Case study

Ovarian metastasis of cutaneous melanoma : literature review illustrated by a case report

Abstract:

The discovery of ovarian metastasis from cutaneous melanoma is an exceptional pathological situation, only few isolated cases were reported in literature. The diagnosis is rarely evoked before surgery, especially when the primary tumoral site is unknown. Clinical presentation isn't specific, the contribution of imaging is limited, only immunohistochemistry is of great contribution to establish the diagnosis of certainty.

The goal of our study is to specify the characteristics of this pathological entity whose prognosis remains bleak despite therapeutic progress.

Key words:

Melanoma-ovarian metastasis-immunohistochemistry-immunotherapy-targeted therapy

Introduction:

With an annual incidence of 15 404 new cases, cutaneous melanoma is responsible for 1783 deaths per year. It is the sixth largest cancer in women. In Africa and in Maghreb, cutaneous melanomas are less frequent but often in a thick nodular type. If the forms diagnosed early are of good prognosis with 91% survival at 5 years, metastatic forms remain of terrible prognosis, despite the advent of new systemic therapies [1,2].

Frequent metastatic sites of cutaneous melanoma are : lung, mediastinum, brain, lever and bone [3]. The occurrence of ovarian metastasis is an exceptional event, only few isolated cases were reported in literature. Clinical and paraclinical aspect of this unusual metastatic location being

non specific, the diagnosis is often carried out after surgery with immunohistochemistry study of surgical specimens [4].

We report the case of bilateral ovarian metastasis with peritoneal carcinomatosis occuring 14 years after diagnosis of primary cutaneous site.

Clinical case:

It's the case of a 26 year-old-woman, without familiar pathological history of melanoma or other neoplasic illness, followed since the age of 12, for cutaneous nodular melanoma at dorsal part of her body, treated by surgical excision. The evolution, 13 years after, was marked by the appearance of left axillary metastatic nodes and bone metastasis in the third right rib of 7cm, also resected. Immunotherapy was started in vain, the patient received 9 cures without response, with progression of the disease and other outbreaks of spread including spinal location, requiring a medullary decompression laminectomy at the level of the tenth dorsal vertebra. One month later, the patient consults for rapid increase in abdominal volume evolving in a context of asthenia and unencrypted weight loss.

Clinical examination found a conscious patient, hemodynamically stable, afebrile. Abdominal examination found a distended abdomen with an abdomino-pelvic mass arriving to umbilicus, regularly shaped, firm in consistency, associated with ascites.

Pelvic ultra-sound found a voluminous abdomino-pelvic mass, solid and cystic, heterogenous, not measurable on ultrasound, with central vascularization on Doppler, associated to an ascites of great abundance reaching the parieto-colic gutters. The CT-scan, shows an abdomino-pelvic mass up and lateral to uterus, fleshy, mixed, measuring 16.5/11.5/17cm, associated to multiple nodes of peritoneal carcinomatosis predominant at the level of the greater omentum with ascites of great abundance.

In addition, vertebral metastasis at the third and tenth dorsal vertebrae were found.

Laparoscopic exploration found a 24cm ovarian mass of whitish colour with brownish areas, roughly rounded, with a bumpy surface (figure 1). The contro-lateral ovary was increased in size, bumpy, containing blackish areas. The peritoneal cavity was a site of diffuse pigmented carcinosis with black omentum (figure 2).

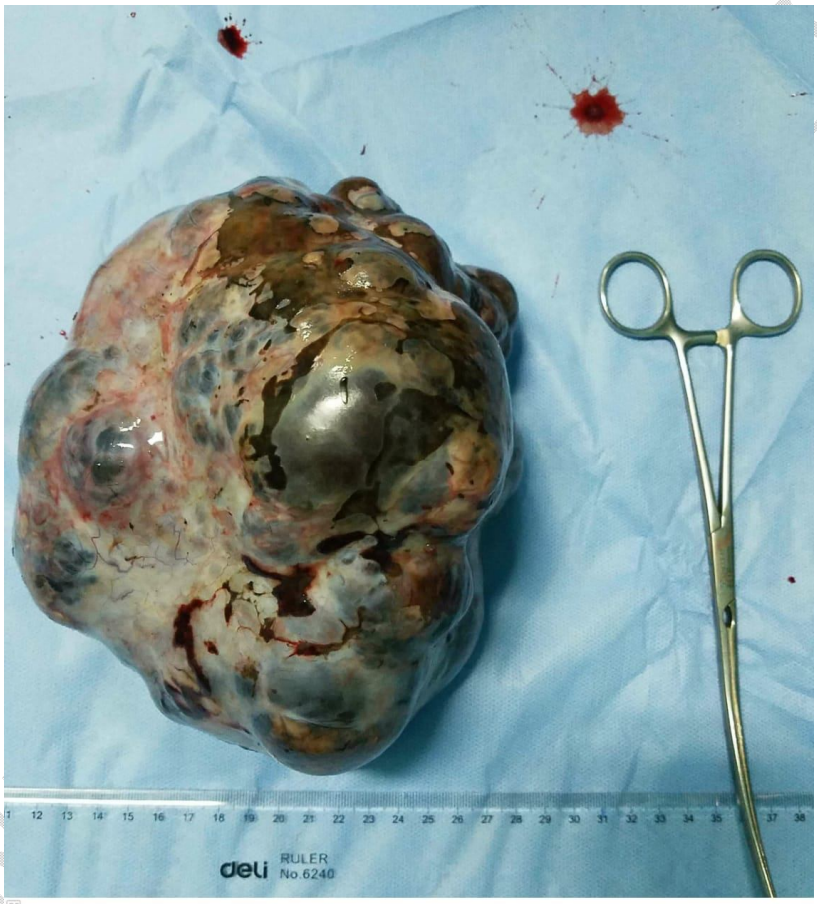

Figure 1 : Right ovarian mass measuring 24/20/14cm, solid and cystic, fleshy with pigmented areas

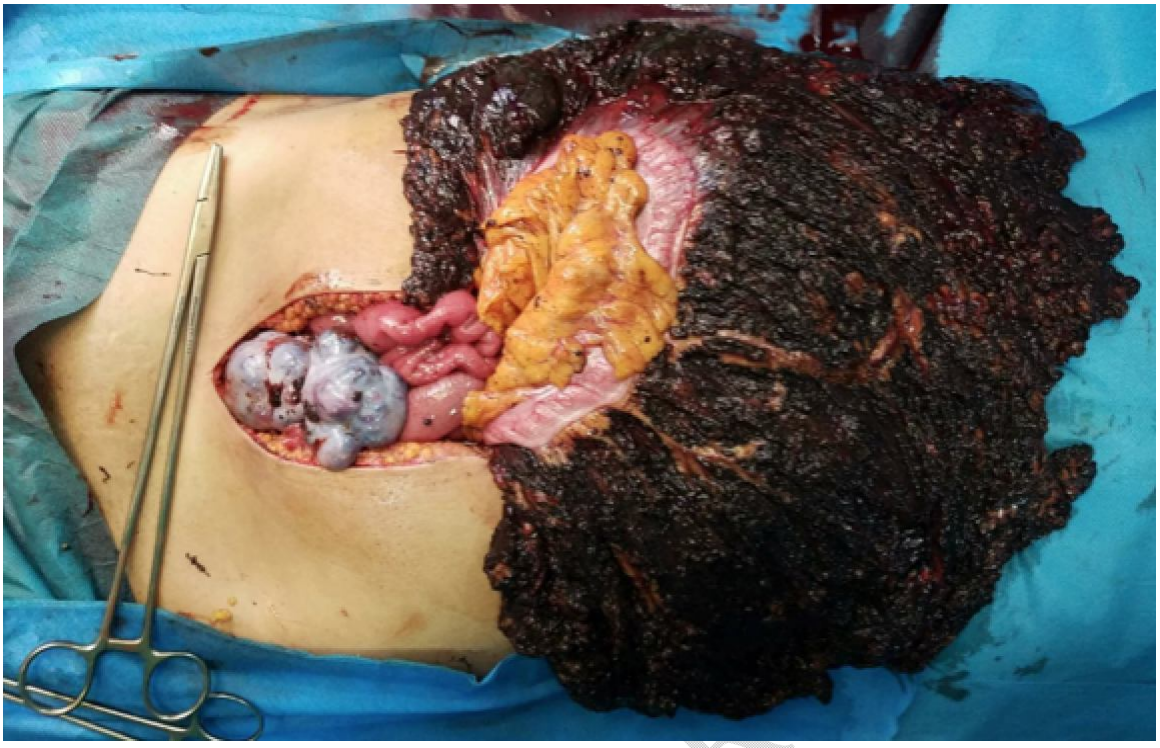

Figure 2 : black omentum invaded by carcinosis

In front of the pigmented aspect of lesions, a secondary ovarian location of the cutaneous melanoma was suspected. We did aspiration of ascites with cytological study of the liquid, followed by a bilateral annexectomy and omentectomy after conversion to laparotomy. The histological study of specimens affirmed the diagnosis thanks to the immunohistochemical analysis which highlighted a strong and diffuse marking of tumour cells by Melan A.

Discussion :

Ovarian cancer is the fifth gynecological cancer and the fourth in terms of mortality. The average age of onset is about 60 to 70 years. Epithelial tumors are the most frequent. Ovarian metastasis represent 6 to 7% of malignant tumors. They are usually of gynecological, gastrointestinal or mammary origin. Ovarian metastasis of cutaneous melanoma are exceptional, with frequency of 3%, only few cases are reported in literature

[3, 4, 5]. However, post-mortem studies have shown a frequency estimed to 18%. This underestimation is undoubtedly explained by the long silent character of ovarian masses in women dying from complications related to other extra-ovarian locations [6]. Ovarian extension occurs through blood, lymph and peritoneum [3]. Delay between the diagnosis of primary lesion and the discovery of ovarian metastasis varies between few months and 18 years [4]. In our case, it was about 14 years. The breach is unilateral in 60% of cases. Ovarian metastasis achieve with predilection for young women comparing to menopaused ones, due to reduction of ovarian blood flow after menopause [3, 4].

Clinical and paraclinical aspects aren't specific, presenting a real problem of differential diagnosis with other ovarian malignant tumors. However, MRI can suspect the diagnosis, by showing spontaneous peripheral hypersignal in T1 and T2 weighting sequences in connection with the presence of melanic pigments [3, 4, 6]. The average size of secondary ovarian tumors, reported in literature, is about 10cm. In our case, the largest tumour size was about 25cm. Histopathological study of specimens may be confusing with germinal, stromal and granulosa tumors. Only immunohistochemistry give the diagnosis of certainty by demonstrating the expression of these tumor markers : S-100, HMB-45 and Melan A [7]. The distinction between primary ovarian melanoma or metastatic may be difficult. The clinical context is evocative if primary cutaneous, adrenal or choroidal location is known, otherwise, or in case of regression of the primary cutaneous lesion, which can occur in 2-9% of cases, some authors have retained the diagnosis of primary location on some criteria such as, the only ovarian location of the tumor and the association with an ovarian teratoma [4]. Otherwise, primary ovarian melanoma is mainly seen in menopaused women.

In our case, the primary cutaneous location was known. The absence of ovarian teratoma on imaging and the pigmented aspect of ovarian and peritoneal lesions in surgical exploration, made it possible to suspect the diagnosis. Although the pigmented character isn't specific, seen only in 35% of cases, and can be seen also in steroid ovarian tumors [7]. Confirmation of the diagnosis has been obtained by immunohistochemistry by showing the presence of Mela A on specimens.

Surgical management consists in performing annexectomy and removal of the reducible lesions. In our case, the complete resection was not possible because of the disseminated character and diffuse peritoneal carcinomatosis. Surgical management seems to improve the prognosis, when it's complete, especially when metastasis are only located in the ovaries. In case of unilateral ovarian location, prophylactic controlateral annexectomy is discussed in postmenopausal women [3]. Assessment of prognosis in forms eligible for optimal surgical management, depend on staging by conventional imaging or PET scan [3, 4].

For more than 30 years, the standard treatment for advanced cutaneous melanoma stages was platinum-based chemotherapy with response rates from 5 to 15% and a median survival from 6 to 9 months, while actually, it currently exceeds 2 years, with even hope to heal some patients. The therapy options have evolved radically since 2011 with the development of two new therapeutic strategies, on the one hand immunotherapy and on the other hand targeted therapy for patients with melanoma related to BRAF 600 mutation, encountered in half of cases, response rate is estimated at 25%. In terms of duration of treatment, targeted therapeutics are continued until intolerance or progression, while immunotherapy can be stopped after obtaining a complete response or stabilization [8].

Our patient was resistant to treatment by immunotherapy, which was interrupted because of the progression of the disease. Chemotherapy, based on carboplatin and taxane, retains its interest in forms with peritoneal dissemination [3].

Nevertheless, the value of systemic treatments in terms of improving survival prognosis, is however not established. 5-year survival varies from 0 to 5% depending on literature data, median survival is from 10 to 20 months [3,6].

Conclusion :

Through this clinical case, we tried to illustrate the features of this exceptional pathological situation. In fact, the diagnosis of ovarian metastasis from cutaneous melanoma is rarely evoked before surgery, especially when primary tumoral site is not identified, clinical presentation being non-specific. MRI can be contributive in some cases. The diagnosis in based on immunohistochemistry study of specimens. Despite the contribution of surgery when it's optimal and the contribution of new systemic therapies, the prognosis remains very grim with less than 5% survival at 5 years. Actually, many predictive markers are under study and many therapeutic combinations are under investigation to try to improve the prognosis of the disease.

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