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Antonio Varricchio*, Lorenzo Di Libero**, Carlo Iannace***

*A.O.U. Federico II, Napoli, Italy

**Clinica Sanatrix spa, Napoli, Italy

***A.O. San Giuseppe Moscati, Avellino, Italy

Reconstruction with cutaneous flap after resection for breast cancer's skin metastases in a chemoresistant patient

We reported a case of a breast cancer's skin metastases in a patient that had sustained 3 lines of chemotherapy. At first she received surgical treatment with Madden's mastectomy with dissection of axillary lymph nodes and positioning of an expander. After that she underwent to chemo- and radiotherapy. The schedules we performed were: FEC, TC, Vinorelbine and Capecitabine. Only after the FEC there was a clinical remission just for 1 year. After that she underwent to surgery for the removal of a lozenge of skin on the right hemithorax, including also the subcutaneous tissue, a strip of muscular tissue, and a residue of the breast implant. The histology showed a multiple-nodules infiltration involving the dermis, the hypodermis, and the muscle. This pattern was valued as a G3 breast cancer recurrence with ER 70%, PgR<5%, Ki67 50% Her2neu-. During the second line chemotherapy with TC she developed an high grade LCIS with lymphovascular infiltration on the left breast; on the right hemithorax there were cutaneous metastases with dermis' infiltration. Surgery with local excision was performed, and a cutaneous flap was realized.

KEY WORDS: Breast cancer, Chemo-radiotherapy, Cutaneous Flap, Local Excision.

Introduction

Cutaneous metastatic carcinoma is an unusual clinical finding. According to an article in the Journal of the American Academy of Dermatology, Lookingbill et al. ¹, the majority of the cutaneous metastases in women was caused by breast cancer (70.7% of cases)². Focusing on breast cancer's skin metastases the chest wall is the most frequent site (39% of cases), the other sites are face (22.2% of cases), abdominal wall (15%), scalp (13.5% of

cases) and neck (9%). The clinical manifestations are various. They may occur as single subcutaneous nodes or single intracutaneous lesions (Paget type) or multiple subcutaneous or intercutaneous lesions or sometimes by rapidly progressive necrotic ulcerating lesions. A rare presentation is the "cancer en cuirasse" that involves the whole chest wall, causing also restrictive lung disease for the difficulty of thorax expansion during inspiration. Sometimes the manifestations are rapidly progressive necrotic ulcerating lesions. The spectre is often complicated by bacterial and mycotic infections that are difficult to treat.

The treatment includes surgery, radiotherapy, systemic therapy, phototherapy ², electrochemotherapy ⁴ (when surgery is not possible) and local treatment with miltefosine ². Surgery can be performed when the skin metastasis is the sole evaluable lesion. In a classic publication, Fentiman ⁵ showed that the prognosis of patients found

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Correspondence to: Varricchio Antonio, Via Amicoli 1, 82010 San Leucio del Sannio (BN), Italy (e-mail: an.varr89@hotmail.it)

to be suffering from skin metastases of breast cancer depended largely on the incidence of more advanced disease. In patients found to have single cutaneous lesions, a 42% 5-year survival and a 22% 10-year survival could be documented in a retrospective analysis of more than 200 patients, while patients suffering from metastases in multiple organs at the occurrence of skin metastases had a 10-year survival rate of 0% and only 10% of the patients survived 5 years.

Case report

The patient S.A.A. female, 59 years old received a diagnosis of breast cancer on November 2008. She was investigated with MRI which showed a big nodule of 3.6 cm with characters of malignancy in the subareolar area of the right breast. There was also the presence of edema involving skin and subcutaneous tissue. The patient received surgical treatment with Madden's mastectomy and dissection of axillary lymph glands with positioning of an expander behind the pectoralis major³. The lesion

was valuated as a DCIS G3 pT2N1 with ER 90%, PgR 70%, Ki 67 50%, Her2 neu -. On January 2009 she began FEC standard schedule (x 6 cycles). She was treated also with radiotherapy. On May 2009 she received ormonotherapy with tamoxifen+LHRH analog. On September 2009 she had a Transvaginal US and an endometrial polyp was discovered. After its removal with hysteroscopy, the biopsy described a proliferating endometrial polyp. On October 2010 the patient received surgery in order to remove a lozenge of skin on the right hemithorax, including also the subcutaneous tissue, a strip of muscular tissue, and a residue of the breast implant. The histology showed a multiple-nodules infiltration involving the dermis, the hypodermis, and the muscle. This pattern was valuated as a G3 breast cancer recurrence with ER 70%, PgR < 5%, Ki67 50% Her2neu-. An adjuvant treatment with TC schedule was implemented, but was interrupted after 4 cycles, because of the progress of disease (PD). This situation was documented with a CT on January 2011, which showed a

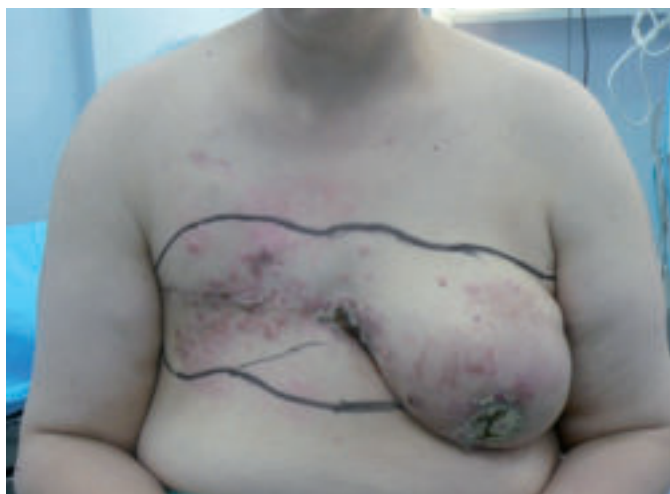


Fig. 1. Presentation of the patient before surgery.



Fig. 3: Schema about surgical treatment. The red arrow indicates the cutaneous flap which will be rotated. The black lines indicate the part we had to remove.

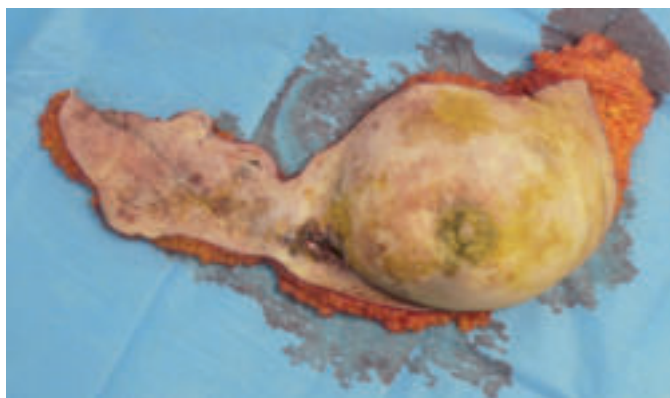


Fig. 2: Specimen.



Fig. 4: An overview on the result.

tumefaction of 2 cm in the left axillary cavity, in association with contiguous subcentimetric nodules.

On July 2011 the patient took an MRI that evidenced multiple millimetric areas of impregnation on the right hemithorax ;on the left there were multiple focuses of impregnation in the subareolar and internal part and near the union between OUQ and LOQ. The PET showed areas of hyperaccumulation in the left retroareolar region (SUV 2,7) and in the ipsilateral axillary cavity (SUV 1,4);there was a diffuse accumulation in the soft tissues of right hemithorax 's anterolateral part (SUV 2) of non-specific meaning. The CT total body was negative for brain lesions, but indicated lymphadenopathies of the front pillar of the left axilla and in the ipsilateral subclavicular region. There was no evidence of pleuropulmonary, mediastinal and splanchnic lesions.

At that time a skin biopsy on the surgical scar on the right hemithorax, and an excisional biopsy on the left were performed. The istology demonstrated an high grade LCIS with lymphovascular infiltration on the left; on the right hemithorax there were cutaneous metastases with dermis' infiltration. The results of IHC were ER 90%, PgR 80%,Ki67 60% HER 2 2+.

On October 2011 she began the chemotherapy with Vinorelbine and Capecitabine.

On February 2012 she received a surgical treatment that included the excision of a lozenge of skin with dermis,subcutaneous tissue and muscle in order to remove the cutaneous metastases and the reconstruction with a cutaneous flap on the right hemithorax. On the left breast a Madden's mastectomy was performed. (see figures below). The patient at that moment presented clinically multiple papulo-nodular lesions on the right; on the left there was an ulcerating process medially and Paget's lesions on nipple and areola. This kind of presentation was complicated by a concurrent infection of the ulceration. On March 2012 the patient was treated with 4 cycles of liposomal doxorubicin and with Paclitaxel for 12 weeks. No other sites of metastases were detected.

Discussion

The first useful step is an early staging to consider the systemic extension of the cancer. Whole body FDG-PET is the most sensitive instrumental investigation for staging primary tumour ⁶ and to detect metastases ⁷ an synchronous tumours. The second step is a correct dissection and biopsy of sentinel lymphnode ⁸ and axillary nodes ⁹; this procedure is important also for the local and regional control of the pathology. The third step is a correct implementation of chemotherapy schedules and an immediate evaluation of progress of disease ; in the case,we reported, 3 lines of therapy were used but the clinical remission, obtained with FEC schedule, was only temporary. Multidrug resistance in this case is the most

important cause of failure of the clinical remission. Assessment of cutaneous metastatic disease can be perplexing because the clinical presentation appears similar to other skin maladies such as cellulitis or lymphedema. Patients present with a variety of symptoms ranging from firm, indurated skin to tiny, seed-like solid papules and large egg-sized lesions. The differential diagnoses of cutaneous lesions are varied. In a breast cancer patient, other possible etiologies besides cutaneous metastases include cutaneous change, either acute or chronic – secondary to radiation therapy – or other infectious processes such as erysipelas, cellulitis or candidiasis. A physician caring for breast cancer patients must be able to distinguish between these. In the present patient, an infectious process was considered, but the clinical picture and history did not completely support this diagnosis. In general, specific clinical features such as lack of a febrile response, absence of leukocytosis and prolonged presence of the lesion (weeks to months) without response to antibiotics should alert the physician to the possibility of cutaneous metastasis ¹¹. Treatment is driven by two goals: (a) improving survival through gaining control of the disease and (b) optimizing quality of life and symptom management. Skin and wound management aims to alleviate symptoms such as copious exudate, malodor, pain, and the risk of hemorrhage. A large excision of the metastases gives the possibility to have a local control on the disease ¹⁰. many radiotherapy regimens are in use in the treatment of skin metastases (after excision) (H. Bartelink, personal communication). Regimens consist of 1x8 Gy, 3x8 Gy, 5x3 Gy, etc. (no comparative studies have been done).

The aggressiveness of the palliative radiotherapy regimen and the use of radiation ports of the whole operation field seem to be related to the time elapsed since the primary curatively intended treatment, e.g. radiotherapy or previous radiation treatment. For example, a skin metastasis manifesting itself within 2 years of previous surgery could be a seeding metastasis (although arguments are to be found that these are primary manifestations of systemic disease), and radiation of the whole operation field could be considered after removal of such a (scar) metastasis.

The problem becomes more difficult when such a metastasis in the operation field occurs after primary surgery including radiotherapy. Treatment of these skin manifestations of breast cancer occurring in the operation (radiation) field calls for local treatment by either radiotherapy or photodynamic treatment.

Conclusions

It's important to retrieve and recognize early the signs of the skin metastases. The first choice is surgery because gives the possibility of a local control of disease. Systemic adjuvant chemotherapy could be used to reach better

results on survival. Radiotherapy can be used to palliate local symptoms and in addition to surgery. Cutaneous flaps are possible for the control of the wound's strips. Systemic therapy with antibiotics can be applied for the treatment of the infections.

Riassunto

Riportiamo un caso di metastasi cutanee in un tumore della mammella di una paziente sottoposta a 3 linee di chemioterapia dopo il primo intervento chirurgico di mastectomia secondo Madden con dissezione ascellare e posizionamento di espansore. Iniziato il trattamento con lo schema FEC si è evidenziata una remissione clinica di circa un anno dopo la quale c'è stata progressione della malattia. Nonostante i trattamenti con TC e Vinorelbina si sono sviluppati un carcinoma lobulare con presentazione pagetoide a sinistra con metastasi cutanee sull'emitto destro, di conseguenza la paziente è stata trattata con mastectomia secondo Madden e dissezione ascellare a sinistra e ampia escissione locale a sinistra, con flap cutaneo di ricostruzione. Successivamente si è sottoposta al trattamento con doxorubicina e paclitaxel senza evidenziare altri siti metastatici.

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