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CASE REPORT

Primary Squamous Cell Carcinoma of the Breast in Two Chinese Women

TW Chan, AKC Leung, KC Ngan

Department of Clinical Oncology, Queen Elizabeth Hospital, Jordan, Hong Kong

ABSTRACT

Primary squamous cell carcinoma of the breast is a rare breast neoplasm. This report describes two Chinese women diagnosed with primary squamous cell carcinoma of the breast. The first patient was a 54-year-old woman with stage pT1cN0M0 triple-negative disease treated with wide local excision and axillary dissection followed by adjuvant chemotherapy with adriamycin and cyclophosphamide, and adjuvant radiotherapy. She was disease-free on follow-up at 19 months. The second patient was a 63-year-old woman presenting with a 10-cm right breast mass. She was given one cycle of neoadjuvant chemotherapy using docetaxel, cisplatin, and 5-fluorouracil without clinical response. Modified radical mastectomy with transverse rectus abdominis myocutaneous flap was performed. Pathology showed stage pT3N0M0 triple-negative disease. Adjuvant locoregional radiotherapy was given. She was disease-free on follow-up at 19 months. As reported in the literature, squamous cell carcinoma of the breast is mostly triple negative, of large size, and has infrequent nodal involvement at presentation. The disease runs a more aggressive clinical course. There is no consensus on the role and mode of adjuvant treatment. The choice of chemotherapy regimen for this histology remains to be defined.

Key Words: *Breast neoplasms; Carcinoma, squamous cell; Cisplatin; Doxorubicin; Radiotherapy*

中文摘要

兩名華藉女性的乳房原發性鱗狀細胞癌

陳添偉、梁國璋、顏繼昌

乳房原發性鱗狀細胞癌是一種罕見的乳腺腫瘤。本文報告乳房原發性鱗狀細胞癌的兩名華藉女性患者。其中一名被診斷pT1cN0M0期三重陰性乳癌的54歲患者，接受廣泛性局部切除乳房腫瘤及腋下淋巴切除術，以及術後用adriamycin及cyclophosphamide的輔助化療和輔助放射治療。患者術後19個月未有復發。另一名63歲患者有10 cm大的腫瘤在右邊乳房。她雖接受docetaxel、cisplatin及5-fluorouracil的新輔助化療，但臨床未見療效。後接受腹直肌皮瓣的改良型乳房根除手術，病理學發現患者有pT3N0M0期三重陰性乳癌，遂接受輔助性局部放射治療。患者術後19個月未有復發。文獻中記載大部份的乳房原發性鱗狀細胞癌病例均為三重陰性、腫瘤偏大，以及病發時很少牽涉淋巴結，這種病會有侵襲性的臨床病程。對於此病，輔助治療的角色及其形式仍未達至共識，而是否應選擇化療的方法亦尚有待確定。

Correspondence: *Dr TW Chan, Room 1112, Block R, Queen Elizabeth Hospital, 30 Gascoigne Road, Kowloon, Hong Kong. Tel: (852) 2958 8888 ; Email: ctw263@ha.org.hk*

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INTRODUCTION

Primary squamous cell carcinoma of the breast is a rare breast neoplasm, accounting for less than 0.1% of all breast cancers.[1] The diagnosis is made when more than 90% of the malignant cells are of the squamous type,[2] with exclusion of a tumour originating from the skin of the breast and metastasis from another primary.

We report on two Chinese women diagnosed with primary squamous cell carcinoma of the breast who received treatment and follow-up at the Department of Clinical Oncology, Queen Elizabeth Hospital, Hong Kong.

CASE REPORTS

Patient 1

A 54-year-old woman presented in August 2009 with two months' history of left breast mass measuring 2 cm. Core biopsy revealed invasive carcinoma. The patient underwent wide local excision of the left breast mass and left axillary dissection. Pathological examination showed stage pT1cN0M0 squamous cell carcinoma with no involvement of the 28 lymph nodes dissected.[3] Tumour cells were negative for oestrogen receptor (OR), progesterone receptor (PR), and C-erbB2. The tumour was partly formed of carcinoma cells with squamous differentiation, including keratinous material, and other part formed of a cavity with its wall replaced by inflammatory tissue with focal residual cystic ductal lining. Ductal carcinoma in situ was focally seen in the medial resection margin. Re-excision was performed and showed no malignancy. The patient then received four cycles of adjuvant chemotherapy with adriamycin and cyclophosphamide followed by adjuvant local radiotherapy to her left breast. Follow-up consultation at 19 months showed no evidence of disease.

Patient 2

A 63-year-old woman presented in December 2009 with a 10-cm right breast mass for six months (Figure 1). Core biopsy confirmed squamous cell carcinoma. The tumour cells were negative for OR, PR, and C-erbB2. In view of the locally advanced disease, neoadjuvant chemotherapy was started using docetaxel, cisplatin, and 5-fluorouracil (5-FU), which is commonly used for treating head and neck squamous cell carcinoma, but was stopped after the first cycle due to deranged renal function and lack of clinical response. Modified radical mastectomy with transverse rectus abdominis myocutaneous flap was subsequently performed. Pathological examination revealed stage pT3N0M0 squamous cell carcinoma, with no involvement of the 10 lymph nodes dissected. Grossly, the tumour exhibited central cystic changes. The tumour was composed of well-differentiated squamous cells in broad anastomosing cords with abundant keratinous material. There were no components of intraductal carcinoma or lymphovascular permeation. The tumour was found to be close to the deep margin. The patient received adjuvant locoregional radiotherapy. Adjuvant chemotherapy was not given because of persistent impaired renal function. Follow-up consultation at 19 months showed no evidence of disease.

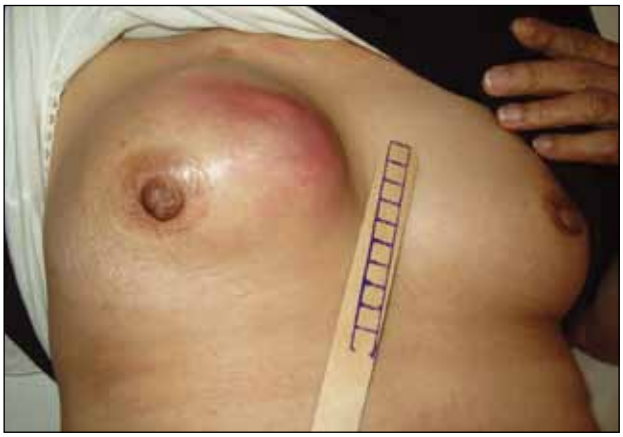

Figure 1. Advanced squamous cell carcinoma of the breast of patient 2.

DISCUSSION

Primary squamous cell carcinoma of the breast is a rare disease entity.[1] Diagnosis of the breast origin of the disease needs exclusion of primary squamous cell carcinoma of the skin and squamous cell carcinoma originating from another part of the body. Some authors suggest that it may originate from metaplasia of ductal epithelium, but others suggest that it may develop from chronic abscess or keratinous cysts of the breast.[4] Metaplastic carcinoma of the breast denotes a heterogeneous group of uncommon malignancies with mixed epithelial and sarcomatoid components; primary squamous cell carcinoma of the breast is considered one of the subsets of this entity.

Clinicopathological Features

The usual age range at presentation is 53 to 64 years.[2,4-6] The tumour presents as a palpable breast lump, which is generally large (usually >4 cm) and cystic in more than 50% of cases.[2] There is no consistent finding on mammography, while ultrasound of the breast may

reveal a solid component (Figure 2). On magnetic resonance imaging, the tumour appears as a well-circumscribed mass with central necrosis.

The cytopathological features of the tumour include numerous malignant squamous cells with keratinising eosinophilic glassy cytoplasm, intercellular bridges, keratin debris, and background necrosis (Figure 3).[5] High nuclear grade, mitosis, and infiltrative growth is noted.[4] Rapidly progressive squamous cell carcinomas are reported to be associated with a prominent spindle cell component. Squamous cell carcinoma of the breast is mostly OR- and PR-negative[1,4,5] without HER2/neu amplification.[2,6]

Data on prognosis have been conflicting. In general, primary squamous cell carcinoma of the breast is reported to run a more aggressive clinical course than invasive ductal carcinoma,[1,2] although some authors suggest that it is more indolent.[4] The tumour is associated with a low rate of lymph node involvement at presentation and a high rate of distant metastasis without lymph node involvement.[1] A five-year overall survival rate of 40.0 to 68.1% has been reported.[1,2,4,5]

Treatment

Because of the rarity of squamous cell carcinoma of the breast, there is no standard treatment strategy. The initial treatment is surgery, and there is no consensus concerning adjuvant therapy.

Surgery

It is recommended that the treatment should follow the guidelines of invasive ductal carcinoma. Complete excision of the tumour as well as mastectomy have been performed as initial surgery.[4] However, there is no evidence to support breast conservation with adjuvant radiation as a clinically acceptable option to mastectomy.[6] Taking into account the low rate of axillary lymph node involvement at presentation, the role of sentinel lymph node biopsy could be considered,[5] and may be more appropriate.

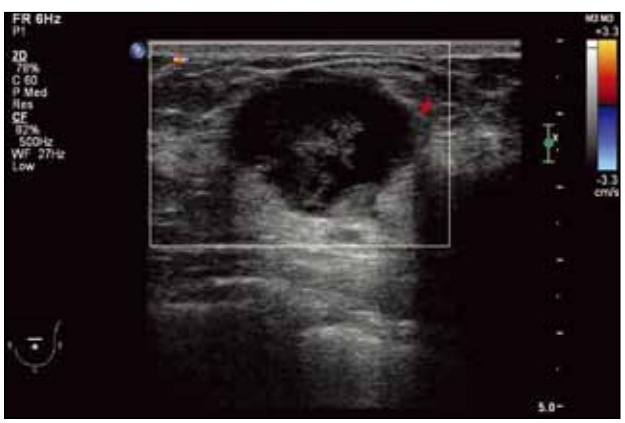

Figure 2. Ultrasound image of the breast mass of patient 1 showing a complex cystic mass with an internal solid component.

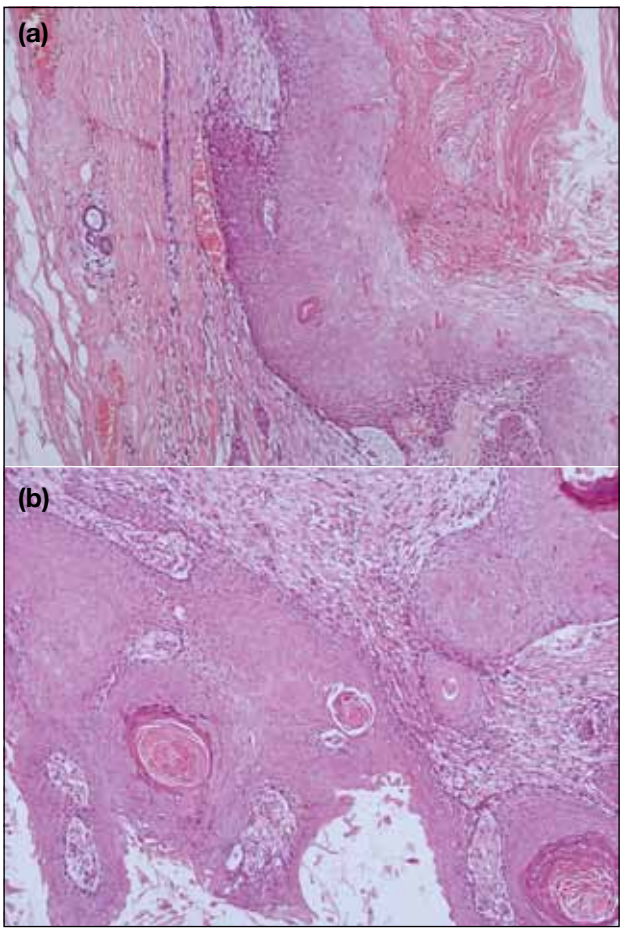

Figure 3. Histological examination of sections of the squamous cell carcinoma of the breast from patient 2. (a) Well-differentiated keratinising squamous cell carcinoma — a normal mammary terminal duct lobular unit is seen on the left side; and (b) keratin pearl formation in well-differentiated keratinising squamous cell carcinoma (H&E, x 100).

Adjuvant Chemotherapy

The current breast cancer chemotherapy regimens clearly have limited activity in breast squamous cell carcinoma.[2,5,6] Chemotherapy regimens used in invasive ductal carcinoma have been given to patients with squamous cell carcinoma of the breast as adjuvant treatment. Examples include 5-FU, adriamycin, and cyclophosphamide with or without taxane. Cisplatinum-based chemotherapy, which is commonly used for

squamous cell carcinoma in other sites, has been offered as an alternative agent and has had some success.[7] Cisplatin and 5-FU have been used as a neoadjuvant chemotherapy regimen, leading to tumour shrinkage and complete resolution of pain and erythema in one report.[8] However, patient 2 in this report who received neoadjuvant chemotherapy with docetaxel, cisplatin, and 5-FU did not achieve any clinical response after one cycle. She did not proceed to further cycles due to chemotherapy toxicity, and her tumour response (or non-response) to chemotherapy could not be confirmed. So far, there has been no evidence to suggest benefit in relapse-free or overall survival for adjuvant treatment using the chemotherapy described.

Radiotherapy

According to reports in the literature, adjuvant radiotherapy has been given to patients, aiming at better locoregional control, but local recurrence has been found to occur frequently in the irradiated field.[2,5] It seems that the tumour may be relatively radioresistant.[2,5]

CONCLUSION

Review of the literature shows that primary squamous cell carcinoma of the breast is a distinct disease entity from invasive ductal carcinoma. This disease usually presents with a large breast mass with infrequent nodal involvement, is of high tumour grade, and hormone receptor– and CerbB2-negative. Primary squamous cell carcinoma of the breast has been reported to run an aggressive clinical course. There is no consensus on the role and mode of adjuvant treatment. Since the disease entity is rare, it would be unlikely to have evidence-based treatment guidelines. Management of these patients should therefore be individualised.

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