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A common cancer in an uncommon location: A case report of squamous cell carcinoma of the nipple



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ABSTRACT

INTRODUCTION: Cutaneous squamous cell carcinoma (SCC) is common however SCC is rarely seen on the nipple, with only ten cases of SCC of the nipple in literature (American Cancer Society, 2015; Scotto et al., 1983; Pendse and O'Connor, 2015; Loveland-Jones et al., 2010; Brookes et al., 2005; Sofos et al., 2013; King and Kremer, 2012; Venkatesh et al., 1994; Hosaka et al., 2011) [1–9].

CASE: An 80 year old female presenting with a chief complaint of an abnormal lesion on the medial portion of her right nipple areola complex. A biopsy showed well-differentiated squamous cell carcinoma. She had an extensive history of prolonged sun exposure predisposing her to cutaneous SCC however none to the breast region. Her mammogram was negative for any invasive disease so a wide local excision was performed with no complications.

DISCUSSION: Due to the rarity of SCC of the breast or nipple, a biopsy is necessary to rule out other more common types of malignancies on the nipple that present with a similar physical appearance. We then examined the many different risk factors for SCC and the different methods for treating SCC whether it is cutaneous or of the nipple or breast. We also discussed the treatment of Paget's disease of the breast (PDB) as SCC of the nipple or breast can be mistaken for PDB.

CONCLUSION: The cases of SCC of the Nipple demonstrate the importance of recognizing changes of the skin even in locations not typically associated with SCC (American Cancer Society, 2015; Scotto et al., 1983; Pendse and O'Connor, 2015; Loveland-Jones et al., 2010; Brookes et al., 2005; Sofos et al., 2013; King and Kremer, 2012; Venkatesh et al., 1994; Hosaka et al., 2011) [1–9]. We concluded with a future suggestion of investigating possible risk factors specific to SCC of the breast or nipple.

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1. Introduction

Skin cancer is the most frequently diagnosed cancer with basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) being the most common [1]. SCC specifically is the second most prevalent of the two [2]. However it is rarely seen on the nipple as can be seen in the limited number of case reports seen in literature which at last count was ten cases [3–11]. Paget's disease of the breast (PDB) on the other hand while rare itself is the most common malignancy of the nipple areola complex [12]. In line with SCARE criteria, we present a case of well differentiated SCC of the nipple in an 80-year-old female patient [24].

2. Case presentation

Our patient is an 80-year-old formerly smoking Caucasian female with a past medical history of fibrocystic disease, diabetes mellitus, hypothyroidism, and asthma. She initially presented due to abnormal lesion on her right nipple areola complex. Patient's history was also significant for basal cell carcinoma and previous sun exposure without protective measures however none of the sun exposure was to her breasts or chest region. She also had a previously suspicious lesion seen on mammogram which turned out to be benign. Her family history was also significant for malignant neoplasm of brain, lymphoma, and throat cancer but no skin cancers. She initially presented to a private practice dermatology clinic with a lesion on the medial portion of her right nipple. The clinic performed a shave biopsy (Picture 1). The pathology report noted a well-differentiated squamous cell carcinoma. She was then referred to our academic surgical oncology clinic (Diagram 1).

On breast examination, the right breast had a 7 × 7 mm scar where the shave biopsy was performed. The nipple showed 50% distortion due to the previous shave biopsy but no retraction or

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Picture 1. Squamous cell carcinoma lesion of the nipple post initial biopsy and prior to surgery.

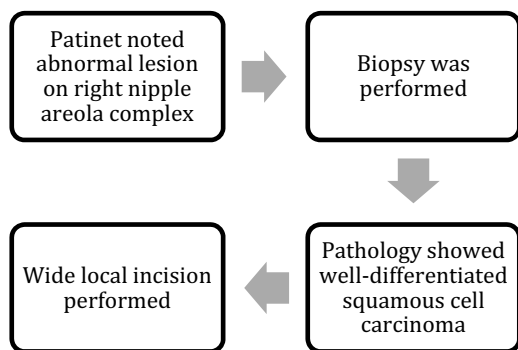
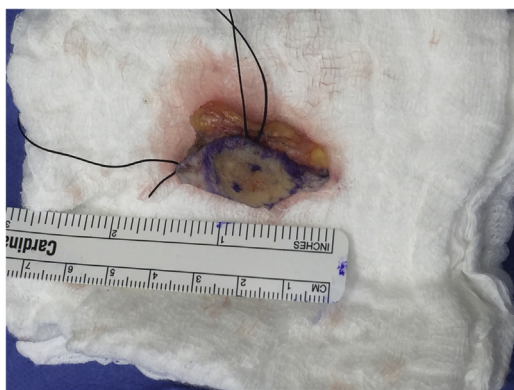


Diagram 1. Patient timeline.



Picture 2. Surface lesion with underlying tissue after surgical removal.

dimpling. Furthermore, there were no palpable lesions, or lymph nodes in axilla or supraclavicular areas. We reviewed her mammograms and found no evidence of pathology. Due to the lack of deeper pathology, it was decided to treat the lesion in a similar fashion to that of cutaneous SCC so a wide local excision of the lesion was performed. A 6-mm circumferential margin around the lesion was decided upon (Picture 2).

Prior to the surgery, she was medically cleared with a complete blood count with differential, comprehensive metabolic panel, prothrombin time, international normalized ratio, two chest x-ray views, and electrocardiogram. On the day of surgery, she received one gram of Mysoline intravenously and sequential compression devices were placed on both lower extremities. She was positioned supinely on the table and general anesthesia was induced. The

skin and subcutaneous tissues were dissected down in an anatomical fashion to a depth of 1.2 centimeters. After the lesion was removed, the incision was inspected and monopolar cautery was used to achieve complete hemostasis. Subcutaneous tissues were approximated with sutures in a layered fashion. There were no complications during or after the procedure. The pathology report noted clear margins and reaffirmed the diagnosis of SCC in situ as well as noting cystic dilation of the ducts beneath the nipple.

Post-surgery, she followed up with us as scheduled. Her lesion healed well at follow up. At her six month follow up, we obtained a new mammogram and compare it to previous mammograms. She was clinically normal with no signs of recurrence and we will continue to follow her.

3. Discussion

In the case of our patient, we already had a biopsy. Without this biopsy, we would have also needed to consider PDB. The biopsy however narrowed down our differential to SCC but we had to determine if the initial source was the skin, nipple or breast. In Table 1, we compare cutaneous SCC and SCC of the nipple.

Cutaneous SCC is common however it usually presents on skin exposed to UV radiation. The rarity of cutaneous SCC on the breast is most likely related to the risk factors associated with SCC. The risk factors of SCC include exposure to ultraviolet radiation, exposure to ionizing radiation, infection with human papillomavirus (especially types 6, 11, 16, and 18), exposure to chemical carcinogens, immunosuppression, chronically injured or diseased skin, and certain precursor lesions (actinic keratoses, arsenical keratoses, radiation-induced keratoses) as well as host factors (eye and hair color, complexion, tanning, ethnic characteristics) [13,14]. The most significant is the exposure to ultraviolet radiation however the nipple areola complex is rarely exposed to large quantities of ultraviolet radiation.

Our patient has several risk factors although none specifically predispose the skin of the nipple areola complex to SCC. She worked as a farmer so has a history of prolonged ultraviolet radiation and unfortunately she did not use any sun protection. This accumulated ultraviolet radiation over the years put her at increased risk of developing skin cancer in general [15]. This accounts for her extensive history of BCC lesions she had removed over the years. The history of BCC however only puts her at a 6% risk of developing SCC [16].

The major treatment approaches for cutaneous SCC include surgical excision, cryotherapy, electrocautery, topical treatments, radiation therapy, or photodynamic therapy. The intensity of treatment is related to the risk level of the lesion with high-risk lesions requiring surgical intervention and assessment of possible systemic spread. The cure rate of primary cutaneous SCC for more than five years is greater than 90% [17].

The next consideration is that the source of the lesion is the nipple. The most common lesion of the nipple is PDB, which is still quite rare. In a case report by Sofos et al., a scaly lesion of the nipple closely resembling PDB clinically but was later diagnosed as SCC of the nipple instead [6]. Early diagnosis of PDB is important since 92% of patients diagnosed with PDB have an underlying mammary carcinoma [18]. The current recommendation for management of PDB is surgical intervention although breast-conserving surgery is an option due to the high chance of an aggressive cancer under the lesion mastectomy is often performed [19]. In an article published in 2012, they suggested an algorithm by which to manage PDB after being confirmed by biopsy [20]. The algorithm denotes the first step after a positive biopsy is a breast exam and mammogram. If these are negative then MRI should be performed. Treatment is

Table 1
Comparison in presentation of cutaneous SCC vs SCC of the nipple [3–11,13,14,23].

	Cutaneous SCC	SCC of the nipple
Incidence	100,000 cases per year	Only 10 cases in literature
Risk Factors	Radiation, Chemicals, Chronic skin inflammation, HPV, Immunosuppression, Precursor lesions, Host factors (complexion, age)	Radiation, Chemotherapy, History of breast cancer, Immunosuppression
Previous History	Scars, Burns, Chronically inflamed skin, Non-healing ulcer	Radiation, Chemotherapy
Presentation	Hyperkeratotic, Ulceration, Erythematous, Eczematous	Eczematous, Scaly, Inflamed, Erythematous, Serous/serosanguinous discharge, Excoriations, Skin retraction around areola
Age	>60 years	Varies
Sex	Similar occurrence in both sexes	8 of 10 cases reported were in females

determined on the stage or histologic findings of any underlying cancer.

With SCC of the nipple being rare, a pattern for prevalence, diagnosis, and specific risk factors nipple have been difficult to establish. Several of the reported cases of SCC of the nipple in the literature occurred post radiation therapy for breast cancer [4,5]. This makes sense as radiation is in general a risk factor for SCC of any type. Radiation therapy of the breast can predispose the nipple to secondary malignancy as it has no protection leading to toxic doses of radiation. However this is not the case in our patient as she has no history of radiation therapy of the breast.

Due to the low incidence of SCC of the nipple, a standardized treatment has not been established. The current literature exhibited a wide range of approaches in treatment but as in cutaneous SCC, a wide local excision has been the primary choice but mastectomy and photodynamic therapy was also reported [3–11]. Of the cases only two reported local reoccurrence, one of the cases was treated via an incomplete local resection that was corrected with repeat resection and the other case was initially treated with a photosensitizer and retreated with cryotherapy [3–11]. Of the cases with no reported reoccurrence, patients were SCC free for six months up to five years as reported in one of the cases with mastectomy [5,9].

Then there is SCC of the breast which just as the other discussed lesion is also rare with it accounting for only <0.04% to 0.1% of all primary breast malignancies [21]. Unlike the other lesions discussed, SCC of the breast typically begins as a lump and as it expands can lead to manifestations visible on the skin [21]. The current recommended approach for SCC of the breast is similar to other malignancies of the breast being a lumpectomy or radical mastectomy with possible addition of chemotherapy or radiation therapy depending on the severity of the malignancy. If treatment is undergone as suggested the outcome consisted of being cancer free [21–23].

4. Conclusion

Our case further adds to the literature involving the rare entities of SCC of the nipple or breast, and cutaneous SCC on skin unexposed to UV radiation such as the nipple areola complex.

The key point learned from this case is that it is important to be vigilant in recognizing changes in skin even in locations not typically considered to be at risk. As is in the case of SCC of the nipple since, the nipple is not commonly exposed to solar radiation. Patients should be advised to follow recommended guidelines about protection from the sun and note any new moles, eczematous lesions, skin thickening or redness on any portion of the body to their primary care physician or if possible a dermatologist.

Another key point is that thus far the surgical approach has been most efficacious. Surgical resection either as a wide localized excision or mastectomy was used in most cases as well as in our own patient [3–11]. Prognosis seen in the other cases that were managed

promptly is good, with patients in other cases being tumor free for at least five years [9]. We will continue to follow our patient with the hope of a similar outcome to those already in literature.

A future topic of consideration would be to determine possible risk factors specifically for rarer forms of SCC beyond those already known to literature for SCC. With several of the cases being related to breast cancer and radiation therapy afterwards, breast radiation therapy can be considered a possible risk factor for SCC of the nipple [4,5]. While this was not so in our case, we hope that by adding our case to the literature, we may stress the importance of a thorough skin evaluation in order to recognize cancers earlier leading to better outcomes.

Conflict of interests

None.

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Ethical approval

No ethical approval needed for the case study presented and submitted.

Consent

Our patient consented for publication of the case.

Author contribution

Kelly Dye MS4: Data collection, data analysis, and writing the paper.

Melissa Saucedo MS3: Data collection and data analysis.

Divya Raju MS3: Data collection and data analysis.

Nail Aydin MD: Study concept, design, data analysis and interpretation, and review of the paper.

Guarantor

Nail Aydin MD FACS.

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