

# A sinister rash in a lady with breast malignancy

Wen Foong Tan, MRCP, Sook Yee Michelle Voo, AdvMDerm

Department of Dermatology, Hospital Queen Elizabeth, Ministry of Health, Sabah, Malaysia

## SUMMARY

Cutaneous metastasis may be the first presentation of an undiagnosed malignancy or a relapse of a previously treated malignancy. We describe a case of a 64-year-old lady with cutaneous metastases from breast carcinoma, who presented with two uncommon rash morphology-carcinoma erysipeloïdes (CE) and annular erythema. Histopathological examination showed infiltration of neoplastic cells in the dermal lymphatics and staging CT showed distant metastases. She is currently on palliative chemotherapy. A high index of suspicion and early referral to a dermatologist is crucial for early diagnosis for a patient who presents with an inflammatory skin lesion that is refractory to treatment, particularly if the patient has a previous history of malignancy.

## INTRODUCTION

Metastases to the skin account for about 0.6-10.4% of all metastases.<sup>1</sup> They may represent the first presentation of an occult malignancy, a relapse of a previously treated malignancy or first indicator of metastasis. The most common internal malignancy that metastasises to the skin in women is breast carcinoma. This may be explained by the location of breast tumours which are superficial and in contiguity with the skin of the chest wall, as compared to visceral malignancy.<sup>1</sup> The presentation of cutaneous metastases may vary from the more common being single or multiple erythematous papules, plaques, nodules or ulcers to the uncommon variants including carcinoma erysipeloïdes (CE), carcinoma telangiectaticum, carcinoma en curaise, alopecia neoplastica, metastasis to the inframammary crease and zosteriform pattern.<sup>1,2</sup>

## CASE REPORT

We describe a 64-year-old lady who presented with a 3-month history of painless swelling of her right upper limb with itchy rash at her trunk. The right upper limb became warm and more erythematous 2 days prior to presentation, associated with fever. She was diagnosed with right upper limb cellulitis and was treated with intravenous cefuroxime. After completion of a course of antibiotic, the swelling over the right upper limb improved and the rash over her chest, right upper limb and back were less erythematous but persisted. Opinion of a dermatologist was sought. Of note, she had a history of invasive ductal carcinoma of the right breast (T2N3M0, HER2 positive, oestrogen/progesterone receptors negative) and had undergone right mastectomy with axillary lymph node clearance 7 years ago, followed by adjuvant chemotherapy (5-fluorouracil, epirubicin,

cyclophosphamide for 3 cycles and docetaxel for 3 cycles), radiotherapy and trastuzumab for 17 cycles. However, she developed right chest wall recurrence 2 years ago and was treated with 6 cycles of docetaxel. She underwent computed tomography (CT) scan at that time which did not show any distant metastases. She denied applying any topical medication on the areas.

On examination, there were well defined irregular erythematous annular patches coalescing into a polycyclic configuration over her chest extending into the left breast (Figure 1a). Her right upper limb was diffusely erythematous and indurated (Figure 1b). Similar annular patches and plaques were seen at the left flank (Figure 2a) and her back (Figure 2b). There was no palpable breast nodules or lymphadenopathy.

Differentials that were considered were CE and radiation dermatitis. Skin biopsies were taken from the erythematous patch over her right upper arm, left chest and left flank. Histological evaluation revealed irregular nests of malignant cells in tubular formation within the dermis and the lumen of vessels. The malignant cells were pleomorphic with fine to coarse nuclear chromatin and prominent nucleoli. Mitotic figures were also seen. The surrounding stroma was desmoplastic with lymphoplasmacytic cells and histiocytes infiltration. Immunohistochemistry studies showed positivity to mammaglobin, HER2 and E-cadherin. The endothelial cells were immunoreactive to CD31. Staging CT showed bilateral pleural effusion and bony metastases.

She was started on capecitabine for 3 cycles, followed by gemcitabine/carboplatin for 6 cycles. The rash over her trunk resolved after completion the chemotherapy. However, she had recurrent pleural effusion and pericardial effusion requiring drainage.

The rash over her chest, abdomen and back recurred 6 months after the gemcitabine/carboplatin chemotherapy and she is currently on treatment with vinorelbine.

## DISCUSSION

Here we highlight the need to consider the diagnosis of skin metastases in patients with underlying solid organ tumour presenting with erythematous, indurated skin eruption. Interestingly, our patient had CE and annular erythema which are two morphological variants of skin metastases. In this case, radiation dermatitis was another differential however, it was less likely as the erythematous indurated appearance of radiation dermatitis usually occurs in the

This article was accepted: 06 January 2021

Corresponding Author: Wen Foong Tan

Email: wftan85@gmail.com



**Fig. 1:** a) Well defined irregular erythematous annular patches coalescing into a polycyclic configuration over her chest extending into the left breast; b) Diffuse erythema and induration of right upper limb.



**Fig. 2a, 2b :** Erythematous annular patches and plaques at the left flank and back.<sup>1</sup>

<sup>1</sup>Written consent had been obtained from the individual for publication of her images.

setting of acute radiation dermatitis. In contrast, chronic radiation dermatitis typically presents more than 90 days after radiation therapy and the cutaneous findings are epidermal thinning, edema, dyspigmentation and telangiectasia.<sup>1,3</sup>

CE also known as inflammatory metastatic carcinoma, is a rare presentation of cutaneous metastasis from a primary internal malignancy. CE is most frequently associated with breast carcinoma with intraductal carcinoma being the most common. Other primary tumour sites include the pancreas, stomach, colon, rectum, lung, ovary, prostate, parotid gland and melanoma.<sup>1</sup> The prevalence of CE as a clinical manifestation of cutaneous metastases from breast carcinoma is about 3%. In CE, malignant cells disseminate from the affected lymph nodes to the cutaneous lymphatics in the dermis and subcutaneous tissue.<sup>2</sup> These malignant cells form tumour emboli that obstruct the lymphatics, giving rise to peau d'orange appearance due to localised lymphedema.

The rash in CE is described as a unilateral erythematous patch or plaque with a well-demarcated border.<sup>1</sup> The rash is usually distributed in proximity to the primary tumour and may progress to involve the back, arm and the contralateral side. CE may mimic other inflammatory conditions such as cellulitis, erysipelas, dermatophytosis, mastitis and contact dermatitis.

Our patient also had annular erythematous patches with polycyclic configuration. This morphology had been described in several reports of local recurrence of breast carcinoma. In these cases, the annular lesions were described to occur adjacent to the previous surgical scar except in one case where there was involvement of the back. This annular morphology is due to the spread of tumour cells via the lymphatics, not direct spread.<sup>4</sup> Tan et al postulated that the remaining cancer cells which did not respond to the initial chemotherapy had invaded the dermal lymphatics giving rise to this annular morphology.<sup>5</sup> Differential diagnoses to

consider include erythema chronicum migrans, erythema annulare centrifugum, drug-induced subacute cutaneous lupus and tinea corporis. Histological examination will help to clinch the diagnosis of cutaneous metastasis.<sup>4</sup>

Histopathological examination of both CE and annular erythema show infiltration of metastatic tumour cells into the superficial and deep lymphatics. The endothelial cells in the involved dermal lymphatics stain positively with CD31 and podoplanin, further supporting the predominant spread via lymphatic channels.<sup>1,4,5</sup> Other markers such as cathepsin D, mammaglobin, E-cadherin, pankeratins, epithelial membrane antigen (EMA), carcinoembryonic antigen (CEA), gross cystic disease fluid protein-15 (GCDFP-15), progesterone and estrogen receptors may improve diagnosis accuracy of breast carcinoma as the primary site.<sup>1,2</sup> In reported cases of annular erythema, there were overexpression of HER2 and negative markers for hormonal receptors.<sup>4</sup>

Features that may suggest the diagnosis of cutaneous metastasis include prolonged duration of rash, absence of fever or leucocytosis, negative cultures, and no improvement despite antibiotic treatment. In these cases, early biopsy facilitates the diagnosis. The prognosis of the patient will depend on the behaviour and type of the primary tumour and its treatment response. With regard to breast carcinoma, cutaneous metastasis portends advanced stage of disease with poor prognosis. The main treatment options include systemic chemotherapy, immunotherapy, hormonal therapy with or without radiation.<sup>2</sup>

## CONCLUSION

Inflammatory skin lesions, in particular those that are refractory to conventional treatment in a patient with history of malignancy could be the first sign of a relapse or metastasis. A high degree of suspicion and prompt referral to the dermatologist may lead to early diagnosis and intervention.

## ACKNOWLEDGEMENT

The authors would like to thank the Director General of Health for permission to publish this paper.

## CONFLICT OF INTEREST

The authors do not have any conflicts of interest to declare.

## INFORMED CONSENT

Written informed consent had been obtained from the individual for the publication of her images.

## REFERENCES

1. Alcaraz I, Cerroni L, Rutten A, Kutzner H, Requena L. Cutaneous metastases from internal malignancies: a clinicopathologic and immunohistochemical review. *Am J Dermatopathol* 2012; 34: 347-93.
2. Mordenti C PK, Concetta Fargnoli M, Cerroni L, Chimenti S. Cutaneous metastatic breast carcinoma: A study of 164 patients. *Acta Dermatoven APA* 2000; 9: 143-8.
3. Hegedus F, Mathew LM, Schwartz RA. Radiation dermatitis: an overview. *Int J Dermatol* 2017; 56: 909-14.
4. Sabater V, Ferrando F, Morera A, Palomar L. Cutaneous metastasis of inflammatory breast carcinoma mimicking an erythema annulare centrifugum: a sign of locally recurrent cancer. *Clin Exp Dermatol* 2016; 41: 906-10.
5. Tan E, Kuper-Hommel M, Rademaker M. Annular erythema as a sign of recurrent breast cancer. *Australas J Dermatol* 2010; 51: 135-8.