



Avens Publishing Group
Inviting Innovations

Journal of Surgery

Special Issue

Surgical Oncology

Editors:

¹Dr. Marlon A Guerrero

²Dr. James A Warneke

¹Assistant Professor of Surgery, University of Arizona, USA

²Associate Professor of Surgery, University of Arizona, USA

A Retrospective Case Series and Literature Review of Primary Squamous Cell Cancer of the Breast

Keywords: Breast cancer; Primary squamous cell cancer; PSCCB

Abstract

Background: Primary squamous cell carcinoma of the breast (PSCCB) is one of the rarest forms of breast cancer, accounting for less than 0.1% of all breast cancers. PSCCB can be aggressive with no typical radiologic findings on mammogram and a wide range of clinical presentations, often leading to delayed or missed diagnoses.

Methods: We performed a retrospective review of patients diagnosed with PSCCB at our institution from 2007 to 2012. Inclusion criteria included females over the age of 18 years old with a primary tumor consisting of >90% malignant cells of squamous origin and excluded squamous cell cancer that had metastasized to the breast or lesions that were not independent of the overlying skin or nipple. In addition, we performed a literature review using the PubMed database.

Results: We identified two patients diagnosed with PSCCB during that timeframe with ages ranging from 35-52 years old. The average size of the mass seen on mammogram was 2.1 cm (range of 1 cm to 3.6 cm). Histologically, all cancers were moderately to poorly differentiated with negative estrogen, progesterone, and HER2 receptor status and an elevated Ki-67. One patient underwent breast conservation with partial mastectomy and axillary sentinel lymph node biopsy with whole breast radiation. The second patient underwent a total mastectomy and axillary sentinel lymph node biopsy without radiation. Neither of the patients had evidence of regional nodal disease at time of surgery nor received any systemic therapy. Both patients were disease free at last follow up which was five to twenty eight months respectively.

Conclusion: Because PSCCB is so rare, prognosis and optimal treatment are still controversial, making treatment options limited. More research is needed to further elucidate the biological behavior of this rare cancer as well prognostic factors that may allow more conservative treatment.

Background

Primary squamous cell cancer of the breast (PSCCB) is an extremely rare form of breast cancer with an incidence of approximately 0.04-0.1% of all breast cancers and more specifically 0.04-0.07% of all ductal carcinomas [1-3,5,7-12]. PSCCB is a diagnosis of exclusion, with the following criteria that must be met: (1) tumor origin does not arise from overlying skin, nipple or adenexal components, (2) greater than 90% of the tumor must be composed of squamous cells, (3) no evidence of ductal or mesenchymal elements within the tissue sample, and (4) no other sites of primary squamous cell cancer are present [2-4]. Compared to other forms of breast cancer, PSCCB tends to be larger on presentation, with more than half being greater than five centimeters [5]. There are no radiologic findings specific for PSCCB, leading to a higher incidence of delayed or missed diagnoses [5]. Previously reported cases of PSCCB have demonstrated a wide



Elizabeth S Lee^{1*}, Tracy M Lundberg², Jessica F Rose¹, Michele B Ley¹, Amy Waer¹, Robert B Livingston³, Alison T Stopeck³, Pavani Chalasani³, Victor J Gonzalez⁴, Lauren G LeBeau² and Rebecca K Viscusi¹

¹Department of Surgery, University of Arizona, College of Medicine, Tucson, AZ, USA

²Department of Pathology, University of Arizona, College of Medicine, Tucson, AZ, USA

³Department of Medicine, University of Arizona, College of Medicine, Tucson, AZ, USA

⁴Department of Radiation Oncology, University of Arizona, College of Medicine, Tucson, AZ, USA

*Address for Correspondence

Elizabeth S Lee, MD, Department of Surgery, University of Arizona, College of Medicine, 1501 N Campbell Ave., PO Box 245058, Tucson, AZ 85724-5058, USA, Tel: 520-626-0887; Fax: 520-626-2247; E-mail: liz8236@email.arizona.edu

Copyright: © 2014 Lee ES, et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Submission: 01 October 2014

Accepted: 30 October 2014

Published: 04 November 2014

range of clinical presentations ranging from PSCCB only detected on an abnormal mammogram with no obvious breast mass to a breast abscess. In addition, due to the rarity of this disease, no clear consensus on definitive treatment or prognosis exists.

We present a case series of two females who were diagnosed with PSCCB from 2007-2012 at our institution illustrating their initial clinical presentation, clinical course and outcomes of treatment, as well as a literature review.

Methods

Using a search of our pathology database, we identified females diagnosed with PSCCB at our institution from 2007-2012. Inclusion criteria included female patients over the age of 18 years old with a primary tumor consisting of greater than 90% malignant cells of squamous origin. Likewise, exclusion criteria included squamous cell cancer that had metastasized to the breast from elsewhere or lesions that were not independent of the overlying skin or nipple. We then performed a retrospective review to evaluate patient characteristics, presentation, tumor characteristics, treatment modalities and outcomes. A literature review was also performed using the PubMed database using the key words “primary squamous cell cancer of the breast”, “primary squamous cell carcinoma of the breast” and “primary squamous cell breast cancer”.

Results

The first patient is a 52 year old healthy, non-smoking, post-menopausal, female with no personal or family history of breast, ovarian, or colon cancer who presented with a progressively enlarging left breast mass that she noticed one month prior to presentation. On examination of her left breast, a 6 centimeter mobile breast mass at the twelve o'clock position was noted with no skin changes, nipple discharge or lymphadenopathy. She underwent a bilateral diagnostic mammogram with a 2.5 centimeter dense mass noted in the left upper outer quadrant of her breast. An ultrasound guided core needle biopsy

was performed that demonstrated a moderate to well differentiated keratinizing squamous cell carcinoma. Furthermore, a bilateral breast MRI was performed that depicted a 3.2 centimeter spiculated mass in the left upper outer quadrant at the two o'clock position with no evidence of lymph node, chest wall or right breast involvement. She underwent a left partial mastectomy with axillary sentinel lymph node biopsy. Final pathology demonstrated a 4.5 centimeter, stage pT2N0M0, moderately differentiated squamous cell carcinoma with negative lymph nodes and margins. ER/PR/Her2-neu were all negative with a Ki-67 proliferation index of 80%. Postoperatively, she was treated with adjuvant whole breast radiation and no systemic therapy. At her 28 month follow up, she continues to be disease free.

The second patient is a 35 year old healthy, non-smoking, premenopausal female with no personal or family history of breast, ovarian, or colon cancer who presented with a right breast mass that she palpated on a breast self-exam. On examination of the right breast, a 2 centimeter mass at the one o'clock position was noted with a negative axillary exam. She had a diagnostic mammogram performed demonstrating a 2.6 centimeter mass in the upper inner quadrant of her right breast adjacent to the chest wall. An ultrasound guided core needle biopsy was performed that demonstrated moderately differentiated keratinizing squamous cell carcinoma. A pre-operative PET scan was negative for metastasis. The patient underwent a bilateral skin sparing mastectomy with bilateral axillary sentinel lymph node biopsy and immediate reconstruction. Pathology demonstrated a right breast 1 centimeter, pT1bN0M0 moderately differentiated squamous cell carcinoma with negative lymph nodes and margins. In addition, ER/PR/Her2-neu receptors were negative with a Ki-67 proliferation index of 40%. Post-operatively, she received no adjuvant radiation or systemic therapy. At her eighteen month follow up, she continues to be disease free.

Discussion

Because PSCCB is so rare, prognosis and optimal treatment are still controversial [1-5,7-12]. There is a small body of research regarding this topic which consists mainly of isolated case reports and a few larger case series. One of the larger series by Hennessey et al. includes 37 cases of PSCCB reported over a 6 year period (1985-2001) from one institution and compares their findings with cases of PSCCB entered into the Surveillance, Epidemiology and End Results (SEER) Database, which is a population based tumor registry sponsored by the National Cancer Institute and includes newly diagnosed cancer cases from 11 SEER participating areas. Out of 281,382 total numbers of breast cancer reported to the SEER database from 1988-2001, there were 137 cases of PSCCB reported [6]. A study by Nayak et al. identified 21 cases of PSCCB over a 15 year period (1985-2010) from one institution [9]. Additionally, Stevenson et al. identified seven cases of PSCCB out of 1647 cases of malignant breast tumors over a 48 year collection period (1945-1993), further demonstrating the rarity of this cancer [13].

In addition, defining PSCCB can be challenging [13]. Currently, there are four pathological criteria that must be met prior to establishing the diagnosis of PSCCB according to Rosen's Breast Pathology, which include: (1) tumor origin does not arise from overlying skin, nipple or adenexal components, (2) greater than 90% of the tumor must be composed of squamous cells, (3) no evidence

of ductal or mesenchymal elements within the tissue sample, and (4) no other sites of primary squamous cell cancer are present [1-6,8-10,13,14]. However, there are questions as to whether PSCCB even exists or is simply a continuum with different degrees of squamous metaplasia within pre-existing adenocarcinoma [13]. This is exemplified in one study in which the ultrastructure of PSCCB is examined under light and electron microscopy and noted to have features of both glandular and squamous cells [13]. The World Health Organization (WHO) classifies PSCCB as a subgroup of epithelial-type metaplastic breast cancer, along with adenocarcinoma with spindle cell differentiation and adenosquamous carcinoma [9]. To further challenge things, the origin of PSCCB continues to remain unclear. In addition to Stevenson et al.'s hypothesis stating that PSCCB could be associated with pre-existing adenocarcinoma, there have been other hypotheses that the cancer arises from metaplasia of the ductal, luminal epithelial or myoepithelial cells, chronic abscesses or possible malignant transformation from epidermal or dermoid cyst [4,8,10].

Detection of PSCCB can be very difficult as there is no specific physical exam or mammographic findings that are typical of this disease process. The majority of the patients present with a palpable mass. However, (name) presented a case report of a patient presenting with a pyogenic abscess. This patient presented with erythema and tenderness to her left breast and had an ultrasound study performed demonstrating a 7 x 6 x 2 cm cystic lesion. This lesion was subsequently drained, however, the patient returned 17 days later and underwent incision and drainage again with final pathology demonstrating PSCCB [3]. Unfortunately, because of its rarity, the diagnosis of PSCCB is usually made later in the disease process with the tumor being on average 4 cm, already putting them within the T2 category [1,10]. One author documented a wide range of tumor size within their study population, ranging from 1.2 to 13 cm's [13]. In addition, on gross pathological exam, 50% of these lesions demonstrate a cystic component [1]. Axillary lymph node metastasis have been reported to range from 10-30% [2,7,10,12]. Hennessey et al.'s demonstrated a higher rate of lymph node metastasis at 50% in 33 patients with PSCCB [6]. PSCCB was noted to skip regional lymph node metastasis and present as a distant lesion at a rate of 30-33% and most notably to the lungs or soft tissue of the neck and mediastinum [2,10]. Furthermore, these tumors are most often estrogen receptor (ER), progesterone receptor (PR) and HER2/neu negative with overexpression of EGFR [7,10].

In regards to imaging, there are no specific radiological findings of PSCCB that have been reported. A study by Sameuls et al. describes the mammography results of two patients with PSCCB as having an oval shape, indistinct, and spiculated mass without calcifications [15]. A second case report by Nair, et al describes their mammographic findings as having a rounded, dense mass with obscured margins and again, no calcifications [7]. These findings are similar to those of our cases that we presented. This further illustrates the elusiveness of this disease process. A fine needle aspiration and/or tissue biopsy needs to be performed in order to make a diagnosis of PSCCB [5]. On cytology, the principle finding is a predominant population of malignant squamous cells and may be enough data for the diagnosis. However, in rare cases of apocrine metaplasia, pseudosarcomatous stromal reaction, carcinosarcoma and fibroadenoma with squamous cell metaplasia may cause a false positive and make diagnosis difficult

[5,13].

Most of the current literature portrays PSCCB as an aggressive cancer with a poor prognosis and outcome [6]. According to Behranwala et al., they found that larger tumor size (greater than five centimeters) and positive lymph node status were prognostic indicators of poor outcome. A study performed by Nayak et al. analyzed the histological features and disease outcome of 21 cases of PSCCB and noted that the predictors of decreased overall survival were patients over the age of 60 years old and >10% spindle cell tumor component [10]. They also demonstrated that lymph node status, mitotic rate, tumor necrosis, clear cell change and anaplastic features were not statistically significant in impacting overall survival or locoregional recurrence disease free survival [10]. The 5-year overall survival rate according to the SEER database on 137 patients with PSCCB from 1988-2001 was 64%. Hennessey et al. compared their institutions findings to the SEER database results and found similar overall survival rates with their median survival at 37 months and a 40% five year survival rate. They also reported that median relapse free survival with localized disease was 20 months [6].

Since very little is known about the natural history of PSCCB, it often leads to multimodality therapy consisting of aggressive surgery followed chemotherapy. Initial surgical management of PSCCB is local disease control appropriate for tumor size with either total mastectomy or partial mastectomy with or without axillary clearance if the tumor to breast ratio is favorable [13]. Some investigators like Sheela et al. state that an axillary lymph node dissection should only be performed if there are clinically positive nodes or suspicious nodes present on imaging [12]. Other investigators including Behranwala et al. and Stevenson et al. report that while approximately 70% of patients with PSCCB do not have axillary lymph node metastasis on axillary dissection, complete axillary clearance should be routinely performed due to the unpredictability of the lymphatic spread [5,13].

Chemotherapeutic choices remain a point of controversy as well as. Because the majority of these cancers are estrogen and progesterone receptor negative, there is no benefit to adjuvant hormonal therapy. In addition, PSCCB does not appear to respond adequately to conventional breast chemotherapy regimens. However, one report states that the use of CDDP, 5-FU and doxorubicin as a commonly used combination [13]. There have been reports that cisplatin based chemotherapeutic agents have been successful in treating PSCCB [10,12,13]. The overexpression of EGFR has been used to the patient's advantage as it has been reported to be more responsive to platinum and taxane chemotherapeutics [6,10,12,13]. With the use of anti-EGFR therapy in combination with taxane/platinum therapy needs to be further explored as it may make treating PSCCB more successful [10]. The use of neoadjuvant chemotherapy still remains unclear and according to Hennessey et al. has not demonstrated any proven benefit as 4 of their 33 patients received neoadjuvant therapy with no resultant tumor response [6]. However, according to a case report by Dejager et al, neoadjuvant cisplatin and 5-FU was given to a patient with a 5.5 cm palpable PSCCB. After 3 cycles of chemotherapy, the mass was reported to be non-palpable and after surgical resection, the patient remained disease free for 2.5 years [4].

The efficacy of radiation therapy in PSCCB is not well documented.

Since locoregional relapse occurred frequently in the irradiated breast field, it is hypothesized that PSCCB is relatively radioresistant [6]. The lack of response to the radiation therapy may be due to the mixed cell type present within the cancer as proposed by Stevenson et al. [13]. In our case series, neither of our patients received systemic chemotherapy and has remained disease free at the time of their last follow up at five and eighteen month, respectively. Furthermore, one patient underwent radiation while the other patient did not, further exemplifying the need for more long term studies of this rare disease.

In conclusion, due to the rarity of PSCCB, there is little consensus on a gold standard treatment or prognosis as evident by the different treatment methods discussed. Because treatment options can be limited, more research is needed to further elucidate the biological behaviors of this rare cancer as well as prognostic factors that may allow us to treat a patient more conservatively.

References

1. Carbone S, Lobo Alvarez R, Lamacchia A, Almenar Gil A, Martin Hernandez R, et al. (2012) Primary squamous cell carcinoma of the breast: A rare case report. *Rep Pract Oncol Radiother* 17: 363-366.
2. Gupta C, Malani AK, Weigand RT, Rangineni G (2006) Pure primary squamous cell carcinoma of the breast: a rare presentation and clinicopathologic comparison with usual ductal carcinoma of the breast. *Pathol Res Pract* 6: 465-469.
3. Comellas N, Marin Gutzke M (2009) Primary pure squamous cell carcinoma of the breast presenting as a breast abscess. *J Plast Reconstr Aesthet Surg* 62: 178-179.
4. Dejager D, Redlich PN, Dayer AM, Davis HL, Komorowski RA (1995) Primary squamous cell carcinoma of the breast: Sensitivity to cisplatin- based chemotherapy. *J Surg Onc* 59: 199-203.
5. Behranwala KA, Nasiri N, Abdullah N, Trott PA, Gui GP (2003) Squamous cell carcinoma of the breast: clinico-pathologic implications and outcome. *Eur J Surg Oncol* 29: 386-389.
6. Hennessey BT, Krishnamurthy S, Giordano S, Buchholz TA, Kau SW, et al. (2005) Squamous cell carcinoma of the breast. *J Clinical Onc* 23: 7827-7835.
7. Nair VJ, Kaushal V, Atri R (2007) Pure squamous cell carcinoma of the breast presenting as a pyogenic abscess: a case report. *Clin Breast Cancer* 7: 713-715.
8. Arrangoiz R, Nigliazzo A, Apelgren K, Saxe A (2009) Squamous cell carcinoma of the breast: a case report and literature review. *Internet J Oncol* 7: 1.
9. Nayak A, Wu Y, Gilcrease MZ (2013) Primary squamous cell carcinoma of the breast: predictors of locoregional recurrence and overall survival. *Am J Surg Pathol* 37: 867-873.
10. Gupta N, Vashisht R, Nimbran V, Gupta R, Dhingra N, et al. (2012) Primary squamous cell carcinoma of the breast: case report and management decisions. *J Cancer Res Ther* 8: 323-325.
11. Tsung SH (2012) Primary pure squamous cell carcinoma of the breast might be sensitive to Cisplatin based chemotherapy. *Case Rep Oncol* 5: 561-565.
12. Sheela CS, Ramakant P, Shah G, Chandramohan V, Abraham D, et al. (2013) Primary squamous cell carcinoma of the breast presenting as a cystic mass. *J Postgrad Med* 59: 155-156.
13. Stevenson JT, Graham DJ, Khyami A, Mansour EG (1996) Squamous cell carcinoma of the breast: a clinical approach. *Ann Surg Oncol* 3: 367-374.
14. Rosen PP (1997) *Rosen's Breast Pathology*. New York: Lippincott, Raven. Chapter 19: 456-461.
15. Samuels TH, Miller NA, Manchul LA, DeFreitas G, Panzarella T (1996) Squamous cell carcinoma of the breast. *Can Assoc Radiol J* 47: 177-182.