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journal homepage: www.casereports.comMetastatic breast disease from cutaneous malignant melanoma[☆]

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ABSTRACT

INTRODUCTION: Malignant melanoma is one of the most rapidly increasing cancer in the world. Breast metastases from melanoma are uncommon but could reflect a widespread disease.

PRESENTATION OF CASE: We report a case of malignant widespread melanoma presenting with bilateral breast nodules in a 39 year-old pre-menopausal Caucasian woman with an history of cutaneous melanoma of the trunk. Breast clinical examination revealed the presence of a hard and mobile lump located on the left breast. Ultrasound detected two bilateral nodules corresponding to oval opacities with well-defined edges and without calcifications or architectural distortion on mammography. Fine needle aspiration cytology performed on both breast nodules confirmed that the breast lesions were metastases from primary cutaneous malignant melanoma. A total-body CT examination detected brain, lung and abdominal lymph nodes metastases.

DISCUSSION: The breast represents an uncommon site of metastatic disease from extra-mammary tumors. Imaging features of breast metastases from melanoma usually do not allow a differential diagnosis with breast primary tumors. Breast metastases may be asymptomatic or palpable as dense and well-circumscribed nodules. Breast metastases indicate a widespread disease and should lead to avoid aggressive surgical procedures because of the poor prognosis of patients affected by metastatic melanoma.

CONCLUSION: The detection of bilateral breast metastases from melanoma is highly suggestive of metastatic multi-organ disease and could be useful to address the therapeutic approach.

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1. Introduction

Malignant melanoma is one of the most rapidly increasing cancer in the world with an increasing incidence rate in recent decades. An estimated 76,250 new melanoma cases have been diagnosed in the United States in 2012 and 9180 are expected to die.¹

Haematic or lymphatic metastases from malignant melanoma occur outes in 20% of cases. Liver, lung and brain represent the common sites of haematic metastases, although any organ could be involved. Metastases to the breast from malignant melanoma or other extra-mammary tumors are rare and represent approximately 1.3–2.7% of all malignant breast tumors. Melanomas and lymphomas are the most commonly reported tumors metastasizing to the breast. Breast involvement often represents the first sign of a primary extra-mammary tumor.^{1–4} For this reason, breast metastases must be suspected in patients with an history of malignant melanoma and the detection of breast lesions always

requires further diagnostic and instrumental procedures aimed to their characterization. Even if breast metastases from melanoma have no specific feature on imaging techniques, cytological or histological examination provides crucial information in order to choose the most suitable therapeutic approach.

In this paper, we report the case of a pre-menopausal woman with an history of malignant cutaneous melanoma of the trunk and a palpable left breast lump 3 years later. The diagnostic and instrumental procedures revealed metastases to the breast and others organs from malignant melanoma.

2. Presentation of case

A 39 year-old pre-menopausal Caucasian woman was referred to our breast clinical center for a palpable lump on left breast.

The patient had an history of a primary cutaneous melanoma of the trunk diagnosed at the age of 36. In December 2009, the lesion was surgically removed from the inter-scapular region and the histo-pathological examination revealed a Superficial Spreading Malignant Melanoma (SSMM) with infiltration of the reticular derma and a thickness of 2.8 mm, Clark IV. The excision margins were not infiltrated. A wide local and sentinel lymph node excisions were performed in the region of the nape and of the trapezius. The histological report was negative for tissue and node involvement.

No further treatment was performed for this disease.

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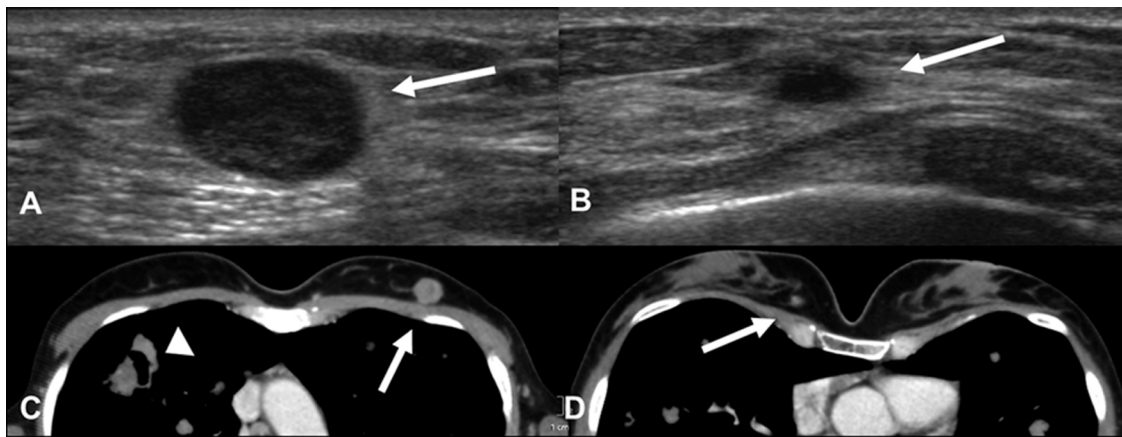


Fig. 1. A and B US examination. Two breast hypo-echoic nodules with regular edges were detected in the superior medial quadrant of the left breast (A, arrow) and on the inferior inner quadrant of the right breast (B, arrow), respectively. B and C CT scans. Corresponding CT findings of the left (C, arrow) and right (D, arrow) breast nodules appearing as hyper-enhanced lesions. An excavate lung metastasis was also evident in the upper lobe of the right lung (C, arrow head).

In December 2012, the patient felt a lump on the left breast. Breast clinical examination confirmed the presence of a hard and mobile lump with normal overlying skin located in the superior medial quadrant of the left breast. Ultrasound detected two bilateral rounded nodules with well-defined edges, hypo-echoic structure and a maximum diameter of 1.4 cm.

The nodules appeared as oval opacities with well-defined edges and without calcifications or architectural distortion on mammography.

A fine needle aspiration cytology (FNAC) was performed on both breast nodules by using a 21G needle. The sample material was macroscopically dark and therefore highly suggestive of melanocytic pigmentation. The cytological and immuno-histochemical reports (S100 protein, Melan-A and HMB-45) diagnosed metastases from primary cutaneous malignant melanoma.

A total-body CT examination was performed a week later. Brain, lung and abdominal lymph nodes metastases were detected (Figs. 1 and 2).

The patient underwent whole brain radiation therapy for brain metastasis (30 Gy in 10 fractions) and she is now undergoing a target drug therapy with Dabrafenib, a reversible selective inhibitor of mutant BRAF.

3. Discussion

Breast represents an uncommon site of metastatic disease from extra-mammary tumors. The most common primary tumor sources for breast metastases are represented by lymphomas, melanomas, rhabdomyosarcomas, lung and ovarian tumors.^{1,2} Patients with breast metastases from melanoma are often pre-menopausal women and considerably younger than patients affected by other tumors with breast metastatic involvement. In about 50% of cases, the upper outer quadrant is involved.^{2,4–8} The age and hormonal setting of our patient seem to confirm these previously reported findings, except for the site of breast lesions, located in the superior medial quadrant of the left breast and in the inferior inner quadrant of the right breast.

Besides, in case of breast metastases from cutaneous malignant melanoma, the most common Clark stage reported at diagnosis is IV, 2–3 mm of depth by Breslow and the mean reported interval from the initial diagnosis is 33 months.

As reported by Majeski, the bilateral breast involvement amounts for about 10% of patients affected by breast metastases from melanoma and suggests a widely disseminated disease as a poor prognostic factor.¹

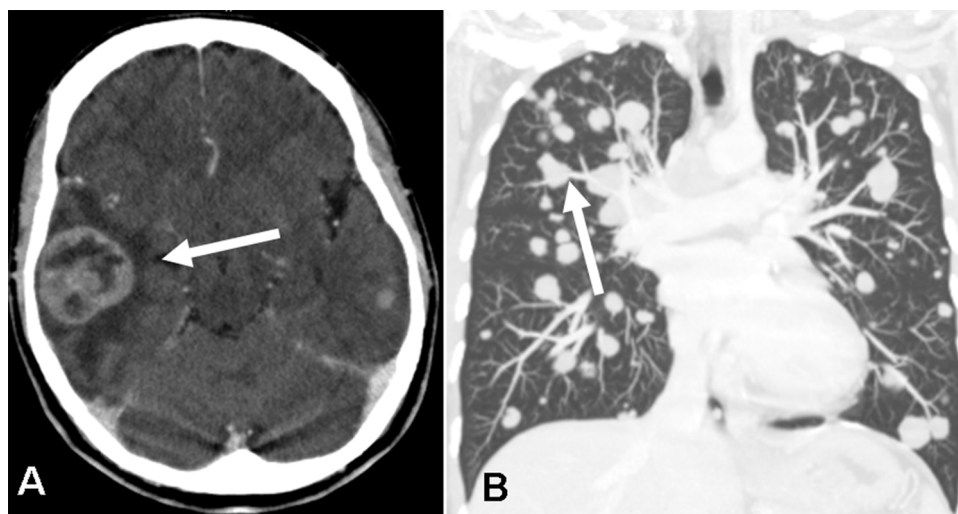


Fig. 2. CT scans. (A) Multiple brain metastases were detected in both cerebral hemispheres (arrow). (B) CT image on the coronal plane showing multiple lung metastases from cutaneous malignant melanoma (arrow).

The clinical examination and imaging features of breast metastases from melanoma usually do not allow a differential diagnosis with breast primary tumors. Breast metastases may be asymptomatic or palpable as dense and well-circumscribed nodules. On ultrasound examination, lesions usually appear as rounded or oval hypo-echoic nodules with a well-defined posterior wall. On mammography, breast metastases appear as well-defined nodular opacities without calcifications or architectural distortion.^{1–3}

For these reasons, clinical history, cytological and histological examinations are crucial for diagnosis.

In our experience, the history of malignant melanoma and the pigmented cytological samples were highly suggestive of breast metastases, therefore histological examination was not required. However, melanin pigment within tumor cells represents a rare feature. In fact, in most cases, metastatic melanoma can mimic a variety of cellular and architecture phenotypes, including primary breast malignancies. Immuno-histo-chemistry allows a correct diagnosis; tumor cell immune-reactivity for S100 protein, Melan-A and HMB-45, along with no expression for cytokeratin staining, proves useful in differentiating malignant melanoma from other malignant tumors.^{8,9}

The diagnosis of breast metastases from melanoma, especially in case of bilateral lesions, requires a whole body evaluation because in most cases they are associated with wide dissemination.

Treatment options for metastatic melanoma include close observation, surgical resection of isolated metastases, chemotherapy and radiation therapy.

With regard to chemotherapy, the response rates to dacarbazine and interleukin (IL-2) therapy are low. However, the treatment of metastatic melanoma has been modified by the introduction of targeted therapy and immunotherapy; in fact, vemurafenib, a BRAF inhibitor, and ipilimumab, an anti-cytotoxic T-lymphocyte antigen 4 antibody, represent the first agents which showed a survival benefit.

Radiation therapy plays a limited role in the control of the natural history of metastatic melanoma, because the radio-sensitivity of melanoma cells is low.^{1,4,9,10} Our patient underwent whole brain radiation therapy because of the presence of multiple brain metastases.

Finally, breast metastases indicate a widespread disease and should lead to avoid aggressive surgical procedures because of the poor prognosis of patients affected by metastatic melanoma.

4. Conclusion

Metastases to the breast should be searched in any patient with an history of cutaneous malignant melanoma and suspected in

case of breast lumps. Any breast lump in these patients should be characterized by cytological or histological examination. In case of confirmed breast metastases from melanoma, no therapeutic approach should be performed before the staging of the disease. In fact, breast metastases could reflect a widespread disease and a poor prognosis, especially in case of bilateral breast lesions.

Conflicts of interest

The authors declare that there is no conflicts of interest.

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Ethical approval

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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