Primary Squamous Cell Carcinoma of the Breast is a Rare and Special Entity. A Case Report from Arab Region with Aggressive Behavior and follow up 25 Months

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Abstract: *Background*: Primary squamous cell carcinoma of the breast (PSCCB) is a very rare malignancy of the breast. Pure squamous cell carcinoma of the breast can originate from skin adnexa, the nipple or the epithelium of deep-seated epidermoid cyst or squamous metaplasia on chronic inflammation background.

Case Report: Our case is a 49-year-old female patient who presented with a highly suspicious lump in her left breast. Bilateral mammography and core biopsy were carried out. The core biopsy was revealed atypical cells and review inconclusive. Incisional biopsy was done and revealed squamous cell carcinoma of the breast (SCCB). Her metastatic work up at presentation was unremarkable. Left-side modified radical mastectomy was carried out. TNM staging was Stage IIa pT2N0M0 GIII, Estrogen receptors (ER) and Progesterone receptors were negative and HER2/Neu was negative as well (Triple negative). Pt had adjuvant chemotherapy and radiotherapy. Eight months later, she developed multiple brain metastasis as solitary site of metastasis, then after four months she developed hepatic and pulmonary deposits. Pt survived only 25 months since disease diagnosis.

We report this case with relatively younger age to confirm that primary squamous cell carcinoma of the breast has special aggressive entity and this conjugant with few series. The treatment of primary SqCC of the breast does not differ from other common histological types of breast cancer so far.

Conclusions: The prognosis of this disease is highly uncertain and the treatment options are unclear and controversial. There is inadequate literature and treatment guidelines. To our knowledge it is the first case to be reported from arab region with aggressive behavior and short survival period.

Keywords: Squamous cell carcinoma of the breast (SCCB), chemotherapy, rare malignancy.

INTRODUCTION

Primary Squamous cell carcinoma of the breast (PSCCB) is a rare tumor and it is constituting less than 0.1% of all breast carcinomas [1]. There are few reported series documenting the management and clinical outcome of these tumors [2]. The rarity of of this type of neoplasms does not allow large or randomized studies to define the optimal treatment. Many of the descriptions of these cancers are from case reports and small series.

Clinical and radiologic appearances are not specific, and tumors are usually hormone receptor negative [3-4]. The prognosis for this type of breast cancer is still a subject of controversy: some reports suggest that it is aggressive, with an outcome comparable to that of poorly differentiated breast adenocarcinoma [2-7]. PSCCB express some markers associated with basal cancers—epidermal growth factor receptor (EGFR), cytokeratin-5 (CK5), and cytokeratin-6 (CK6), however, their clinical features suggest that they represent a unique subtype. As a result of lack of data, the issue of whether to prescribe neoadjuvant or adjuvant treatment and what type of therapy for PSCCB remains unresolved [7].

To help settle these controversies, we are presenting this case report to add to the experience of others and to tackle the need for further studies to explore the best theraputic approach and to detect the outcome of this population even it is rare. This case is the first case with this rare type and agressive behaviour to be reported from arab region with follow up peroid 25 months.

CASE REPORT

A 49-year-old premenopausal lady was referred from rheumatology deptarment to the breast clinic with a lump in the Left (Lt) breast on November 6th/2015. Pt is known case of Rheumatoid artheritis since 10 years, and she is treated and followed by the rheumatology team. The pt pointed out to her rheumatologist during her regular visit that she discovered a painless breast lump during her shower. The lump was gradually progressive in size, not associated with pain, redness, or nipple discharge and there was visible mild

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retraction of the skin at the site of the lump. Then, She started to worry and follow it.

The patient noticed her lump six months before she mentioned the subject to her doctor and seven months before she presented to the breast clinic. She was upset and not feeling well, her husband died of metastatic cancer colon one year before, and she suffered a lot during his palliative phase. Pt was fatalistic about cancer disease, and never had previous self or clinical breast examination or never attended for screening mammography.

There was no family history of breast malignancy. Physical examination revealed firm, rubbery, non-tender and non-mobile lesion of 4 × 3 cm in lower outer quadrant (LOQ) of the It breast. Right (Rt) breast was unremarkable, with no clinically detectable masses can be appreciated. Bilateral axillary lymph nodes were not enlarged. Pt denied any chest, abdominal, urinary or neurological symptoms and her clinical abdominal examination was unremarkable. There was no other skin lesion in the whole body. Head and neck examination was unremarkable as well.

Mammogram of the Rt breast demonstrated a scattered fibro glandular densities (BIRAD II) with no underlying architectural distortion noted, and no speculations. Lt breast showed large well defined macrolobulated nearly homogenous mass in the lower outer qudrant (LOQ) with foci of macroclacifications were seen within it (Figure **1**). It measures 4.5cmX2.7cm with no speculations. Another two smaller lesions are seen in the Lt breast oval shaped with fatty component, one in the upper outer qudrant (UOQ) 11X11 mm and the other in upper inner qudrant (UIQ) (13x7mm) no intralesional calcifications were noted in those small masses.spherical mass lesion with ill-defined speculated margins. The skin and the nipple-areola complex were not involved.

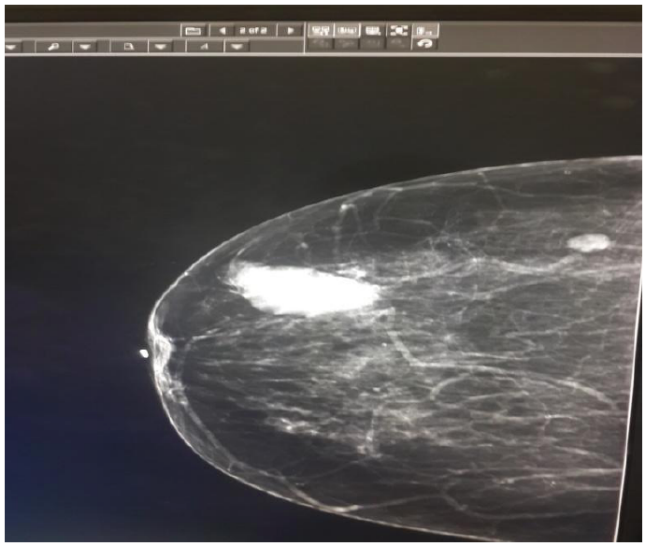


Figure 1: Lt Breast mammogram which showed Lt Breast well circumscribed high-density mass with micro classifications.

Ultrasound of the Lt breast revealed well defined (wider than longer), hypoechoic mildly heterogeneous solid intramammary mass lesion with posterior acoustic enhancement located in (5 o'clock of the Lt breast) and no adjacent parenchymal distrotion (Figure **2**). Ultrasound true cut biopsy was carried out (Figure **3a, b**), and pathological examination revealed atypical cells and inadequate tissue. Incisional biopsy was carried out two weeks later and 2 cm long tissue was obtained, three samples were taken for histopathological examination from the palpable mass and the other two from the two suspicious lesions detected by mammography. Grossly, Three irregular pieces showed gray white appearance with few cystic areas and collectively measuring about 3.5X2.5 cm. Microscopic description showed multiple squamous epithelium lined sturcture with small ducts as well as cystic structures lined by atypical squamoid cells. Also seen are vague squamous pearls and individual cells kertanization. Some solid foci show ductular differentionation. Stroma is fibrous in nature with chronic inflammation (Figure **4a**). Histopathological diagnosis was malignant epithelial neoplasm with squamoid differentionation, consistent with metaplastic carcinoma. The tumor cells were positive for cytokeratin and negative for estrogen (ER), progesterone receptors (PR) and the human epidermal growth factor receptor 2 (HER2).

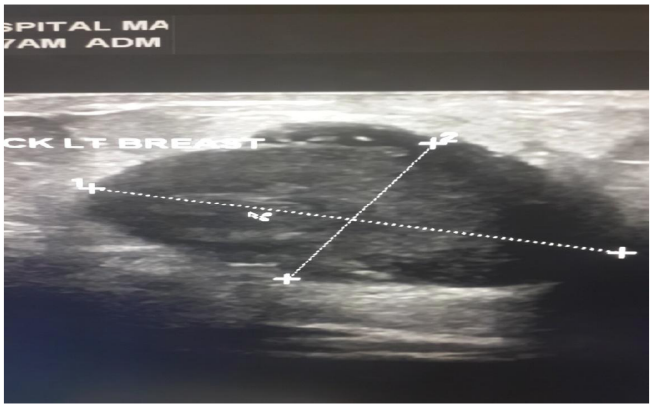
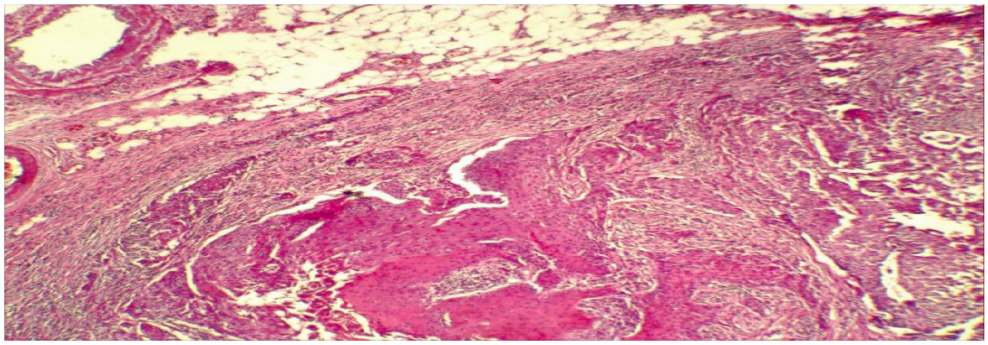


Figure 2: Lt breast US shows hypoechoic mildly heterogeneous solid intramammary mass lesion with posterior acoustic enhancement located in (5 o'clock of the Lt breast) and no adjacent parenchymal distortion.



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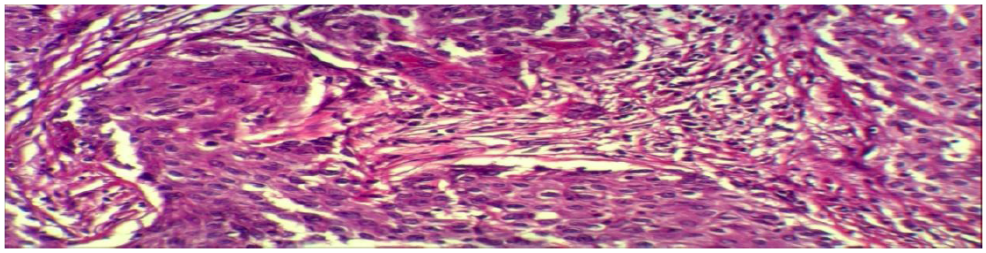

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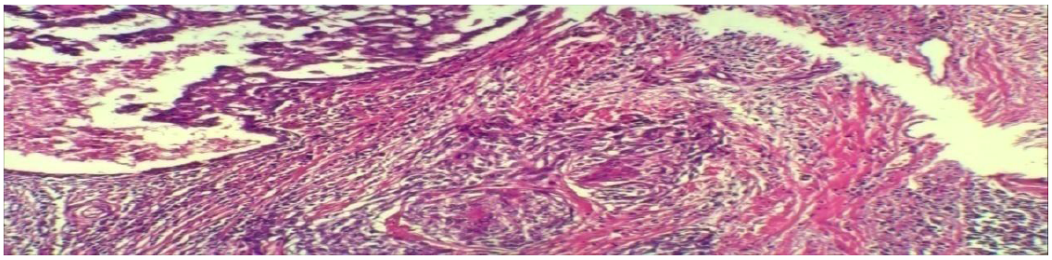
Figure 3: a: Section from breast mass showing invasive moderately differentiated squamous cell carcinoma (H&E, 4X).
b: High power of the fig.3a shows invasive moderately diffrentiated squamous cell carcinoma (H&E, 20X).

Subsequent computed tomography scan (CT) chest, abdomen, and pelvis were carried out and were free of metastasis. Whole body Bone scan was done as well and revealed no evidence of osseous metastasis, however there was abnormal tracer accumulation by the 4th lumbar vertebrae suggestive degnerative changes. Both knees joints showed increased uptake which may be due to degnerative changes. Pt was followed and treated by rheuamtologist longtime ago.

Echocardiography and complete blood work were done and were unremarkable. Tumor markers cancer antigen (CA) 15.3 was 6.8 IU/L, CA 125 was 11.4 IU/L, and carcinoembryonic antigen (CEA) was 3.6 IU/L. We discussed the treatment plan with the pt, and her perferance was mastectomy, we explained to her in advance that it is a rare type and we dont have an evidence so far about the best approach.

Pt's case was discussed in multidisciplinary team (MDT) cancer management, and was elected for modified radical mastectomy (MRM) followed by postoperative treatment based on the histopatholgical findings. Lt MRM with axillary lymph nodes dissection was performed after 35 days from pt presentation to our breast clinic. Gross description revealed solid and cystic grayish white mass 3X2.5 cm pT2N0M0 LNS 0/21. Microscopically, the tumor was composed of sheets and clusters of round to polyhedral cells with pleomorphic hyperchromatic nuclei and a moderate amount of eosinophilic cytoplasm. Individual cell keratinization and keratin pearls were also seen (Figure **4b**). Some of the ducts showed squamous metaplasia and well differentiated squamous cell carcinoma. Intraductal carcinoma components <10% with no lymphovascular invasion. Stroma at places shows spindle cells. No evidence of metastasis in all 21 LNs. The tumor cells were positive for cytokeratin and negative for estrogen, progesterone receptors and HER2 (score 0). Overlying skin and areola was uninvolved by tumor and free surgical margins. The tumor size collectively from the biopsy (2 cm) and mastectomy is 6.5X5 cm, Pt's TNM classification is pT3N0M0, Stage IIB. Triple negative. pt elected for adjuvant chemotherapy Adriamycin 50mg/m2 and Endoxan 600mg/m2 X 4 Recycle/21days followed by Taxotere75mg/m2X4 Recycle/21days followed by chest wall irradiation 40Gy/20ttt/4ws. Pt tolerated her adjuvant therapy very well with grade II hematologic toxicity and grade II fatigue, peripheral neuritis and mucositis. All the toxicities were manegable, and Pt admitted in the hospital twice because of febrile neutropenia induced by chemotherapy. Pt recoverd very well and we put her under prophylactic G-CSF for the rest of the cycles. Pt had her local radiotherapy with good tolerance and GII skin toxcity.



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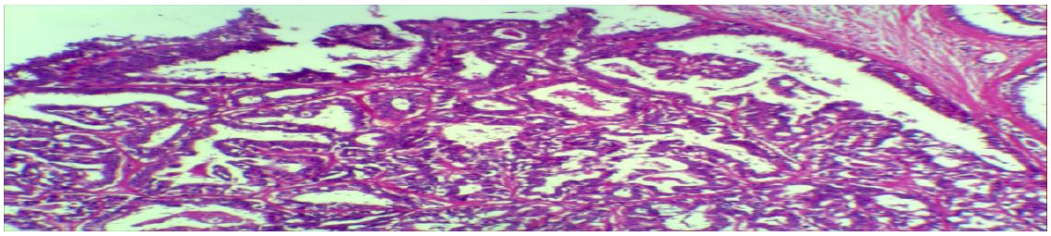

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Figure 4: a: Invasive squamous cell carcinoma adjacent to intraductal papillary carcinoma (H&E, 10X). **b**: Section shows intraductal papillary carcinoma close to the main tumor (H&E, 10X).

Pt finished her treatment on June/2016. Pt was under follow up every three months as planned by our policy. Eight months later she presented to Emergency Room (ER) with distrubed conscious level, CT brain scan was carried out revealed multiple brain deposits (Figure **5**). Pt was treated with dehydrating measures and Whole brain irradiation 30Gy/10ttt/2ws. Pt improved but suffered from post irradiation cogentive effect. CT scan of whole body was unremarkable at that time. Pt had brain mets as solitary site of metastsis. Four months later after havin brain mets, Pt developed abdominal pain and CT scan revealed hepatic and pulmonary deposits (Figures **6** & **7**). She received palliative Cisplatin/5FU regimen for 3 cycles with disease progression. We stopped chemotherapy and shift to Capcitabine 1250mg/m2 BID single agent. Pt received 3 cycles with mild response then Pt developed sever pneumonitis and admitted in Intensive care unit (ICU) for two weeks, then pt Pt died on December 19/2017 with overall survival 25 months only after her pathological diagnosis.

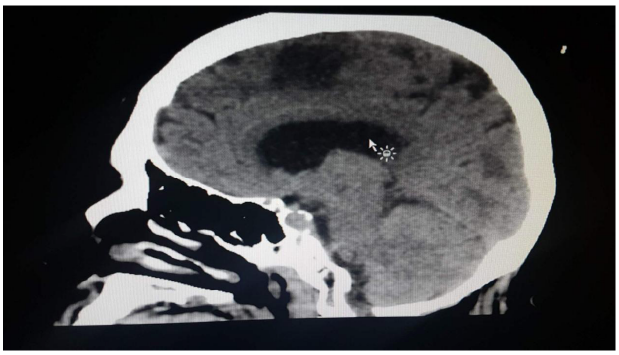

Figure 5: contrast enhanced CT image with multiple brain deposits.

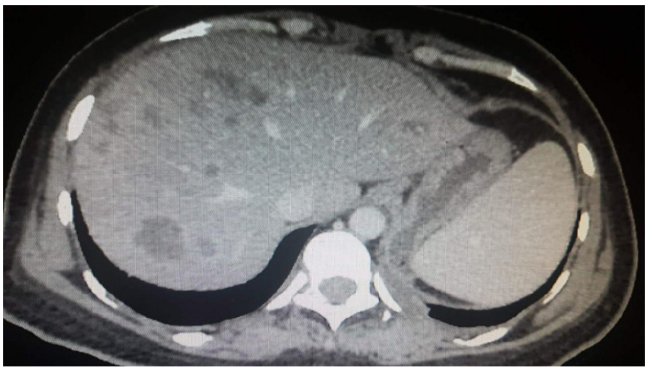

Figure 6: contrast enhanced CT image of the abdomen showed hepatic metastasis.

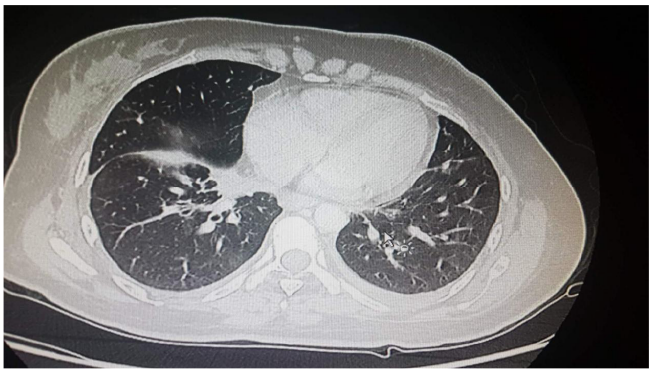

Figure 7: CT image showed pulmonary metastasis.

DISCUSSION

PSCCB is very rare. The etiology and pathogenesis of PSCCB is still unclear. PSCCB is the tumor of elderly age group [8]. Tumors, frequently reach large volumes and can be as large as 5 cm and more. Our

patient was 49 years old and she had a mass of 6.5X3cm. There are no typical findings or characteristic features on the mammogram [9]. Some tumors have been reported to have irregular borders [9]. Only one reported case as far we know of SCCB has shown microcalcifications on mammogram [10] Ultrasound may show a cyst or an inflammatory process. In our case the mammogram showed large well defined macrolobulated nearly homogenous mass in the lower outer qudrant with foci of macroclacifications were seen within it. In our case, core biopsy guided by US showed suspicious atypical cells, and was inconclusive. Incisional biopsy confirmed the diagnosis of PSCCB.

PSCCB are reported to result in less lymphatic spread than adenocarcinomas. In 10–30% of cases there is lymph node infiltration at the time of surgery [11, 12]. In contrast, about 30% of patients will develop distant metastasis. In the report of Menes *et al*., [13] SCCB was found to be associated with a lower rate of lymph node metastasis at presentation (22% versus 40-60% for invasive duct carcinoma), and a significant rate of distant metastasis without lymph nodes involvement. The initial management has generally been modified radical mastectomy with adjuvant radiotherapy and chemo/hormonal therapy. Breast conservation therapy is not usually possible because most patients presented with locally advanced disease [14]. In our case, the pt had MRM with axillary node dissection and, there was no lymphatic involvement, LNs were 0/21. Our pt had neither LNs involvement or systemic metastasis at presentation.

Squamous cell carcinomas are generally hormone receptor-negative [4]. The management of SCCB is still not clear, it is recommended so far to give patients similar adjuvant therapy as any breast cancer pt based on her staging and risk score. However, the sensitivity of squamous cell carcinomas to chemotherapy and radiotherapy is uncertain. The 5-year survival is 67% [14,15]. In our pt, the tumor was triple negative, and she wasn't candidate for hormonal or biological therapy. She received adjuvant chemotherapy AC X4, followed by Tx4. Pt developed brain mets shortly after finishing her adjuvant therapy. It is unusual to have brain mets as solitary site with Stage II disease without systemic involvement and indicate aggressive behaviour. Four month later she developed pulmonary and hepatic deposits. Pt was referactory to platinum based chemotherapy and had modest response to Xeloda as well. Some series suggest indolent clinical course and a relatively good prognosis in PSCCB [16] however in our case, she was younger age and short peroid of survival comparable to usual breast cancer cases and other series of PSCCB and this compatible with some investigators thought squamous cell carcinoma of the breast had an aggressive course with outcome comparable to poorly differentiated breast adenocarcinoma [17,18].

CONCLUSION

Pure squamous cell carcinoma of the breast is a rare type of malignancy. Its prognosis and appropriate approach for treatment is still debatable. New case reports and clinical trials would help to determine the right approach to this disease. Future research should focus on the molecular biology to develop tumor specific therapy.

REFERENCES

[1] Louwman MW, Vriezen M, van Beek MW. Uncommon breast tumors in perspective: Incidence, treatment and survival in the Netherlands. Int J Cancer 2007; 121: 127-135. https://doi.org/10.1002/ijc.22625

[2] Tavassoli FA, Devilee P, editors. Tumours of the Breast and Female Genital Organs. Lyon, France: IARC Press; 2003. World Health Organization Classification of Tumours. Pathology and Genetics; p. 1-433

[3] Vu-Nishino H, Tavassoli FA, Ahrens WA, Haffty BG. Clinicopathologic features and long-term outcome of patients with medullary breast carcinoma managed with breast-conserving therapy (BCT). Int J Radiat Oncol Biol Phys 2005; 62(4): 1040-1047. https://doi.org/10.1016/j.ijrobp.2005.01.008

[4] Kim MJ, Ro JY, Ahn SH, Kim HH, Kim SB, Gong G. Clinicopathologic significance of the basal-like subtype of breast cancer: a comparison with hormone receptor and Her2/neu-overexpressing phenotypes. Hum Pathol 2006; 37(9): 1217-1226. https://doi.org/10.1016/j.humpath.2006.04.015

[5] Behranwala KA, Nasiri N, Abdullah N: Squamous cell carcinoma of the breast: Clinico-pathologic implications and outcome. Eur J Surg Oncol 2003; 29: 386-389. https://doi.org/10.1053/ejso.2002.1422

[6] Yerushalmi R, Hayes MM, Gelmon KA. Breast carcinoma—rare types: review of the literature Ann Oncol 2009; 20(11): 1763-1770. First published online July 14, 2009. https://doi.org/10.1093/annonc/mdp245

[7] Tayeb K, Saadi I, Kharmash M, El Omari-Alaoui H, El Ghazi E, Mansouri A,: Primary squamous cell carcinoma of the breast: Report of three cases. Cancer Radiother 2002; 6: 366-368. https://doi.org/10.1016/S1278-3218(02)00258-5

[8] Cardoso F, Leal C, Meira A, Azevedo R, Mauricio MJ, Leal da Silva JM, Lopes C, Pinto Ferreira E. Squamous cell carcinoma of the breast. Breast 2000; 9: 315-319. https://doi.org/10.1054/brst.1999.0145

[9] Gupta G, Malani AK, Weigand RT, Rangenini G. Pure primary squamous cell carcinoma of the breast: A rare presentation and clinicopathologic comparison with usual ductal carcinoma of the breast. Pathol Res Pract 2006; 6: 465-69. https://doi.org/10.1016/j.prp.2006.01.006

[10] Moisidis E, Ahmed S, Carmalt H, *et al.* Primary squamous cell carcinoma of the breast. ANZ J Surg 2002; 72: 65-67. https://doi.org/10.1046/j.1445-2197.2002.02298.x

[11] Murialdo R, Boy D, Musizzano Y, Tixi L, Murelli F, Ballestrero A. Squamous cell carcinoma of the breast: a case report. Cases Journal 2009; 2: 7336-7339.

[12] Grenier J, Soria JC, Mathieu MC, Andre F, Abdelmoula S, Velasco V, Morat L, *et al*. Differential immunohistochemical and biological profile of squamous cell carcinoma of the breast. Anticancer Res 2007; 27(1B): 547-555.

[13] Menes T, Schachter J, Morgenstern S: Primary squamous cell carcinoma (SqCC) of the breast. Am J Clin Oncol 2003; 26: 571-573. https://doi.org/10.1097/01.coc.0000045809.85995.3B

[14] Hennessy BT, Krishnamurthy S, Giordano S, Buchholz TA, Kau SW, Duan Z, Valero V, Hortobagyi GN. Squamous cell carcinoma of the breast. J Clin Oncol 2005; 23: 7827-7835. https://doi.org/10.1200/JCO.2004.00.9589

[15] Geyer FC, Weigelt B, Natrajan R, Lambros MB, de Biase D, Vatcheva R, Savage K, *et al*. Molecular analysis reveals a genetic basis for the phenotypic diversity of metaplastic breast carcinomas. J Pathol 2010; 220(5): 562-573. https://doi.org/10.1002/path.2675

[16] Banerjee S, Reis-Filho JS, Ashley S, Steele D, Ashworth A, Lakhani SR, Smith IE. Basal-like breast carcinomas: clinical outcome and response to chemotherapy. J Clin Pathol 2006; 59(7): 729-735. https://doi.org/10.1136/jcp.2005.033043

[17] Yamaguchi R, Horii R, Maeda I, Suga S, Makita M, Iwase T, Oguchi M, *et al*. Clinicopathologic study of 53 metaplastic breast carcinomas: their elements and prognostic implications. Hum Pathol 2010; 41(5): 679-685. https://doi.org/10.1016/j.humpath.2009.10.009

[18] Tsung S. Primary Pure Squamous Cell Carcinoma of the Breast Might Be Sensitive to Cisplatin-Based Chemotherapy. Case Rep Oncol 2012; 5(3): 561-565. https://doi.org/10.1159/000343745

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