

Case Report

Sebaceous carcinoma of the breast nipple: a case report and literature review

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Abstract: Sebaceous carcinoma (SC) of the breast nipple is a rare malignant tumor, and only five cases, including the present one, have been reported in the English-language literature. The present report describes a case of SC of the breast nipple in a 51-year old Chinese woman. The lesion presented a gradually enlarging nodule in the right breast nipple, with transparent yellow exudate overflowing from the cutaneous lesions. The histopathological results revealed that the tumor cells were arranged in nests consisting of sebocytes with vacuolated or multivesicular/foamy cytoplasm and atypical nuclei, accompanied with definite foci of keratinization and keratin pearls. Complete resection of the lesion and SLNB were accomplished, and no recurrence was observed during the follow-up. This is the first case of SC in the nipple-areolar complex diagnosed in Peking Union Medical College Hospital in Beijing of China for the period from 1995 to 2016, and therefore, it contributes to a better understanding of its clinicopathological characteristics and improved recommendations for diagnosis and treatment it contributes to the recommendations for diagnosis and treatment.

Keywords: Sebaceous carcinoma, breast nipple, clinicopathological characteristics

Introduction

Cutaneous sebaceous carcinoma (SC) is a rare, potentially aggressive neoplasm. It accounts for less than 1% of all cutaneous malignancies in the world and is traditionally subcategorized into two groups based on the site of origin: ocular (periocular) and extraocular [1]. As is known, cutaneous SC occurs most often in the periocular area, whereas extraocular cutaneous SC accounts for only 25% of the tumors and usually localizes in the head and the neck region. To the best of our knowledge, the case reported here is the third case in the English literature of cutaneous SC arising from the nipple [1, 2] without association with Muir-Torre syndrome (MTS). It is important that the carcinoma derived from the breast nipple skin and was characterized by totally different diagnosis and treatment options which are different from breast cancer traditionally.

Results

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The surgical pathology files of all cutaneous SC cases diagnosed in Peking Union Medical

College Hospital during the period from 1995 to 2016 were retrospectively reviewed. A total of nine cases had been diagnosed as cutaneous SC. Among them, in six of the cases, the disease occurred in the periocular region, whereas in the remaining three cases, it arose from the nipple, the nose, and the lower limb. The clinicopathological characteristics of the patient with cutaneous SC arising from the nipple were examined.

A 51-year-old woman presented with a six-month history of a red-yellow, gradually enlarging papule located eccentrically on her right nipple with mild itch and pain. Before admittance to the hospital, the nodule had slightly increased in size, measuring approximately 1.5 cm in diameter, with skin redness and swelling. Transparent yellow exudate was observed on the top of the cutaneous lesions. She had no other cutaneous or breast tumors, regional lymphadenopathy, or any clinical evidence of other internal malignancy. However, since her renal transplantation in 2009, the patient started to receive oral administration of immunosuppressive drugs till now, including tacrolimus, mycophenolate mofetil, and prednisone.

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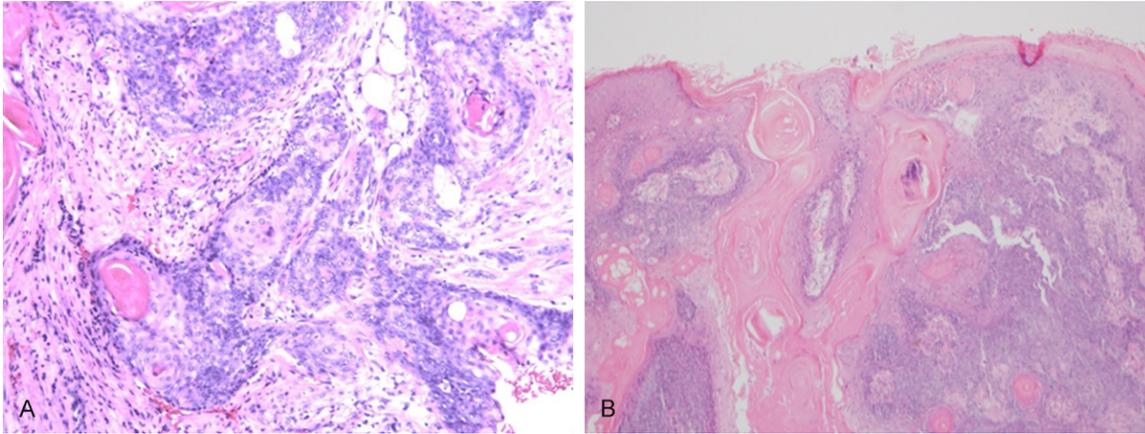


Figure 1. A. Histopathological examination of the tumor consisting of sebocytes with vacuolated or multivesicular/foamy and atypical nuclei. B. Nipple involvement visible under low magnification of a sample of sebaceous carcinoma tissue.

An ultrasound examination was performed, and a low-echo mass with dimensions of 2.3 × 1.4 cm and clear boundaries was identified. The nipple lesion was resected size with 1 × 0.5 cm at the beginning in Beijing chaoyang hospital and a histopathological examination was conducted as described below.

The histopathological examination (**Figure 1A** and **1B**) revealed a cutaneous lesion involving the epidermis, dermis, and subcutaneous tissue. Tumor cells were arranged in nests consisting of sebocytes with vacuolated or multivesicular/foamy cytoplasm and atypical nuclei. Areas of squamous differentiation with foci of keratinization and keratin pearls were also present. Frequent mitotic figures and scattered necrotic cells with increased nucleus:cytoplasm ratios were found.

Furthermore, immunohistochemical staining was performed. The tumor was negative for ER and Her-2 (**Figure 2A** and **2B**), and positive for p63 (**Figure 2C**), with a Ki-67 index of 15% (**Figure 2D**). A scattered positive reactivity of p53 (**Figure 2E**) was also observed.

Above all histopathological findings confirmed a definite diagnosis of cutaneous SC of the nipple.

Seven days after the first operation, the patient returned for further treatment since the wound was not healing. Then, a wider excision of the lesion over the nipple-areolar complex and sentinel lymph node biopsy were per-

med. Both the frozen and the paraffin sections showed negative margin and sentinel lymph node. Thus, our patient did not undergo further lymph node dissection. The lesion was completely removed and the wound healed well (**Figure 3**). Moreover, no recurrence of tumor or metastasis was detected during the 24 months of follow-up, and no clinical evidence of Muir-Torre syndrome (MTS) was found either.

Discussion

Cutaneous SC is a rare neoplasm with a reported incidence varying from 0.2% to 5% of all malignant cutaneous neoplasms [3-5]. The results of a previous study indicated that extraocular cutaneous SC was much less common than cutaneous SC in the periocular region [6]. The previously reported primary sites of extraocular SC include the external genitalia, the parotid and submandibular glands, the buccal mucosa, the external auditory canal, the trunk, the extremities, the breast, the laryngeal or pharyngeal cavities, and the lungs [5-10]. SC arising from the nipple is extremely rare, and, due to its rarity, no standard guidelines for its diagnosis and treatment are available.

Extraocular SC deriving from the nipple usually originates from the skin appendages, whereas sebaceous carcinoma of the breast always derives from the mammary glands without connection to the overlying skin or the nipple [11]. Due to their different origin, these two subtypes of carcinoma have diverse clinical presentation. The former usually presents as a

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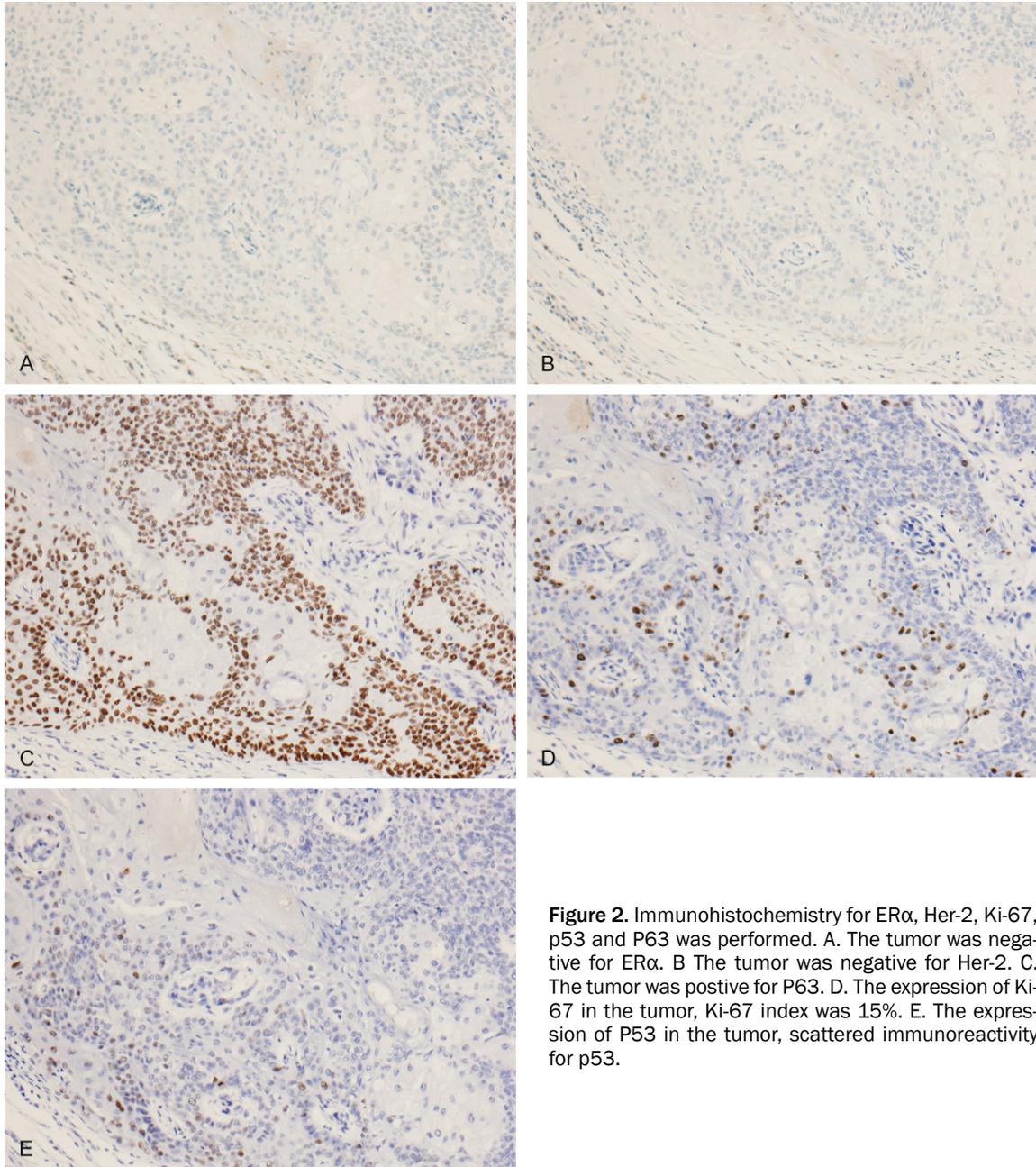


Figure 2. Immunohistochemistry for ER α , Her-2, Ki-67, p53 and P63 was performed. A. The tumor was negative for ER α . B The tumor was negative for Her-2. C. The tumor was positive for P63. D. The expression of Ki-67 in the tumor, Ki-67 index was 15%. E. The expression of P53 in the tumor, scattered immunoreactivity for p53.



Figure 3. Healed wound after a wider excision of the lesion over the nipple-areolar complex.

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pink to red-yellow nodule, whereas the latter always develops as a mass of the breast. Extraocular SC is considered less aggressive in terms of local recurrence and metastasis, and thus has a better prognosis than SC of the breast. Therefore, a local excision such as segmentectomy with a negative margin is sufficiently effective for the treatment of extraocular SC in nipple-areolar complex. However, SC of the breast is usually manifested as a lump in the breast and may metastasize to the axillary lymph nodes. Thus, mastectomy may be necessary for its successful therapy. Apart from the clinical presentation, the differential diagnosis must be based on the pathological findings of whether the manifestations are limited to the skin and the subcutaneous tissue or the mammary gland with/without the axillary lymph node is involved. We speculate that it is reasonable to perform sentinel lymph node biopsy (SLNB) for extraocular SC of the nipple not only for differentiation, but also for avoiding unnecessary axillary lymph node dissection (ALND).

Importantly, extraocular SC can exhibit diverse clinical presentations and is commonly confused with other lesions, especially with basal cell carcinoma (BCC), squamous cell carcinoma (SCC), Paget's disease [12] and nipple duct adenoma, which may appear similar in clinical images [1]. For this reason, it is crucially important to recognize other cutaneous neoplasms that could be confused with SC. In pathological examination, IHC stains are often less necessary for distinguishing SC from other tumors. The identification of the characteristic histological features and the detection of the presence of tumor cells with multivesicular/foamy cytoplasm facilitate the differentiation of SC from other common tumors with simple cytoplasmic clarity, such as BCC, the pagetoid variant of Bowen's disease, SCC, poroma/porocarcinoma, trichilemmal tumor, and Paget's disease [13]. In our case, the presence of tumor cells with vacuolated or multivesicular/foamy cytoplasm and frequent mitotic figures was obvious. In consistent with our study, SC immunochemically tends to exhibit triple-negative immunoprofile with p63 expression. However, IHC stains are often less necessary for distinguishing SC from other tumors. As is known, extraocular SC can be associated with MTS [6, 14-16], which is an autosomal domi-

nant genodermatosis characterized by the association of sebaceous tumors (adenoma, epithelioma, or carcinoma) and occasionally keratoacanthomas with a variety of visceral malignancies. MTS is caused by mutations in one of several mismatch repair genes. The cutaneous lesion may occur before or after the internal malignancy. Thus, if the presence of MTS is suspected, further assessment should be performed, including a detailed assessment of the family history of cancers; abdominal/pelvic ultrasound; feces occult blood test (FOB); computed tomography (CT) scan of the chest, abdomen, and pelvis; and tumor markers tests, including determination of the serum levels of CA125, CA19-9, and CEA. Our patient was subjected to abdominal/pelvic ultrasound and an FOB test, which detected no clinical evidence of other internal malignancy and absence of history of malignancy. It is noteworthy that the patient had a history of renal transplantation and long-term oral administration of immunosuppressive drugs. This is the first case report of extraocular SC that developed after immunosuppression therapy in the specialized literature in English. More evidence is required to elucidate whether immune suppression is related to the occurrence of this malignancy.

Extraocular SC is believed to have a somewhat better prognosis than ocular SC, with less chance of local recurrence and metastatic tendency [3, 7, 8, 17, 18]. Distant metastasis from extraocular SC has been reported in less than 10% of the cases globally. However, given the limited number of reported cases and the scarce clinical follow-up data available, the true etiology of this neoplasm might still remain undetermined [8, 17, 19]. Therefore, periodic physical examination, laboratory tests, and close follow-up are necessary to detect the recurrence and metastasis of SC as well as for the timely identification of the potential occurrence of MTS.

In conclusion, histopathological examination is the only way for definite diagnosis of cutaneous SC, which is an extremely rare cutaneous neoplasm that occurs at the areola-nipple complex. Radical resection of the lesion and SLNB are both recommended in patients with SC at the areola-nipple complex owing to the potential for local recurrence and regional lym-

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ph node and distant metastasis. Furthermore, in some cases, mastectomy may need to be performed. In addition, a long-term follow-up period is necessary for monitoring of potential MTS occurrence.

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Disclosure of conflict of interest

None.

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