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Case Report

Basaloid ductal carcinoma in situ arising in salivary gland metaplasia of the breast: a case report

Eun Jeong Jang[1], Su Hwan Kang[2], Young Kyung Bae[1]

[1]Department of Pathology, Yeungnam University College of Medicine, Daegu, South Korea; [2]Department of Surgery, Yeungnam University College of Medicine, Daegu, South Korea

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Abstract: Salivary gland metaplasia is a newly recognized, adenosis-like lesion which could not be classified according to known categories of adenosis of the breast. We report a case of basaloid ductal carcinoma in situ (DCIS) arising in a background of salivary gland metaplasia in a 49-year old woman who visited our hospital for a right breast mass. Breast ultrasonography showed a multi-lobulating mixed hypoechoic and isoechoic mass measuring 2.9 cm in size at the periareolar area. Histologically, the lesion showed a well-defined DCIS with basaloid tumor cells and central comedo-type necrosis surrounded by salivary gland metaplasia composed of glands or ducts not specific to the breast, ducts with cribriform proliferation of luminal epithelial cells, and ducts with varying degrees of proliferation of basaloid cells including solid nests of basaloid cells. Salivary gland metaplasia is a most unusual lesion of the breast characterized by salivary gland-type acini and ducts with various proliferations of luminal and basaloid cells, and accompanied by malignant tumor of basal cell type.

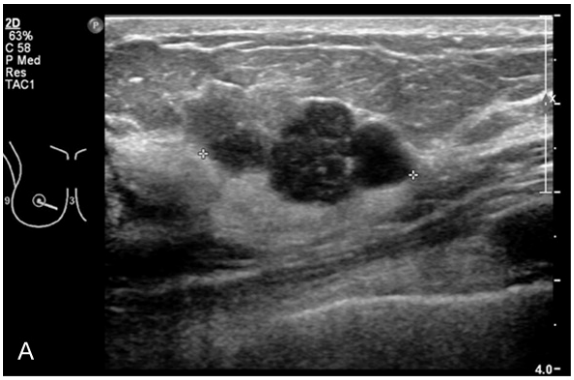
Keywords: Breast, ductal carcinoma in situ, salivary gland, metaplasia, basaloid

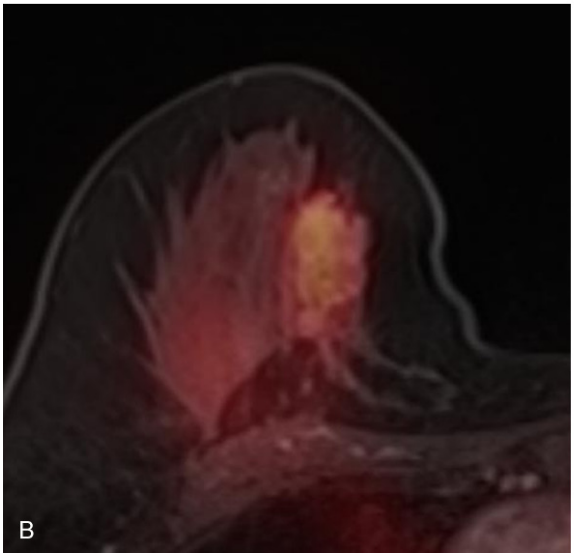
Introduction

The breast and salivary gland are both exocrine glands sharing similar morphologic features. Salivary gland-type tumors may occur in the breast; however, their incidence and clinical behavior are different from those arising in salivary gland [1, 2]. The occurrence of salivary gland-type tumors, including pleomorphic adenoma, adenoid cystic carcinoma, acinic cell carcinoma, mucoepidermoid carcinoma, adenomyoepithelioma, and benign and malignant myoepithelioma, reflects phenotypic progression (salivary gland differentiation) of neoplastic breast epithelium [3]. Presence of benign salivary-type acini and ducts in the breast without accompanying salivary gland-type tumors had been reported [3, 4]. The lesion represented pure serous acinar cells consistent with normal salivary gland tissue, and was found incidentally and limited to a few lobules in the breast of patients with infiltrating ductal carcinoma. The authors suggested that it would be a heterotopic salivary gland or salivary gland-like metaplasia of the breast lobule. Flynn et al. [5] recently reported three cases of basal cell adenocarcinoma arising in salivary gland metaplasia of the breast. Basal cell adenocarcinoma is a salivary gland-type tumor; however, it has not been previously reported in the breast. Of particular, in their report, the salivary gland metaplasia appeared as a diffuse adenosis-like lesion not generally observed in the breast. We experienced a case of basaloid ductal carcinoma in situ (DCIS) arising in the background of an uncommon adenosis-like lesion referred to as salivary gland metaplasia by Flynn et al. [5]. The salivary gland metaplasia was accompanied by varying degrees of proliferation of basaloid and luminal epithelial cells, and represented unique features which could not be classified according to known categories of adenosis of the breast.

Case report

A 49-year-old woman visited our hospital for a right breast mass found one week ago. Regarding past medical history, she had undergone hysterectomy due to uterine leiomyoma six years ago. Mammography showed extremely dense fibroglandular tissue without suspicious





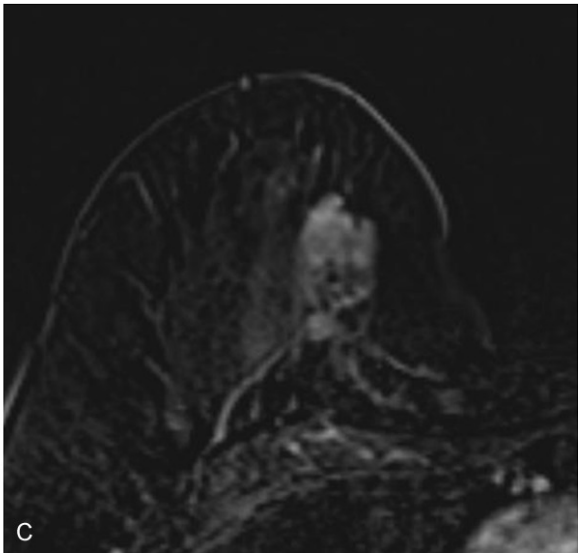


Figure 1. (A) Breast ultrasonography showed a multi-lobulating mixed hypoechoic and isoechoic mass measuring 2.9 cm in size at the periareolar area. (B) F-18 fluorodeoxyglucose (FDG) positron emission tomography/magnetic resonance imaging (PET/MRI)-mammography and (C) the second post-contrast subtraction series of dynamic T1 weighted breast MRI demonstrated an irregularly shaped mass with increased F-18 FDG uptake.

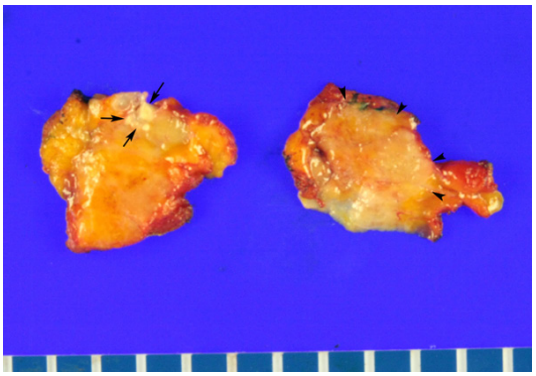


Figure 2. The cut surface of the specimen shows an ill-defined mass-like lesion (arrow heads) with pale-yellow small nodular aggregates consistent with ductal carcinoma in situ (arrows).

lesion or microcalcification. Breast ultrasonography showed a multi-lobulating mixed hypoechoic and isoechoic mass measuring 2.9 cm in size at the periareolar area (**Figure 1A**). No axillary lymphadenopathy was observed. F-18 fluorodeoxyglucose (FDG) positron emission tomography/magnetic resonance imaging (PET/MRI)-mammography (**Figure 1B**) and the second post-contrast subtraction series of dynamic T1 weighted breast MRI (**Figure 1C**) demonstrated an irregular shaped mass with increased F-18 FDG uptake.

Core needle biopsy was performed for the right breast lesion and she was diagnosed with DCIS. There was no clinical evidence of axillary node involvement or distant metastases. Lumpectomy was initially attempted, however, the patient finally underwent mastectomy because, on frozen section, the lumpectomy margin was positive for a proliferative lesion that needed to be differentiated from low grade DCIS. Two sentinel lymph nodes were retrieved for frozen biopsy and both were proved to be negative for tumor metastasis.

Grossly, the cut surface of the lumpectomy specimen showed an ill-defined firm mass-like lesion measuring 3.0 cm in maximum diameter, with pale-yellow small nodular aggregates

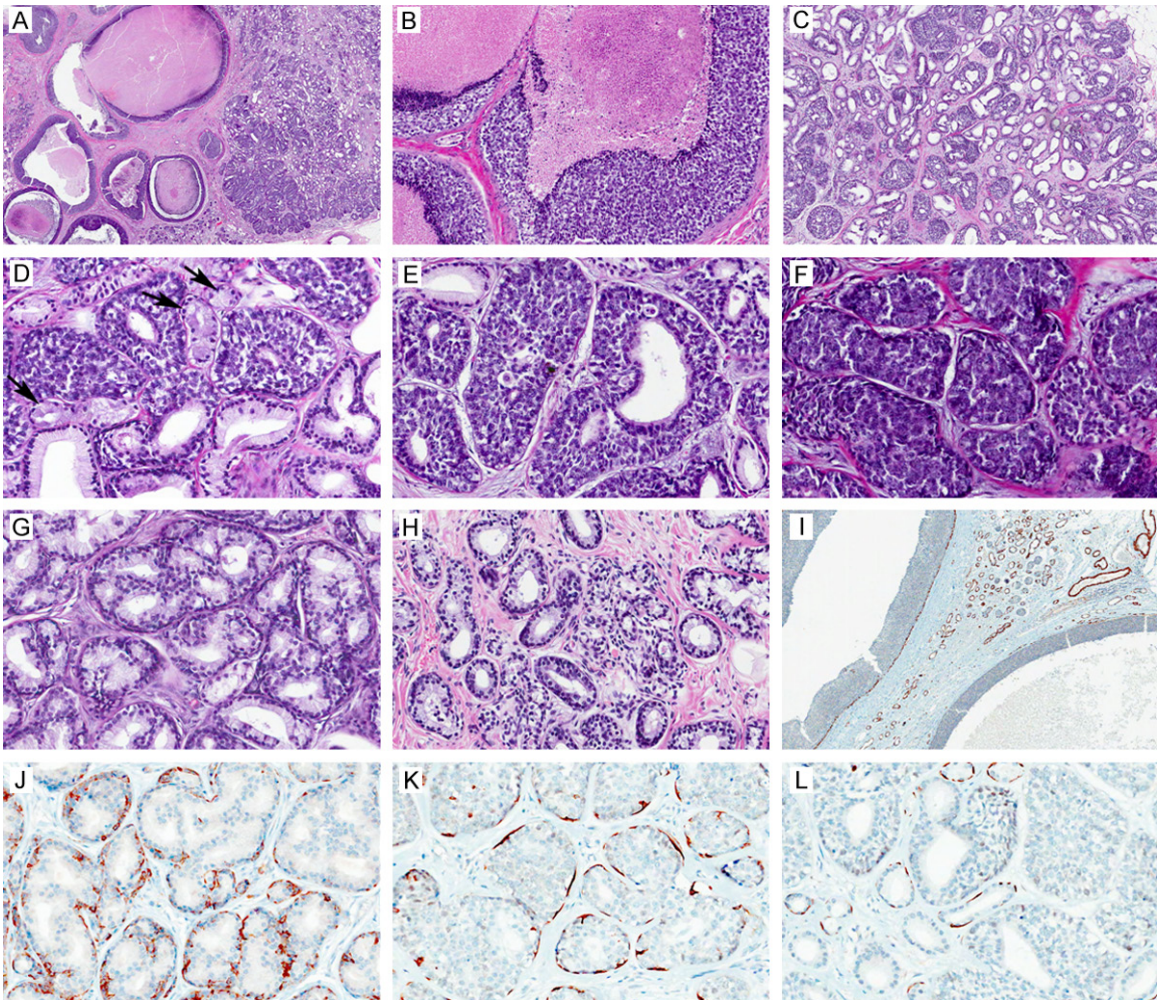


Figure 3. Representative histological findings and immunohistochemical results. A: In low-power field, ductal carcinoma in situ (DCIS) is surrounded by salivary gland metaplasia (×10, H&E). B: DCIS shows solid growth of basaloid tumor cells and comedo-type central necrosis (×100, H&E). C: Salivary gland metaplasia shows varying degrees of proliferation of luminal epithelial cells and basaloid cells within ducts (×40, H&E). D: Salivary gland-type acini (arrows) are admixed with nests with proliferation of basaloid cells (×200, H&E). E: Large nests of basaloid cells show residual luminal cells in their center (×200, H&E). F: Occlusive proliferation of basaloid cells results in solid nests without luminal cells (×200, H&E). G: Cribriform proliferation of luminal cells is observed in some ducts (×200, H&E). H: At the peripheral portion, a normal mammary lobule (arrows) is surrounded by salivary gland-type ducts (×200, H&E). I: In DCIS, some distended ducts (left side) are surrounded by a layer of myoepithelial cells, however, others (right side) are devoid of myoepithelial lining (×40, smooth muscle myosin heavy chain (SMM-HC)). J: Ducts with cribriform proliferation of luminal cells have a distinct myoepithelial lining (×200, SMM-HC). K and L: Some ducts or nests in salivary gland metaplasia are lined by myoepithelial cells, however, others do not have a myoepithelial lining (×200, calponin).

(**Figure 2**). On scanning view, the lesion was composed of DCIS surrounded by a diffusely proliferative, adenosis-like lesion (**Figure 3A**). DCIS showed comedo-type necrosis and solid growth of basaloid cells with dark, monotonous nuclei and scant cytoplasm (**Figure 3B**). The DCIS lesion measured 1.3 cm in the longest diameter on the slide. The surrounding breast showed a haphazardly (not lobulocentric) proliferative lesion composed of salivary gland-type acini and ducts not specific to the breast, ducts with cribriform proliferation of luminal epithelial cells, and ducts with varying degrees of proliferation of basaloid cells including solid nests of basaloid cells (**Figure 3C-G**). This unusual proliferative lesion coincided with salivary gland metaplasia of the breast reported by Flynn et al. [5]. Normal mammary lobules were entrapped by the metaplastic ducts at the periphery of the lesion (**Figure 3H**). The area

with salivary gland metaplasia measured 3.0 × 2.7 cm on the slide.

Histological and immunohistochemical findings showed that basaloid cells were distinct from myoepithelial cells. Tumor cells of DCIS were positive for p63, but negative for calponin and smooth muscle myosin heavy chain (SMMHC). Some of the distended ducts consistent with DCIS appeared to be devoid of myoepithelial lining; however, a clear cut invasive pattern was not evident (**Figure 3I**). Some glands or nests in salivary gland metaplasia were lined by myoepithelial cells; however, others did not show a distinct myoepithelial lining (**Figure 3J-L**). The dispersed glands were negative for S-100 protein. The tumor cells of DCIS were triple-negative for estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2), and diffusely positive for p53, epidermal growth factor receptor (EGFR), and Ki-67 (>50% of tumor cells positive). Postoperative course of the patient has been unremarkable without evidence of disease recurrence.

Discussion

Salivary gland metaplasia is a recently introduced terminology in the breast. We recently experienced a very interesting case with a broad spectrum of proliferation, including acini and ducts histologically unfamiliar to the breast, ducts with proliferation of basaloid cells or luminal cells, small solid nests of basloid cells due to obliteration of the lumina, and ductal carcinoma in situ composed of basaloid tumor cells. The proliferation simultaneously affected many ducts and gradual proliferation of basaloid cells from mild to solid was the most distinct finding of this case. We were not able to classify the background lesion using a conventional classification system of the breast; therefore, we consulted Dr. Fattaneh Tavassoli, a breast pathologist at Yale University School of Medicine, USA, about this uncommon histology of the breast. She named the lesion "salivary gland metaplasia" by referring to her previous case report [5]. She and her colleagues reported three cases of basal cell adenocarcinoma arising in salivary gland metaplasia of the breast. In their cases, solid nests of basaloid neoplastic cells were admixed with salivary gland-type acini as well as intercalated-, striated-, and excretory-type ducts. In the area showing salivary gland metaplasia, a transition from ducts with distinct basal cells to ducts with proliferation of the basal cells either in a pure form or variably admixed with residual luminal cells was a striking feature, as noted in our case. Similar to our case, luminal cells also showed variable degrees of proliferation.

Flynn et al. [5] suggested that genetic instability developed in the metaplastic salivary gland tissue appeared to incite proliferation of the luminal, basal or both cell populations in the ducts with ultimate predominance of basal cells. Judging from the histologic types of malignant tumors arising in these cases and our case (basal cell adenocarcinoma and basaloid DCIS), basaloid cells appear to be more vulnerable to neoplastic transformation in the salivary gland metaplasia. The only difference between their cases and our case is presence or absence of invasiveness in the neoplastic basal cells. In the cases reported by Flynn et al. [5], the nests of neoplastic basal cells showed irregularly coalesced nests with variable necrosis. They diagnosed the area as basal cell adenocarcinoma which had never been reported in the breast. By contrast, our case showed a well-defined area of DCIS surrounded by salivary gland metaplasia. The distended ducts in DCIS were composed of basaloid tumor cells with comedo-type central necrosis and lined by a myoepithelial layer. Flynn et al. [5] described the basal cells as being distinct from myoepithelial cells and used as implicated in salivary glands. In our case, immunohistochemical staining showed that in the salivary gland metaplasia, ducts have luminal, basal, and myoepithelial cells in varying proportions. The basaloid cells did not express myoepithelial markers such as calponin and SMMHC, however, in DCIS, the basaloid tumor cells were positive for p63 immunostaining. Absence of myoepithelial lining in some ducts of DCIS and salivary gland metaplasia may indicate attenuation of myoepithelial cells during metaplastic and proliferative processes. There was no invasive pattern of the nests or stromal reaction suggestive of invasion.

Microglandular adenosis with atypical proliferation should be included in the differential diagnosis of salivary gland metaplasia. Microglandular adenosis also shows dispersed proliferation of small glands permeating through

both fat and fibrous tissue, and in situ or invasive carcinoma may rarely develop in the background of microglandular adenosis [6]. However, in microglandular adenosis, the glands are lined by a single layer of monotonous cuboidal cells expressing S-100 protein. In our case, most of the dispersed glands without proliferation had two-cell layers consisting of luminal and myoepithelial cells, and the luminal cells did not express S-100 protein.

Also included in the differential diagnosis is a solid variant of adenoid cystic carcinoma of the breast. In contrast to solid proliferation of basaloid cells as a component of salivary gland metaplasia and DCIS in our case, adenoid cystic carcinoma, even in the solid variant, has typical glandular-cribriform architecture composed of two cell types with unequivocal myoepithelial cell component, and basaloid cells outline spaces containing basal membrane-like material.

Basaloid cells can be seen in other salivary gland-type tumor of the breast, such as low-grade mucoepidermoid carcinoma, as well as adenoid cystic carcinoma [1]. These tumors are typically triple-negative for ER, PR and HER2. The basaloid DCIS in our case also showed triple negativity for these markers.

Salivary gland metaplasia is a most unusual lesion and little is known about its mechanism of development. Evaluation of molecular changes in different types and stages of intraductal proliferation and comparison of the changes of salivary gland type ducts with those of mammary ducts would be helpful for understanding molecular mechanisms of salivary gland metaplasia and development of carcinoma in the background of salivary gland metaplasia.

Disclosure of conflict of interest

None.

Address correspondence to: Dr. Young Kyung Bae, Department of Pathology, Yeungnam University College of Medicine, 170 Hyeonchung-Ro, Nam-Gu, Daegu 705-703, South Korea. Tel: +82-53-640-6755; Fax: +82-53-622-8432; E-mail: ykbae@ynu.ac.kr

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