI-RADS 5) in the mammography, according to the terminology adjusted by the American College of Radiology [8]. Fine needle aspiration was applied to all the patients, but was diagnostic only in case 2 where it revealed a Hodgkin's lymphoma. Treatment included modified radical mastectomy with axillary dissection (cases 4 and 5), simple mastectomy (case 7), wide local excision (cases 1 and 6) and quadrantectomy (cases 2 and 3).

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Table 1. — *Clinical, mammographic and pathological features of patients.*

n	Age	Sex	Patient's history	Clinical presentation	Mammographic findings	Treatment	Histology report
1	67	F	No history of systemic or primary disease	Hard mass 4x5 cm involving the skin of the right nipple - nipple inversion, FNAC negative	Nipple lesion, diameter 3 cm, BI-RADS* "4"	Local wide excision	Non-Hodgkin's lymphoma, large B-lymphocytes
2	26	F	Known Hodgkin's disease	Palpable lump in the upper-outer quadrant (left) FNAC positive	Breast lesion, diameter 2 cm, BI-RADS* "5"	Quadrantectomy and adjuvant radiation therapy	Hodgkin's lymphoma, nodular-sclerosing type
3	17	F	No history of systemic or primary disease	Palpable lump in the upper-outer quadrant (left), FNAC negative	Breast lesion, diameter 2 cm, BI-RADS* "4"	Quadrantectomy, postoperative systemic therapy for primary disease	Hodgkin's lymphoma, lymphocyte-predominant type, high grade
4	70	F	No history of primary disease	Hard palpable mass upper-outer quadrant 2 x 2 cm fixed to the overlying skin, FNAC negative	Lesion in the tail of the left breast, diameter 3 cm, BI-RADS* "5", with axillary lymph node involvement	Modified radical mastectomy with axillary dissection	Diffuse infiltration from a non-differentiated non-melanotic melanoma
5	67	F	10 years of known history of C.L.L.	Suspicious palpable irregular mass 3x3 cm of upper-outer quadrant (right) FNAC negative	Right breast lesion diameter 3 cm, BI-RADS* "5", with axillary lymph node involvement	Modified radical mastectomy with axillary dissection	Histological appearance of leukemia infiltration of the breast
6	42	F	History of resected intestinal leiomyosarcoma 3 years before	Hard palpable mass 3 x 3 cm in the upper-outer quadrant (left), FNAC negative	Lesion in the left breast, diameter 3 cm, BI-RADS* "5"	Wide local excision	Breast leiomyosarcoma
7	65	M	No history of systemic or primary disease	Suspicious hard palpable mass 3 x 3 cm, FNAC not diagnostic	Not applicable	Simple mastectomy and left nephrectomy	Metastatic renal adenocarcinoma

*BI-RADS: Breast Imaging Reporting and Data System (terminology adapted from American College of Radiology); 4) suspicious-looking abnormality; 5) highly suggestive of malignancy.

^ CLL: chronic lymphocytic leukemia.

° FNAC: fine needle aspiration cytology; M: male; F: female.

Reviewing the literature of the past 30 years (Table 2) it is obvious that about 500 cases of metastatic involvement of the breast have been reported up to date. The most common primary malignancies are melanoma, lymphomas, lung cancer, ovarian carcinomas and soft tissue sarcomas.

Discussion

Metastatic disease of the breast is often an unexpected diagnosis in a female patient presenting with a breast mass. A clinical presentation with pain, tenderness and discharge is distinctly unusual [2, 9]. Toombs *et al.* [5] report that a solitary lesion is the most common clinical presentation, while multiple, well-defined nodules have been seen in 11% of cases and diffuse involvement in 4%. The lesion tends to be superficially located in the upper outer quadrant, with adherence to the skin in 25% of cases and with axillary lymph node involvement frequently encountered [6]. In the six female patients reported in our study, the clinical presentation was a hard

or irregular palpable mass in all of them, involving the upper outer quadrant in five (83%), with invasion of the overlying skin in 33% (cases 2 and 4) and involving the axillary lymph nodes in two (33%). In McCrea *et al.*'s series [10] 40% of the patients had no previous history of malignancy and the newly diagnosed neoplasms comprised approximately equal numbers of patients with hematological malignancies and with solid tumors. In our patients, four patients (57%) had no previous history of malignancy. Three patients had non-hematological tumors (cases 4, 5 and 6), while four had hematological malignancies (2 Hodgkin's and 1 non Hodgkin's lymphoma and 1 leukemia). In men, the prostate is the most common primary site [11, 12, 23] and the differentiation between primary breast carcinoma and metastatic prostatic carcinoma is very important because the first is likely to have a more favorable prognosis. In our results, we report a rather rare case involving a 65-year-old man with no previous history of malignancy who presented with a suspicious hard mass in the breast. The pathological findings revealed that it was a metastatic deposit from a renal

Table 2. — Review of the literature.

Authors - Date of publication	Brief review
Toombs B.D. <i>et al.</i> 1977 [5]	131 clinical cases reported in the literature; 21 new cases added. The most common sources were malignant melanomas and lymphoma/leukemia.
Nielsen M. <i>et al.</i> 1981 [15]	15 cases presented; 2 primary thyroid carcinoma's, 2 adenocarcinoma of the colon, 3 bronchogenic carcinoma's, 4 malignant melanoma's, 1 squamous cell carcinoma of the esophagus, 1 adenocarcinoma of the stomach, 1 renal cell carcinoma and 1 carcinoid of the terminal ileum.
Murakami T. <i>et al.</i> 1985 [16]	2 men who presented with breast malignancies in the course of their prostatic carcinoma are described.
Wierani F. <i>et al.</i> 1988 [17]	2 cases of melanoma
Kelly C. <i>et al.</i> 1988 [18]	2 cases of oat cell carcinoma
Chaignaud B. <i>et al.</i> 1994 [19]	9 women (ages 25 to 67 years) were identified with breast masses, the biopsies of which proved to be metastatic from other sites
Domanski H.A. <i>et al.</i> 1996 [20]	6 cases of metastatic neoplasms diagnosed by FNAB: squamous carcinoma of the cervix, endometrial adenocarcinoma, gastric signet-ring cell carcinoma, small cell carcinoma of the lung, large cell carcinoma of the lung and plasma cell myeloma.
Muttarak M. <i>et al.</i> 1998 [21]	3 bronchogenic carcinomas, 1 papillary adenocarcinoma of the ovary, 1 adenocarcinoma of the colon, 1 squamous cell carcinoma of the nasal cavity and squamous cell carcinoma of the cervix.
Cangiarella J. <i>et al.</i> 1998 [22]	7 cases of malignant melanoma metastatic to the breast diagnosed by fine-needle aspiration biopsy are presented.
Deshpande A.H. <i>et al.</i> 1999 [14]	3 of the cases were previously diagnosed as squamous cell carcinoma (SCC) of the cervix, mucinous cystadenocarcinoma (MCA) of the ovary, and melanoma; 3 cases presented initially with a breast mass. These included melanoma, non-Hodgkin's lymphoma and plasmacytoma.
Chhieng D.C. <i>et al.</i> 1999 [13]	3 cases of renal cell adenocarcinoma metastatic to the breast, with a prior history of renal cell adenocarcinoma treated with radical nephrectomy.
Yan Z. <i>et al.</i> 2000 [23]	A case of a metastatic prostatic adenocarcinoma presenting as bilateral palpable mammary masses.
Oksuzoglu B. <i>et al.</i> 2003 [24]	500 patients reported in the English literature; 5 new cases added: 2 rhabdomyosarcomas, 2 ovarian carcinomas and 1 colon carcinoma.
Yeh CN <i>et al.</i> 2004 [7]	3 hepatocellular carcinomas, 2 gastric carcinomas, 2 malignant melanomas, 1 colon carcinoma, 1 lung adenocarcinoma, 1 ovarian carcinoma, 1 uterine leiomyosarcoma, 1 nasopharyngeal carcinoma, 1 esophageal squamous carcinoma, 1 embryonal rhabdomyosarcoma, and 1 cervical carcinoma.

adenocarcinoma. Reviewing the literature we found a report of three cases of prior renal cell adenocarcinoma treated with nephrectomy that metastasized to the breast [13].

Mammographic findings for metastatic lesions in the breast are similar to those of primary breast cancer, but they are well circumscribed and are not associated with micro calcifications or secondary skin or nipple changes, and exhibit unusually rapid growth [3]. The mammographic findings in the six female patients we report, had similar patterns with those found in primary breast cancers (BI-RADS 4 and 5).

Deshphande *et al.* [14] report that preoperative fine

needle aspiration cytology (FNAC) of extramammary tumors metastatic to the breast may display cytologic features ranging from those not usually seen in primary breast malignancies to those that are indistinguishable from primary breast carcinoma. Preoperative FNAC is invaluable and completes the diagnosis made with clinical and radiological correlation, because the management of the patient differs entirely from that of a primary neoplasm. In our seven patients FNAC was positive in only one woman (case 2).

Conclusion

Metastatic disease to the breast from nonmammary neoplasms is infrequent, and accurate diagnosis is important as treatment and outcome of primary and secondary malignancies of the breast are completely different. It is evident that nearly every malignancy can metastasize to the breast, indicating disseminated metastatic disease and poor prognosis.

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