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Case Report

In- transit metastasis: Case report of a rare phenomenon in primary cutaneous squamous cell carcinoma

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ABSTRACT

Metastatic foci situated in dermal or subcutaneous tissue without the involvement of overlying skin, between the closest lymph node and primary tumor is called in transit metastasis. Although in transit metastasis has been commonly described in malignant melanoma, there are rare cases of squamous cell carcinomas, presenting with the same. It is an uncommon form of metastasis through lymphatics and is found in immunocompromised individuals. We present a case report of squamous cell carcinoma, presenting in an elderly male, as multiple nodules beneath skin. With this case, we highlight the variety of forms of spread in cutaneous squamous cell carcinoma and its prognostic importance.

1. Introduction

Cutaneous squamous cell carcinoma being the second most common non melanoma skin cancer, has a lifetime incidence between 7 and 11%.[1–3] The appearance of cutaneous SCCs varies greatly, presenting as firm, hyperkeratotic, ulcerated, skin-colored papules or plaques found on sun-exposed skin and may be itchy or painful. Nodular squamous cell carcinomas are characterized by nodules with keratin crust or scale, a central keratin mass, prominent vascularity or haemorrhage, and multiple colors.[4] Currently, it is stated that these SCCs are rather metastatic: either from a visceral malignancy or as an in-transit metastasis from a prior SCC, similar to melanoma.[5,6] The percentage of local and distant metastasis increases up to 15 to 38% in cases of high-risk squamous cell carcinoma. In immunosuppressed patients, the metastatic rate of Cutaneous SCC is reported as 12.9%, twice the rate of non-immunosuppressed patients.[7] In-transit metastases are rare and present as dermal and subcutaneous metastatic foci located between the tumor and the closest regional lymph node.[8] This case has been presented hoping that such atypical presentations of a common tumor of skin should not be missed out and be properly managed.

2. Case History

A 72 year old male, with no known co morbidities, presented with multiple swellings over left shoulder and left side of chest since 2 months. He had a history of blackish lesion just lateral to left nipple, noticed 6 months back. All the nodular lesions were of varying sizes, ranging from, 1cm to 8cm in the greatest dimension, largest lesion being ulcerated with bleeding. (Figure 1) On examination, left axillary lymphnodes were enlarged. FNAC was done on the nipple lesion and the prominent cutaneous nodules, which was reported as Moderately differentiated Squamous cell carcinoma (Figure 2).

USG of left breast showed, heteroechoic lesion with in 2-3 O clock position in the peri areolar region. There was no

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obvious infiltration into muscular plane or abnormal internal vascularity in the left breast. Metastatic work up with CT Chest showed lung metastasis with hilar lymphadenopthy. Considering the bleeding from the lesion palliative surgery - Wide local excision with left axillary lymphnode dissection and coverage of the defect with LD flap and the specimen sent to the Histopathology department of our institution. (Figure 3)

Specimen received in the department showed multiple nodules, on cut section shows, homogenous subcutaneous whitish growth with pushing borders. (Figure 4)

Formalin fixed paraffin embedded sections stained with Hematoxylin & eosin, from the multiple nodules showed features of invasive squamous cell carcinoma, but none showed the malignancy originating from the overlying epidermis. There were nodules and islands and sheets of moderately differentiated malignant squamous cells, with scattered mitotic figures and a few keratin pearls. More sections were studied and areas were re sampled, which showed tumor emboli in the dermal lymphatics, in different foci (Figure 5a-d). The sections taken from nipple lesion showed invasive squamous cell carcinoma, evidently arising from the lining epithelium, which, along with the chronicity of lesion, established that the primary site of origin was the nipple lesion.

Sections from the axillary lymphnode dissection specimen showed metastasis from squamous cell carcinoma. The patient was worked up extensively for finding out a primary elsewhere, and was not seen. The case was reported as Primary cutaneous Squamous cell carcinoma, arising from the left peri areolar skin, with multiple nodules on the ipsilateral chest wall skin, showing in transit metastasis. 2/2 axillary nodes show metastasis from the same neoplasm.

Fig. 1: Clinical picture of the nodular lesions and the crusted ulcerated lesion near the left nipple

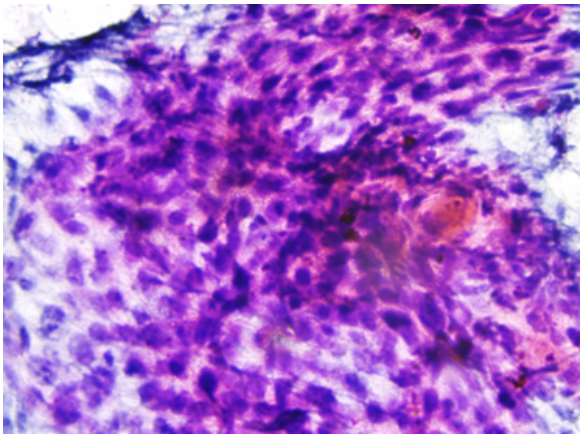

Fig. 2: FNAC microphotograph of largest nodule showing squamous cell carcinoma; 40X

Fig. 3: Intraoperative photograph of the lesions

3. Discussion

The American Joint Committee on Cancer, 8^{th} edition, have described In-transitmetastases for malignant melanoma and such cases are classified as stage 3 disease. They are defined as intralymphatic metastases occurring more than 2 cm from the primary tumor, whereas intralymphatic metastases occurring within 2 cm of the primary tumor are termed satellites.[8]

Any microscopic focus of metastatic tumor cells in the skin or subcutis adjacent or deep to but discontinuous from the primary tumor are called as microsatellites.

In transit metastasis usually present as 0.1 to 1.2 cm exophytic dermal and sub-cutaneous papules or nodules that locate approximately more than 2 cm away from the primary tumor. The mean number of lesions was reported as 3-5.[9]

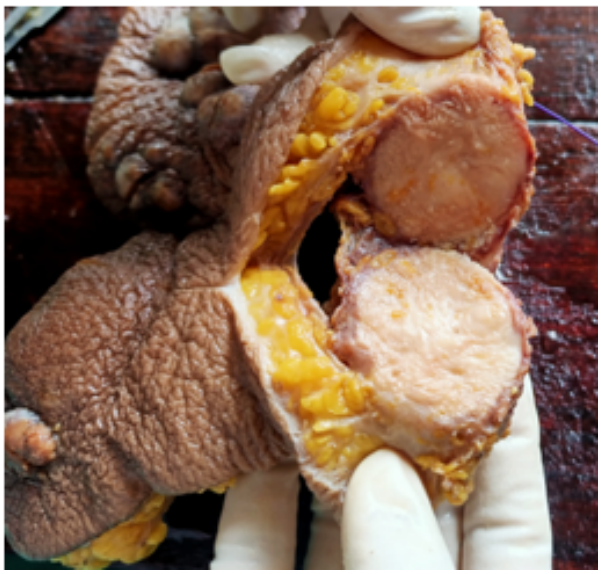

Fig. 4: Gross appearance of the nodules

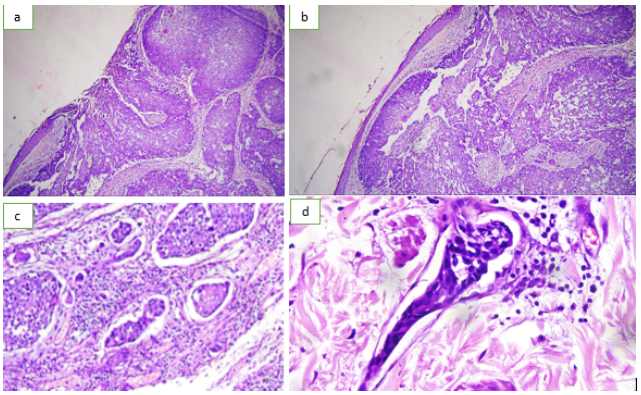

Fig. 5: a: Sections from the areolar lesion, Neoplasm seen arising from the epidermis extending into dermis; H&E Stain, 10X; **b:** Microphotograph of Areolar growth, H&E, 10X; **c:** Sections showing lymphatic tumor emboli; H&E, 40X; **d:** Tumor lymphatic emboli beneath an intact epidermis; H&E, 40X

The lesion in our case started in the left peri areolar skin 6 months before, and within a duration of 2 months, a second nodule appeared at a distance of 7cm from it. This was followed by appearance of other multiple nodules and later axillary node involvement.

The mean age of patients with in-transit metastasis is 61. Men are more commonly affected than women. In transit metastasis development is more in high risk squamous cell carcinomas. Squamous cell carcinomas with poor prognosis are associated with features such as the lip, ear, forehead, scalp, and temple locations; size greater than 2 cm in diameter; thickness greater than 2 mm; perineural, lymphatic, or vascular invasion; poorly differentiated or undifferentiated; certain histologic types; occurrence in an immunosuppressed patient; human papillomavirus infection; recurrence; inadequate tumor resection; and expressions of certain tumor genes.[10] In transit metastasis phenomenon can be seen in the umbilical region, which are defined as skin nodules developing from the dermal and subdermal lymphatics in the abdominal region prior to reaching the regional inguinal lymph nodes.[11]

It is noted that, histologic differentiation of primary tumor and in-transit metastasis has been reported to be mostly well differentiated in the literature. In our case, the neoplasm was moderately differentiated. Diagnosing in-transit metastasis can be challenging, and requires clinicopathological correlation to distinguish it from local recurrence and perineural spread of tumor. New diagnostic criteria, incorporating clinical and histological features, are proposed. (Table 1)[12]

Table 1: Diagnostic criteria for in transit squamous cell carcinoma

Clinical criteria	Metastasis should lie separate from scars of previous treatment (excluding donor site for flaps)
	Metastasis should lie between the initial tumor and possible draining lymph nodes
Histological criteria	Deposit should lie separate from scars of previous treatment (excluding flaps)
	Deposit should not have epidermal origin
	Tumor should not be present exclusively in perineural locations
	Metastasis should bear at least focal histological similarity to initial tumor

Being a rare pattern of lymphatic metastasis, the pathophysiological mechanism of in transit metastasis can be explained by the clonal evolution model of metastasis mechanisms, where the tumor cells invades the skin through dermal lymphatics. As a risk factor, lymphedema is been described, which ends with a delay in lymphnode involvement and results in increased extravasation of tumor cells within the lymphedematous limb.[10]

Treatment choices for in-transit metastasis are Mohs surgery or excision surgery, radiotherapy, excision followed by radiotherapy, amputation, intralesional or systemic chemotherapy (cis-platinum, 5-fluorouracil [5-FU], bleomycin, and methotrexate), oral retinoids (13-cisretinoic acid) immunotherapy (interferon-2a), reduction of immunosuppressive medication, and anti–epidermal growth factor receptor (EGFR) agents.[13]

4. Conclusion

As only a few case series and reports have been described such rare pattern of lymphatic metastasis, there are limited data on features and prognosis of the same. Diagnosis of in-transit SCC relies on clinicopathologic correlation. Prognosis was poor with 5-year overall survival of 13%.[12] Important to have a low index of suspicion when evaluating

new skin lesions in elderly / immunocompromised patients. Subcutaneous SCCs may be a sign of cutaneous or extra-cutaneous metastasis and are particularly aggressive and recurrent, it is important to treat such cancers aggressively to optimize patient outcomes.

5. Abbreviations

SCC- Squamous Cell Carcinoma.

6. Source of Funding

None

7. Conflicts of Interest

None

References

1. Nuño-González A, Vicente-Martín F, Pinedo-Moraleda F, López-Estebaranz J. High-risk cutaneous squamous cell carcinoma. *Actas Dermo-sifiliográficas*. 2012;103(7):567–78. doi:10.1016/j.ad.2011.09.005.
2. Martorell-Calatayud A, Jimenez OS, Mojarrieta JC, Barona CG. Cutaneous squamous cell carcinoma: defining the high-risk variant. *Actas Dermosifiliogr*. 2013;104(5):367–79. doi:10.1016/j.adengl.2011.12.012.
3. Karia PS, Han J, Schmults CD. Cutaneous squamous cell carcinoma: estimated incidence of disease, nodal metastasis, and deaths from disease in the United States. *J Am Acad Dermatol*. 2012;68(6):957–66. doi:10.1016/j.jaad.2012.11.037.
4. Lin MJ, Pan Y, Jalilian C, Kelly JW. Dermoscopic characteristics of nodular squamous cell carcinoma and keratoacanthoma. *Dermatol Pract Concept*. 2014;4(2):9–15. doi:10.5826/dpc.0402a02.
5. Copcu E, Dikicioglu E, Sivrioglu N, Meteoglu I. Subcutaneous nodules on the face: Acantholytic in-transit cutaneous metastasis. *Dermatol Surg*. 2004;30(11):1415–9. doi:10.1111/j.1524-4725.2004.30438.x.
6. Howe NR, Lang PG. Squamous cell carcinoma presenting as subcutaneous nodules. *J Dermatol Surg Oncol*. 1991;17(10):779–83. doi:10.1111/j.1524-4725.1991.tb03259.x.
7. Rowe DE, Carroll RJ, Day CL. Prognostic factors for local recurrence, metastasis, and survival rates in squamous cell carcinoma of the skin, ear, and lip. *J Am Acad Dermatol*. 1992;26(6):976–90. doi:10.1016/0190-9622(92)70144-5.
8. Hayes AJ, Clark MA, Harries M, Thomas JM. Management of in transit metastases from cutaneous malignant melanoma. *Br J Surg*. 2004;91(6):673–82. doi:10.1002/bjs.4610.
9. Carucci JA, Martinez JC, Zeitouni NC, Christenson L, Coldiron B, Zweibel S, et al. In-transit metastasis from primary cutaneous squamous cell carcinoma in organ transplant recipients and nonimmunosuppressed patients: clinical characteristics, management, and outcome in a series of 21 patients. *Dermatol Surg*. 2004;30(4 pt 2):651–5. doi:10.1111/j.1524-4725.2004.30151.x.
10. Wain EM, Webber NK, Stefanato CM. Multiple in-transit cutaneous metastases from a primary cutaneous squamous cell carcinoma. *Clin Exp Dermatol*. 2009;34(4):522–4. doi:10.1111/j.1365-2230.2008.02967.x.
11. Macripo G, Caliendo V, Grassi M, Lista P, Ribero S, Giacone E, et al. Squamous cell carcinoma of the umbilicus: management of an unusual localization. *Tumori*. 2011;97(2):236–8. doi:10.1700/667.7791.
12. Kocaturk E, Ulkumen P, ltac UK, Yuksel T, Kunter A, Erhan S, et al. In-Transit Metastasis from Primary Cutaneous Squamous Cell Carcinoma in a Nonimmunosuppressed Patient. *Dermatol Surg*. 2016;42:1285–92.
13. Padmavathy L, Rao LL, Sylvester. In-transit metastases from squamous cell carcinoma penis. *Indian J Dermatol*. 2012;57:291–3. doi:10.4103/0019-5154.97674.

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