Microcystic Adnexal Carcinoma of the Nipple

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A 36-year-old woman came to our OPD with presentation of a solitary, indurated, nonpainful subcutaneous plaque on the left nipple area for 2 months. There was neither discharge nor ulceration. Axillary's lymph node was not palpable. Histopathological examination directed the diagnosis to microcystic adnexal carcinoma. A wide excision was performed with negative margin. The preoperative and intraoperative investigations of sentinel lymph node in axilla was not involved. No recurrence was noticed in 16-month follow-up. We represent a case of microcystic adnexal carcinoma in an unusual location. Diagnosis of microcystic adnexal carcinoma should be taken into account in a nipple nodule or a breast lump. (Dermatol Sinica 22 : 153-158, 2004)

Key words: Microcystic adnexal carcinoma, Nipple

INTRODUCTION

Microcystic adnexal carcinoma is a rare, locally aggressive tumor with high potential for local recurrences. This tumor presents usually as a solitary, slowing growing, firm, indurated plaque on face, particularly around the upper lip.¹,² Lesions may occasionally be found on extrafacial locations, including the nipple, axilla, and lower extremities. In the nipple location, it has been named syringomatous adenoma of
the nipple. However, because of the metastatic potential, the diagnosis of microcystic adnexal carcinoma is more appropriate. We present a case of microcystic adnexal carcinoma of the nipple in a 36-year-old woman and its immunohistochemical studies. The origin of this tumor according to the results of stains and the differential diagnosis in this unusual location are discussed.

**CASE REPORT**

A 36-year-old married woman presented with enlargement of left nipple for 2 months. On physical examination, there was a painful cord-like mass, which measured 0.5 x 0.3 cm in size, covered with normal skin in the left nipple (Fig. 1). There was no history of trauma, and the patient's medical and family histories were otherwise insignificant. No axillary lymphadenopathy was palpable. A breast sonogram showed a low echoic homogenous mass with smooth margin and the mammogram showed several tiny microcalcifications in the left nipple with dense breast parenchyma (Fig. 2).

Excisional biopsy showed one tumor with gray white color and elastic consistency. Microscopic section revealed a large, poorly circumscribed tumor that invades deeply. The upper part shows several cornifying cystic structures. Solid aggregates clusters or strands of tumor cells within hyalinized stroma around the lactiferous sinus in the middle part. The lower part reveals small irregular comma-shaped gland-like structures lined by a two-cell layer within a desmoplastic stroma (Fig. 3, 4). Focal

![Fig. 1](image1.png)
*A palpable cord-like mass covered with normal skin was located in the left nipple of a 36-year-old woman.*

![Fig. 2](image2.png)
*The mammogram showed several tiny microcalcifications in the left nipple with dense breast parenchyma.*

![Fig. 3](image3.png)
*H & E stain (40X) There is a large, poorly circumscribed tumor that invades deeply. There are cornifying cystic structures, solid strands of tumor cells around the lactiferous sinus, duct and gland-like structures lined by a two-cell layer within a desmoplastic stroma.*
infiltrate adjacent to the nerve is noted. This tumor demonstrated reactivity with cytokeratin, epithelial membrane antigen (EMA), Periodic acid-Schiff (PAS) and distase-resistant PAS (PASD), S100 protein, and carinoembryonic antigen (CEA) (Fig. 5). But the tumor expressed negative immunoreactivity for vimentin and gross cystic disease fluid protein (GCDFP-15). All of the above findings are consistent with the diagnosis of microcystic adnexal carcinoma.

The patient had a wide excision including nipple and areolar area (4x4x4 cm). A sentinel axillary lymph node showed negative finding in frozen sections according to the identification of the sentinel lymph node through the preoperative lymphoscintigraphy and intraoperative gamma probe procedure. There was a complete resection with negative margin in pathologically frozen and paraffin sections. After the operation, the patient lived her life well. After follow up for 16 months, no recurrence was noted.

DISCUSSION

Microcystic adnexal carcinoma (MAC), also named sclerosing carcinoma of sweat ducts or syringomatous adenoma, was first described by Goldstein, et al in 1982.1,2 Because of the cell of origin has not been adequately determined, the descriptive term "Microcystic adnexal carcinoma" was preferred. This tumor is seen most commonly on the skin of the head and neck regions, especially upper lip, chin, nasolabial fold, or cheek. The report of nipple lesion is rare.3-6 In 1983, a locally infiltrating neoplasm of the nipple was reported and named as "syringomatous adenoma of the nipple" by Rosen.7 In this report, he described duct-like structures and keratinizing cysts were present throughout the lesion that has similar histopathologic features with MAC. Therefore, some scholars consider the syringomatous adenoma of the nipple to be a synonym for microcystic adnexal carcinoma of the nipple.8

MAC most often presents as a flesh-colored, indurate plaque with ill-defined margins. Typical symptoms are sensations of pain and paresthesia, which are thought to be secondary to perineural invasion. The average age is in mid-40s. Although bland in its pathological appearance, MAC is an aggressive neoplasm that invades deeply and has a high propensity for local recurrence. The recurrence time range from less than 5 months to 28 years, with a median of 3 years.9 Regional or distant metastasis is uncommon.7,10 The pathogenesis was poorly understood, although radiation exposure may be a predisposing factor.11,12

Histologically, MAC is a poorly circumscribed tumor that may extend into the dermal, subcutaneous, perineural and skeletal muscle
planes. There are three components within a desmoplastic stroma: cornifying cystic structures near the surface, solid aggregations of cells in the center, and gland-like structures in the lower part. The individual tumor cells are cytologically bland without significant atypia, and mitoses are rare. Perineural invasion may be seen, a feature that may account for the high tendency for recurrence.

There are continuous debates about the origin of MAC. In 1986, Cooper believed the cystic-like structures to represent a propensity to "keratinization" in the acrosyringium of eccrine sweat ducts. CEA showed immunoreactivity in the glandular structures but not the pilar structures. The findings support that MAC exhibits differentiation toward both eccrine and pilar structures. Wick et al reported on immunohistochemical studies of MAC, that demonstrated reactivity for CEA, EMA, Leu-M1, and cytokeratin. They concluded that MAC was a hybrid of sweat glandular and follicular neoplasm. In 1993, LeBoit studied 17 samples of MAC histopathologically and immunohistochemically. They demonstrated that MAC is an underrecognized neoplasm, which differentiates toward both hair follicles and sweat glands and ducts. However, in the other opinion, there are convincing signs of follicular, sebaceous, and apocrine differentiation in this distinctive malignant neoplasm. The cornifying cysts are infundibular, and the solid and tubular structures are apocrine. It is a nature like, embrologically, histologically, between follicular and apocrine units. MAC may be inferred to be apocrine in nature not only because of the relationship of the folliculo-sebaceous-apocrine apparatus, but also because of a predilection for apocrine gland areas including face, breast, and axilla. Therefore, the exact direction of its sudoriferous differentiation (i.e., apocrine vs. eccrine) cannot be determined with certainty.

Immunohistochemistry is helpful in the diagnosis of MAC and may clarify the cellular origin. In our case, it demonstrated reactivity with cytokeratin, EMA, PAS, PASD, CEA, and S100 protein. But the tumor expressed negatively for vimentin and GCDFP-15. The positive cytokeratin and EMA stains showed the tumor with both pilar and sweat gland differentiations. PAS and distase-resistant PAS both have stronger reactions in eccrine glands than apocrine glands. CEA and S100 protein showed immunoreactivity in the glandular structures but not the pilar structures. In our case, GCDFP-15 showed negative reactivity under positive control with apocrine gland. GCDFP-15 stain showed negative or positive reaction in the tumors of eccrine differentiation, but positive in the tumors of apocrine differentiation. However, positive GCDFP-15 reactivity has been reported as well. Tubular structures of MAC may be mostly lined by ductal, rather than glandular, epithelium. GCDFP-15, which could distinguish gland epithelium rather than eccrine or apocrine ducts, has a higher opportunity to show negative reactivity. We suggested, on the basis of the immunophenotype, that MAC expresses both eccrine and pilar differentiation, but there are still debates whether it is of eccrine or apocrine differentiation. It is hard to convincingly establish whether MAC express eccrine or apocrine differentiation, particularly when the ducts of either gland are indistinguishable.

According to the report of LeBoit, many cases were initially misdiagnosed. The misdiagnoses included syringoma, papillary eccrine adenoma, benign adnexal tumor, adnexal carcinoma, and morpheaform basal cell carcinoma. They suggested that small specimen sizes from biopsies as well as the bland appearing cytologic features contribute to these high misdiagnoses. Application of immunohistochemical techniques and adequate biopsy specimens could help us to differentiate between MAC and other similar lesions.

The diagnosis of MAC should be considered when a syringomatous or trichoeipithelioma-like proliferation extends to the base of the specimen. A complete excision should be contemplated. The features of MAC, including lack of circumscription, deep dermal involvement, both pilar and ductular differentiations,
rare atypia and mitoses, and perineural involvement, all aid in diagnosis. The resemblance to desmoplastic trichoepithelioma may be considerable, especially if a superficial specimen is taken for biopsy. Like desmoplastic trichoepithelioma, it shows horn cysts, strands of basaloïd cells, and a dense desmoplastic stroma. It differs, however, by showing ductal structures and a deeply infiltrating growth. CEA showed negative in desmoplastic trichoepithelioma. Syringoma can be distinguished from MAC by its smaller size, its greater symmetry, and the lack of prominent horn cyst formation and infrequent single-file strand formation. Syringomatous carcinoma shows tubular structures throughout the entire lesion and the tubules do not contain eosinophilic material. Cornifying cysts are also uncommon. To be distinguishing from other malignant tumors like basal cell carcinoma and adenosquamous carcinoma, MAC lacks nuclear atypia and mitotic figures.

MAC in the nipple lesion may be confused with ordinary nipple duct adenoma and well-differentiated (tubular) carcinoma. Nipple duct adenoma is a circumscribed complex proliferation of ducts of variable sizes with occasional squamous and apocrine metaplasia and keratin cysts. Unlike MAC, nipple duct adenoma often presents with ulceration and bleeding and without evidence of perineural and smooth muscle bundle invasion. Well-differentiated tubular carcinoma occurs deeper in the breast and is commonly located in the upper outer quadrant or away from the nipple. If tubular carcinoma does extend to the nipple, it may produce nipple retraction and Paget's disease. It does not have the feature of keratin cysts. Moreover, nuclear atypia and mitotic activity are more common in tubular carcinoma than MAC.

The appropriate initial managements for this lesion includes a preoperative deeper biopsy. The surgeon must recognize the deep infiltrative tendency and features of perineural invasion of this tumor. Careful preoperative counseling should take place so that the patient can be prepared for the possibility of a very large surgical defect. The goal of achieving tumor-free margins, either by frozen section or by Mohs micrographic surgery, should be attempted. Recent reports indicate similar cure rates between Mohs micrographic surgery and wide excision. The defect surface area after full extirpation following Mohs microsurgery was a mean of 4 times that of the clinically apparent size. The 10-year recurrent rate of both treatments groups is 18%.

MAC is a tumor with an infiltrative growth pattern and a predilection for neural involvement. Although the origin of this tumor is controversial, our immunohistochemical findings support that MAC exhibits differentiation toward both eccrine and pilar structures. Mohs micrographic surgery should be considered to be a preference for tumor excision if available. Irrespective of the method of treatment or the status of resection margins, all patients should be monitored closely for several decades for tumor recurrence.

REFERENCE


