

A large metastatic intramammary lesion of an occult melanoma



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OBJECTIVE: *Malignant melanomas presenting with unknown primaries are uncommon. In the majority of cases metastases of occult melanoma were detected in skin or in lymph nodes. Melanoma can rarely occur as a primary or metastatic intramammary tumor.*

CASE REPORT: *We report the case of a 58-year-old Caucasian woman who came to our department with a voluminous mass in her right breast. Histopathological examination found metastasis of epithelioid melanoma with unknown primary lesion. Our patient underwent a radical enlarged mastectomy, but due to the extension a radical removal was not possible.*

DISCUSSION: *In 2.2% of cases, melanoma may present with a metastasis without an identifiable primary lesion; this case should be considered a stage IV melanoma (Tx; N1; M1) due to the extension of the lesion and the infiltration of adjacent structures.*

CONCLUSIONS: *In literature, the presence of a breast metastasis of melanoma with unknown primary origin was reported just in one case. The execution of histopathological analysis is mandatory for a correct differential diagnosis with primary carcinoma of the breast. Palliative metastasectomy should be discussed with multidisciplinary melanoma board.*

KEY WORDS: Breast metastases, Metastatic melanoma, Unknown primary site

Introduction

Worldwide incidence of melanoma is continuously increasing and nowadays melanoma represents the most common cancer among young adults. Despite increasing awareness through promotion of screening campaigns and other initiatives, the number of deaths due to melanoma is predicted to rise ¹. Prognosis of melanoma is strictly related to the stage at diagnosis: primary lesion characteristics and grade of lymph nodal involvement are the

most important factors influencing survival ^{2,3}. Melanoma can metastasize both through hematic and lymphatic pathways, developing immune escape strategy during its progression ⁴. For these reasons an accurate clinical-imaging examination is indispensable for a correct staging ^{5,6}; this is particularly true for melanoma arising in anatomical district with a complex hematic and/or lymphatic drainage ⁷⁻¹¹. An accurate micro-staging of primary lesion and the execution of sentinel lymph node biopsy in thin and thick melanomas have an important prognostic significance, guiding the subsequent therapeutic management ^{12,13}.

In 2.2% of cases, melanoma may present with its metastases without an identifiable primary lesion ¹⁴. Lymph node and skin metastases are the most frequent sites in which melanoma metastases are reported, while the incidence of breast metastases from extramammary cancers is rare ¹⁵. In case of stage IV metastatic melanoma, metastasectomy improves prognosis of patients with a

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long disease free interval after treatment of their primary tumours if all clinically evident tumor can be resected^{16,17}. Otherwise, palliative metastasectomy should be reserved to carefully selected patients¹⁸. We report the case of wide hemorrhagic metastasis of melanoma of unknown origin in the breast and its diagnostic and therapeutic management.

Case Report

A 58-year-old postmenopausal Caucasian woman came to emergency department of "Policlinico di Bari" in October 2016 because of a voluminous mass grown in her right breast. The physical examination revealed a poorly circumscribed mass of over 25 cm, fixed to surrounding tissues, covered with stretched skin and spider veins and with spontaneous bleeding, extending from right breast up to right axillary region. The patient had no previous history of melanoma or any other cancer. Computed Tomography (CT) with contrast agents showed a wide solid heterogeneous expansive (25 x 25 x 20 cm) process arising from right mammary gland and extended up to right humeral region and to the anterior chest wall. This solid mass infiltrated the muscle grand pectoral, the structures around the pulmonary apex, the muscular structures of the right gleno-humeral joint and the external and internal intercostal muscles, along the entire right thoracic wall. The right parietal pleura was thickened and with nodularity in correspondence with

the infiltration of the intercostal muscles and it was reported a pleural effusion in the right cost-vertebral angle with a maximum thickness of 4 cm. It also determined pathological fracture of the manubrium and sternal body. The images have demonstrated the presence of intralesional calcifications and a large (14x14x8 cm) loculated fluid collection with a fluid-fluid level, suggesting an active hemorrhage. Our patient underwent an incisional biopsy of the wide mammary lesion. The histopathological examination demonstrated the presence of malignant spindle cell with hyperchromatic and pleomorphic nuclei and large and eosinophil cytoplasm. Immunohistochemistry was positive for protein S-100 and HMB45, confirming the diagnosis of malignant melanoma. Molecular biology sequencing showed a BRAF^{V600E} mutation. The final diagnosis was metastasis of epithelioid melanoma with unknown primary lesion. The case was presented to the multidisciplinary melanoma board of our institution and the patient began a treatment with Dabrafenib (150mg/day) and Trametinib (2mg/day).

In November 2016, the clinic-instrumental evaluation demonstrated an enlargement of the lesion due to the increase in the size of hemorrhagic collection. For this reason it was decided to undergo the patient to radical enlarged mastectomy with removal of the massive fluid collection. During surgery a prominent infiltration of thoracic wall of muscular and bone tissue was observed. Due to the mass extension and to the structures involved a radical removal was not possible. The histopathologi-

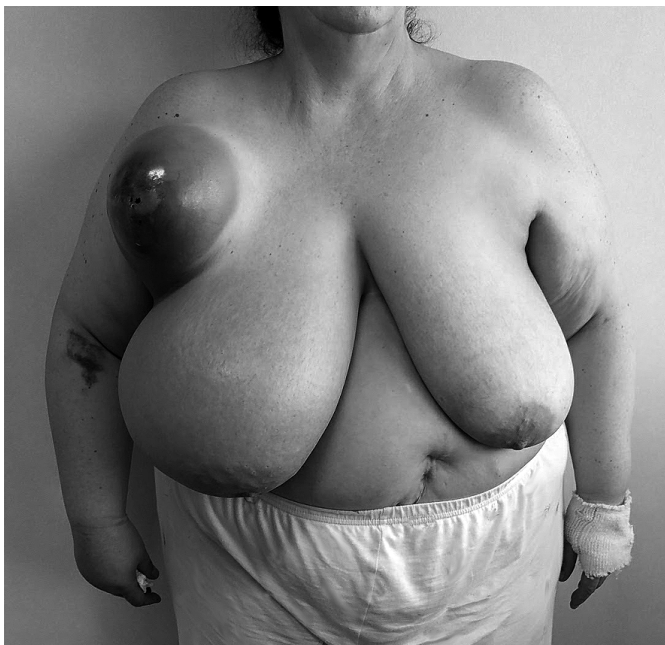


Fig. 1: A 58-year-old woman with a voluminous mass in her right breast, not sliding on the surrounding tissues, covered with stretched skin and spider veins and with spontaneous bleeding, extending from right breast up to right axillary region.

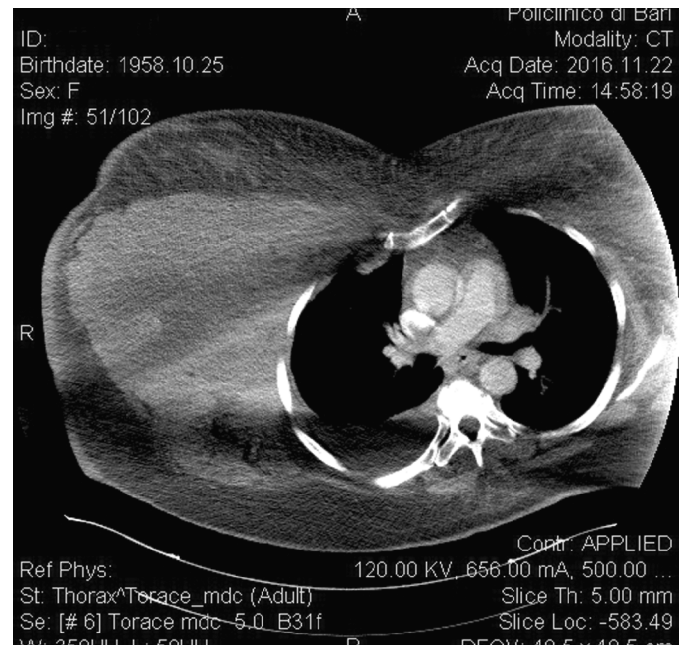


Fig. 2: Inhomogeneous mass at the right anterior chest wall with bones and muscles structures infiltration referable to melanoma metastasis.

cal analysis found a 38 x 33 x 17 cm mass, including a pseudocyst area of 10 cm with colliquative necrosis. The lesion infiltrated the chest muscles, skin and nipple and tumor cells were present in surgical deep margins. The specimens confirmed the diagnosis of metastasis of epithelioid melanoma with unknown primary lesion.

In the following days, the patient underwent a complete dermatological, ophthalmological, pneumological (with bronchoscopy and thoracentesis) and gastroenterological (with gastroscopy and colonoscopy) examination without finding of primary lesion. Also, total body scintigraphy did not show any primary lesion or metastasis in parenchymal organs. Our patient decided for a voluntary discharge against medical advice 15 days after the surgery.

Discussion

Malignant melanomas presenting with unknown primaries are uncommon¹⁹. In the majority of cases metastases of occult melanoma were detected in skin or in lymph nodes, while their presence in visceral organs is even more rare²⁰. Rarely melanoma can occur as a primary intramammary tumor²¹. The presence of a breast metastasis of melanoma with unknown primary origin was reported just in one other case, in which the melanoma metastasis was described as well-delimited oval mass of 1.6x1x1.3 cm in the inferior external quadrant not infiltrating adjacent anatomical structures²². Our patient presented at diagnosis a much more extended lesion, infiltrating chest muscles, skin and nipple. For this reason, diagnosis, prognosis and treatment of our patient is peculiar.

In fact, CT images demonstrate a rich vascularization and the infiltration of adjacent anatomical structures, but it was not useful in the differential diagnosis among metastases of melanoma, primary carcinoma of the breast and any other metastases of extramammary tumors. Only the execution of histopathological examination combined with immunohistochemistry confirmed the diagnosis of melanoma. In our case protein S-100 and HMB45 were expressed; the concomitant expression of these markers has demonstrated a good accuracy in the diagnosis of melanoma²³.

Although the staging of melanoma of unknown primary origin is difficult because of the impossibility to determine if a patient has a regional or distant metastases²⁴, this case should be considered a stage IV melanoma (Tx; N1; M1) due to the extension of the lesion and the infiltration of adjacent structures. The prognosis of patient with melanoma of unknown primary origin is controversial: some authors referred a better prognosis when compared with patients with a melanoma of known primary at the same stage²⁵, while others reported a similar prognosis between the two cohorts²⁶. Nonetheless, the treatment of these patients should be

the same as the treatment of patients with known primary lesion at the same stage.

Due to the presence of a BRAF V600E mutation, our patient underwent a treatment with Dabrafenib and Trametinib, without significant results on containment of tumor progression. We subsequently performed a complete mastectomy because of the increasing of hemorrhagic collection but the infiltration of pleura and chest muscles did not permit the complete removal of metastasis and the patient underwent a partial metastasectomy for palliative reasons¹⁸. A further locoregional treatment of melanoma metastasis with Electrochemotherapy with bleomycin²⁷ and a systemic treatment with low dose chemo-modulating Temozolomide in combination with Fotemustine²⁸ were planned; but these innovative approaches were not used due to the voluntary discharge of the patient.

Conclusions

Primary or metastatic involvement of breast in melanoma is particularly rare. The execution of histopathological and immunohistochemical analysis is mandatory for a correct differential diagnosis with primary carcinoma of the breast and any other metastases of extramammary tumors. The treatment of metastatic melanoma with unknown primary origin should follow the guidelines laid down for melanomas with known primary lesion at the same stage. Palliative mastectomy should be reserved to selected patients.

Riassunto

Il melanoma maligno, nel 2.2% dei casi, si presenta in forma metastatica con localizzazione primaria non identificabile, si parla in questi casi di metastasi da melanoma primitivo occulto. Le metastasi di melanoma sono localizzate più frequentemente a livello cutaneo e linfonodale, mentre la presenza di metastasi mammarie è poco frequente. In letteratura è riportato un solo caso di metastasi intramammarie da melanoma primitivo occulto, in questo lavoro ne presentiamo un nuovo caso. Si tratta di una donna caucasica di 58 anni che è giunta alla nostra attenzione per una voluminosa massa a livello della mammella destra. L'esame istologico della lesione ha diagnosticato la presenza di metastasi mammaria da melanoma cutaneo. La paziente è stata quindi sottoposta ad un accurato esame dermatologico, oftalmologico, pneumologico e gastroenterologico ma non è stata identificata la lesione primitiva. Si tratta di un caso molto particolare e di difficile gestione ed inquadramento terapeutico per le dimensioni della massa e l'estesa infiltrazione alla parete toracica anteriore. La paziente è stata sottoposta a mastectomia radicale allargata, ma a causa dell'estensione della lesione non è stata possibile un'escis-

sione radicale. Sebbene la stadiazione del melanoma occulto sia difficile a causa dell'impossibilità di determinare se si tratti di metastasi regionali o a distanza, questo caso dovrebbe essere considerato uno stadio IV (Tx; N1; M1) per l'estensione e l'infiltrazione delle strutture adiacenti. Nei casi di metastasi intramammarie l'esame istopatologico è dirimente per una corretta diagnosi differenziale con il carcinoma mammario primitivo. La mastectomia palliativa dovrebbe essere attentamente valutata con un team multidisciplinare per la cura del melanoma.

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