Jpn J Clin Oncol 2005;35(4)202–206
doi:10.1093/jjco/hyi068

Different Manifestations of Malignant Melanoma in the Breast: a Report of 12 Cases and a Review of the Literature

Sıdıka Kurul[1], Faruk Taş[2], Nesimi Büyükbabani[3], Ayşe Mudun[4], Can Baykal[5] and Hakan Çamlıca[6]

[1]Division of Surgical Oncology, [2]Division of Medical Oncology, Institute of Oncology, [3]Division of Cutaneous Pathology, Department of Pathology, Istanbul Medical School, [4]Department of Nuclear Medicine, Istanbul Medical School, [5]Department of Dermatology, Istanbul Medical School and [6]Division of Biostatistic and Cancer Epidemiology, Institute of Oncology, Istanbul University, Istanbul, Turkey

Received January 19, 2005; accepted March 7, 2005

Background: The breast is associated with a large number of diseases. Besides being the host of many benign and malignant tumors, breast skin and parenchyma are also metastatic sites for various tumors such as leukemia, lung cancer and melanoma.
Methods: Malign melanoma has different manifestations in the breast. All these manifestations are important not only as initial presentations of the disease, but also as indicators of the progression period of the disease.
Results: This study reports on 12 cases of cutaneous malignant melanoma in breast skin and tissue. Nine of these cases are primary cutaneous melanomas, while the others are breast metastases from a distant site cutaneous melanoma. In two of the nine primary cutaneous melanomas in-transit metastasis to the breast developed during the follow-up period.
Conclusions: In this paper, the diagnostic and surgical approach to primary and metastatic melanoma of the breast, and the importance of the breast during the follow-up period are reviewed.

Key words: Cutaneous melanoma – breast – distant metastasis – in-transit metastasis

INTRODUCTION

The breast is associated with a large number of diseases. Besides being the host of many benign and malignant tumors of breast skin and parenchyma, it is also a metastatic site for various tumors such as leukemia, lung cancer and melanoma (1–12).

The incidence of malignant melanoma is increasing in southern European countries including Turkey. Cutaneous malignant melanoma (CMM) and the breast can be interrelated in various contexts: primary melanoma of the breast skin (1,13–16), melanoma metastasis to the breast (2–10,15), in-transit metastases (IMs) to breast tissue and breast skin (8,12), and finally primary breast melanoma (5–11). Each of these presentations is important when determining the strategies in differential diagnosis, surgical treatment and especially during the follow-up period of CMM.

In this paper, different manifestations of cutaneous melanoma of the breast are assessed and 12 cases are presented with a review of the literature.

For reprints and all correspondence: Prof.Dr. Sıdıka Kurul, Plastic Surgeon, Istanbul University, Institute of Oncology, Dept of Surgical Oncology, Capa, 34390 Istanbul, Turkey. E-mail: skurul@istanbul.edu.tr

MATERIAL AND METHODS

Between 1995 and 2003, >550 cases of malignant melanoma were treated and followed by the Melanoma Group at the Institute of Oncology, Istanbul University, Istanbul. Of these, only 12 cases presented with breast involvement (Table 1). Six females and six males with an average age of 46 years (range 23–73 years) had CMM (10 patients with superficial spreading melanoma, two nodular melanoma), of thickness ranging from 0.90 mm to 7 mm (mean 2.95 mm). Distant metastatic work-up was negative except in one patient (case 12).

These patients were divided into two categories according to the primary location of CMM: (i) primary CMM of the breast (n = 9) and (ii) metastatic melanoma of the breast (n = 3).

Primary CMM of the Breast

Seven cases had their primary tumors located on the inner quadrant of the skin of the left breast, while the other two tumors were localized over the right breast. After re-excision of the primary site, surgical defect was closed with primary suture in five patients, and skin graft reconstruction was performed in the rest. All patients except one underwent sentinel lymph node biopsy (SLNB) with combined technique (radiocolloid and blue dye). As case 9 was clinically at stage III, axillary lymph node dissection was performed without SLNB.

Table 1. Clinicopathologic findings in 12 patients with malignant melanoma

Case no.	Location of the primary tumor	Histology of the tumor	Surgical treatment of the primary tumor	Stage	Adjuvant treatment	Interval between primary surgery and breast recurrence	Type of breast metastasis	Treatment for breast involvement	Follow-up status
1	Lower inner quadrant of the left breast skin	SSMM 0.9 mm Ulceration (+)	WLE + primary suture + SLNB	IB	–	–	–	–	Disease free for 32 months
2	Upper inner quadrant of the left breast skin	SSMM 1.2 mm	WLE + skin grafting + SLNB	IB	–	–	–	–	Disease free for 5 years
3	Upper inner quadrant of the left breast skin	SSMM 1.95 mm Ulceration (+)	WLE + skin grafting + SLNB	IIA	–	–	–	–	Died after 26 months with DMs
4	Upper outer quadrant of the right breast skin	SSMM 4.1 mm	WLE + primary suture + SLNB	IIB	–	–	–	–	Disease free for 12 months
5	Upper inner quadrant of the left breast skin	SSMM 1.2 mm	WLE + primary suture + SLNB ALND	III	INF	–	–	–	Disease free for 24 months
6	Lower inner quadrant of the left breast skin	SSMM 4.39 mm Ulceration (+)	WLE + primary suture + SLNB, ALND	III	INF	–	–	–	Disease free for 18 months
7	Lower inner quadrant of the left breast skin	SSMM 7 mm Ulceration (+)	WLE + skin grafting bilateral axillary SLNB+right ALND	III	DTIC	–	–	–	Died after 10 months with DMs
8	Upper inner quadrant of the right breast skin and right scapula	SSMM 4 mm SSMM 3 mm	WLE + skin grafting + SLNB	IIB	–	17 months	Two skin IMs+single breast IM	Simple mastectomy	Died after 19 months with DMs
9	Upper inner quadrant of the left breast skin	Nodular Clark IV	WLE + primary suture + ALND	III	DTIC	17 months	Skin lMs + DMIM	Simple mastectomy	Dead after 22 months with DMs
10	Midback	SSMM 4 mm	WLE + skin grafting + SLNB + bilateral ALND	III	INF	13 months	Skin IMs+DMIM+four intramammary lymph node metastases	1. Extended mastectomy + skin grafting 2. Re-excision + skin grafting	Dead after 31 months with in-transit and DMs
11	Midback	Nodular unmeasurable	WLE + skin grafting	IIB(?)	–	27 months	Single breast distant metastases	WLE	Disease free Alive for 33 months
12	Lower extremity	SSMM 5.50 mm CL IV	WLE	IIB	–	24 months	Single breast distant metastases	WLE	Alive for 10 months with DMs

WLE, wide local excision; SLNB, sentinel lymph node biopsy; ALND, axillary lymph node dissection; SSMM, superficial spreading malignant melanoma; IMs, in-transit metastasis; DMlM, diffuse microscopic in-transit metastases in the breast parenchyma; DMs, distant metastases.

Figure 1. A 35-year-old female (case 10) with CMM of the mid-back on whom WLE, skin grafting and bilateral axillary lymph node dissection were performed. In-transit metastases on skin and breast parenchyma developed under IFN treatment. Although extended mastectomy with skin graft, and radiation therapy were performed, local recurrences occurred. Re-excision and skin grafting were performed (12). In the late period of illness, in-transit metastases invaded both the previously treated area and opposite breast.

Figure 2. A 73-year-old man (case 8) with in-transit metastases (IMs) both in breast skin and breast tissue (star, previous skin graft; arrow, skin mark of palpable breast mass); mastectomy was done. Biopsy specimen showed that there were two IMs in the skin, and one nodular IM in the breast tissue.

The pathological examination of the sentinel node revealed micrometastates in three cases. Axillary lymph node dissections were performed in these cases and no additional metastatic lymph nodes were observed in the histological examination.

Metastatic Melanoma of the Breast

There were three patients in this group. As previously published (12), in case 10 with stage III mid-back CMM, wide local excision (WLE) and bilateral axillary lymph node dissection was performed. During the follow-up period, skin IMs were diagnosed by biopsy over the right breast. Extended mastectomy and skin graft reconstruction were done to this patient. Pathological examination of the breast showed diffuse in-transit metastasis (DMIM) and intra-mammary lymph nodes metastases together with skin IMs. Although the patient received adjuvant radiation therapy, IMs occured both on the previously grafted/irradiated area and healthy skin. Wide local excision and skin graft reconstruction were performed again. The patient died of recurrent disease on both ipsilateral and contralateral hemithorax (Figure 1) and systemic dissemination 31 months after last surgery.

RESULTS

Clinical follow-up was available in all patients ranging in duration from 10 to 60 months (median 24 months). Five patients died of disseminated disease. The other seven cases are alive; six without clinical evidence of disease and one with disease at the time of this report.

During the follow-up period of patients with primary CMM of the breast, two patients died 10 and 26 months after surgery due to distant metastases with no evidence of loco-regional recurrence. Two other cases showed breast involvement. Single (Figure 2) and DMIM developed in the breast parenchyma and skin. IMs developed in cases 8 and 9, respectively. Generally IMs, which are the specific type of metastases in CMM, appear between the primary site and the site of nodal basin. Simple mastectomy was performed to these patients. They died due to systemic disease 19 and 22 months after last surgery.

In patients with metastatic melanoma of the breast, two cases showed single breast metastasis from CMM located on the mid-back (Figure 3) and on the lower extremity. Metastasectomy was performed to these patients. These patients were still alive at 10 and 33 months from last surgery.

Five patients showed breast parenchyma involvement and the intervals between diagnosis of primary tumor and breast involvement were 13, 17, 17, 24 and 27 months in this series.

DISCUSSION

Cutaneous malignant melanoma showed different manifestations in the breast not only at initial presentation but also during the follow-up periods of each patient.

Melanoma of breast skin accounts for <5% of all malignant melanomas, and large series of primary breast skin melanoma are particularly rare (1,13–16). While, in the past, the surgical treatment of primary CMM of the breast represented a challenging situation (14,15), recent thinking suggests that there is no significant difference between melanoma of breast skin and melanoma of other skin parts (1,13,17). As in our eight cases, only WLE of the primary site and SLNB are sufficient as surgical treatments. If axillary lymph node involvement is detected, clinically or pathologically, lymph node dissection should also be performed.

Unfortunately, there are no detailed specific documents in the literature about follow-up. Papachristou et al. (14) has reported the largest series in the literature, but has not documented information about local-regional problems during the

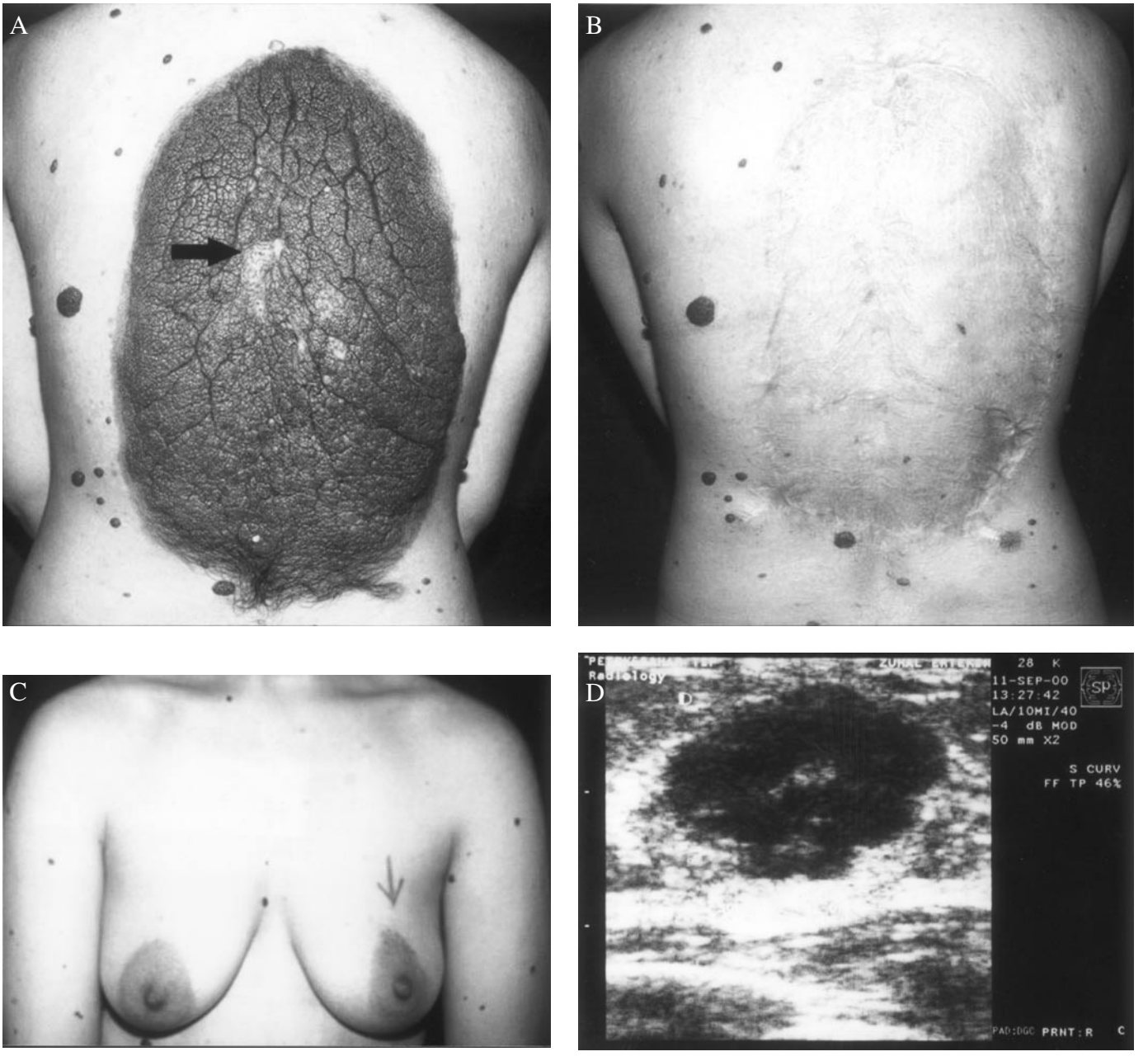

Figure 3. A 23-year-old woman (case 11) with malignant melanoma originated from giant congenital compound nevus. (A) The arrow indicates a previous biopsy site. (B) WLE and skin graft reconstruction was done. (C) 27 months after definitive surgery, a palpable breast mass (2×2 cm in diameter) was found on clinical examination (arrow indicates the breast mass). (D) Breast ultrasonography showed a single cystic lesion (13×11 cm in size) with contour lobulation and internal septations. Fine-needle aspiration biopsy revealed metastatic CMM and metastasectomy was performed.

follow-up period. Lee et al. (15) reported that in five of seven patients with breast CMM who were treated by WLE, local recurrence, satellosis and subcutaneous nodules were observed. Skarin (13) reported a case with CMM of the breast presenting as contralateral breast metastasis.

In our series, two of nine cases (cases 8 and 9) with breast CMM showed IMs both in breast tissue and skin. In case 8, a single IM in the breast parenchyma was detected by clinical examination together with synchronous cutaneous IMs (Figure 1). Jochimsen and Brown (8) reported a similar case, but they did not name it IM to the breast. Case 9 demonstrated multiple IMs on the areola and DMIM in the breast tissue similar to case 10.

As previously published (12), DMIM to the breast parenchyma (cases 9 and 10) is an interesting presentation of CMM. In both cases, histological examination of the mastectomy specimen showed diffuse melanoma cell deposits in the lymphatic channels of the breast tissue with cutaneous IMs. In addition to DMIM, case 10 also had four intra-mammary lymph node metastases. Some authors (6,13,15) noted that

metastasis in an intra-mammary lymph node and lymphatic spread in the breast could occur not only in CMM but also in other metastatic tumors or primary breast carcinoma. In this case, although preoperative lymphoscintigraphy which was done for SLNB did not show any draining lymphatic channel to the breast or internal mammary chain, intra-mammary lymph node metastasis developed 13 months after the SLNB. In-transit metastases invaded not only the chest wall but also the opposite breast (Figure 2). The last presentation of this patient could be due to the previous axillary node dissection which altered the lymphatic pathways. Rees et al. (19) and Sood et al. (20) demonstrated that lymphadenectomy has indeed been responsible for the altered drainage pattern.

The last subject of this paper is distant metastasis to the breast from extra-mammary CMM. Tumors metastatic to the breast are quite unusual, but malignant melanoma is an exception. Arora and Robinson (6) described 15 consecutive patients with CMM metastatic to the breast together with other sites of metastases at the time of breast involvement. Pressman (5) and others (2–4,7–9,21), reported isolated distant metastasis to the breast from extra-mammary CMM. In our series, only two patients showed distant metastasis to the breast from extra-mammary CMM with an interval between primary and breast metastasis of 24 and 27 months, respectively. One of these cases also had disseminated disease at the time of breast involvement.

In any CM case with a palpable breast mass, mammography and/or ultrasonography should be obtained to reveal the number of metastatic lesions (10,13). Following confirmation of histological diagnosis by fine needle aspiration cytology (FNAC), WLE or quadrantectomy is sufficient for surgical treatment in cases with no evidence of multiple metastatic lesions (2–4,7,13,21). In the cases presented, the same procedures were performed for diagnosis and treatment.

The aim of this study was to highlight that the treatment of breast CMM is the same as that for any other skin part and that particular attention should be paid to the importance of breast examination during follow-up visits. Not only in visible IMs, but also when there is evidence of mild skin abnormalities such as light blue spots over the breast skin, histological confirmation should be performed. In these cases, simple mastectomy might be considered as a palliative surgical treatment for the possibility of DMIM in spite of normal breast radiology. Finally, special attention should be given to patients with solitary breast metastases from CMM, as their prognosis may be more favorable than in patients with massively infiltrated breast.

References

1. Foley AL. A new technique for closing wounds after surgery for breast melanoma. *Plast Reconstr Surg* 1995;95:418–9.
2. Cangiarella J, Symmans WF, Cohen JM, Goldenberg A, Shapiro RL, Waisman J. Malignant melanoma metastatic to the breast: a report of seven cases diagnosed by fine-needle aspiration cytology. *Cancer* 1998;84:160–2.
3. Deshpande AH, Munshi MM, Lele VR, Bobhate SK. Aspiration cytology of extramammary tumor metastatic to the breast. *Diagn Cytopathol* 1999;21:319–23.
4. Majeski J. Bilateral masses as initial presentation of widely metastatic melanoma. *J Surg Oncol* 1999;72:175–7.
5. Pressman PI. Malignant melanoma and the breast. *Cancer* 1973;31:784–8.
6. Arora R, Robinson W. Breast metastases from malignant melanoma. *J Surg Oncol* 1992;50:27–9.
7. Plesnicar A, Kovac V. Breast metastases from cutaneous melanoma: a report of three cases. *Tumori* 2000;86:170–3.
8. Johimsen PR, Brown RC. Metastatic melanoma in the breast masquering as fibroadenom. *J Am Med Assoc* 1976;236:2279–80.
9. Barker JNWN, Girling AC. A case of malignant melanoma masquerading as disseminated mammary carcinoma. *Histopatology* 1989;14:219–21.
10. Ho LW. MR appearance of metastatic melanotic melanoma in breast. *Clin Radiol* 2000;5:572–3.
11. Padmore RF, Lara JF, Ackerman DJ, Gales T, Sigurdson ER, Ehya H, et al. Primary combined malignant melanoma and ductal carcinoma of the breast. A report of two cases. *Cancer* 1996;78:2515–25.
12. Kurul S. Diffuse microscopic in-transit metastases from malignant melanoma of the breast. *Plast Reconstr Surg* 2000;106:513–4.
13. Skarin A. Malignant skin lesion. Case 1. Nevoid malignant melanoma of the breast presenting as a contralateral breast metastasis. *Clin Oncol* 1999;17:3850–2.
14. Papachristou D, Kinne D, Rosen P, Ashikari R, Fortner JG. Cutaneous melanoma of the breast. *Surgery* 1979;85:322–8.
15. Lee YTN, Sparks FC, Morton DL. Primary melanoma of the breast skin. *Ann Surg* 1977;185:17–22.
16. Bono A, Baldi M, Maurichi A, Tomatis S. Distribution of melanoma on breast surface suggests its etiology. *Int J Cancer* 2003;105:434.
17. Gershenwald JE, Thompson W, Mansfield PF, Lee JE, Colome MI, Tseng CH, et al. Multi-institutional melanoma lymphatic mapping experience: the prognostic value of sentinel lymph node status in 612 stage I or II melanoma patients. *J Clin Oncol* 1999;17:976–83.
18. Karakousis CP, Choe JK, Holyoke ED. Biologic behavior and treatment of in-transit metastasis of melanoma. *Surg Gynec Obstet* 1980;150:29–32.
19. Rees WV, Robinson DS, Holmes EC, Morton DL. Altered lymphatic drainage following lymphadenectomy. *Cancer* 1980;45:3045–9.
20. Sood A, Youssef IM, El-Zeftawy H, Axelrod D, Siegel B, Abdel-Dayem HM. Alternative lymphatic pathway after previous axillary node dissection in recurrent/primary breast cancer. *Clin Nucl Med* 2004;29:698–702.
21. Mayayo AE,Gomez-Aracil V, Mayayo AR, Azua-Romeo A. Spindle cell malignant melanoma metastatic to the breast from pigmented lesion on the back. A case report. *Acta Cytol* 2004;48:387–90.