



# Eccrine ductal and acrosyringeal metaplasia in breast carcinomas: report of eight cases

Tibor Tot<sup>1</sup>

Received: 8 October 2018 / Revised: 7 November 2018 / Accepted: 14 November 2018 / Published online: 22 November 2018  
© Springer-Verlag GmbH Germany, part of Springer Nature 2018

## Abstract

Eccrine ductal and acrosyringeal metaplasia was described in 2006 as the presence of tumor structures that resemble the epithelium of the eccrine skin ducts and their opening within the epidermis, the acrosyringeum. Here, we report the clinical, morphological, and phenotypic characteristics of eight breast carcinomas that we collected over the past years showing this metaplasia. Unlike squamous metaplasia, acrosyringeal and eccrine ductal metaplasia are luminated structures comprising cells with eosinophilic cytoplasm that are easily detectable in routine histological slides. These lesions invariably appeared in triple-negative carcinomas, but the cases differed in their clinical, radiological, and histological manifestations. Correct interpretation of these changes may facilitate identification of some metaplastic carcinomas.

**Keywords** Breast cancer · Eccrine metaplasia · Acrosyringeal metaplasia · Metaplastic cancer

## Introduction

In embryological terms, the breast is a specialized skin appendix. Despite this fact, metaplastic changes resembling skin appendices other than apocrine metaplasia are surprisingly rare in both normal breast tissue and breast carcinomas.

Eccrine ductal and acrosyringeal metaplasia was described in 2006 [1] as the presence of epithelial structures that resemble the epithelium of the eccrine skin ducts and their opening within the epidermis, the acrosyringeum. These changes have not been further characterized in the literature, with the exception of a single publication questioning rather than confirming the existence of such lesions [2]. In addition, these lesions have been briefly mentioned in a book chapter [3] and in a publication in the Korean language [4].

After the initial publication in 2006, we decided to collect these exceptionally rare cases and we herein report the clinical, morphological, and phenotypic characteristics of eight breast carcinomas showing eccrine ductal and acrosyringeal metaplasia.

## Material and methods

We found five cases exhibiting eccrine ductal and acrosyringeal metaplasia in our database containing a consecutive series of 2244 breast carcinoma cases operated on in Dalarna County, Sweden, during the period 2008–2017. We added the two cases that were previously published [1], one of which is from the consultation files of the author, and an additional consultation case diagnosed before 2008. All of our own cases were documented in large-format histology slides, the technical details of which have been described elsewhere [5]. The consultation cases were worked up using conventional histology methods. We assessed the estrogen and progesterone receptor status as well as the HER2 status of the tumors, Ki67 proliferation index, and expression of cytokeratins 5/6 and 14, and EGFR with routine immunohistochemistry. The proportion of metaplastic structures was estimated on a whole slide image. Cases with metaplastic structures < 30% were classified as breast carcinoma not otherwise specified (NST) with metaplasia while the others as metaplastic carcinomas except the tumors fulfilling the World Health Organization criteria for a specific subtype of metaplastic carcinomas. Tumors were graded in accordance with the Elston-Ellis grading system. For assessing the subgross distribution of in situ and invasive tumor components, tumor size, and disease extent, we followed our previously published criteria [5]. The follow-up data were collected from the patient's files.

---

✉ Tibor Tot  
tibor.tot@ltdalarna.se

<sup>1</sup> Pathology & Cytology Dalarna, County hospital Falun, Falun, Sweden

Informed consent was obtained from all the patients operated on in our institution.

## Results

### Clinical characteristics

All the patients were females, with an age range of 42–70 years (mean 57.6 years). Three of the cases were interval cancers detected 6, 10, and 18 months after the screening event, respectively, while three were detected by mammography screening. One of the cases represented a local recurrence 12 months after initial surgery. Another case represented in situ carcinoma detected in the mastectomy specimen of a patient who was a BRCA1 gene carrier, and the lesion was seen preoperatively only on magnetic resonance imaging. Five of the cases were palpable lesions. The mammographic manifestation of the tumors varied as circular masses, architectural distortions, or microcalcifications. Most of the tumors were located in the upper lateral breast quadrants. Follow-up data could be obtained in 6 patients. One of the patients died of the disease while another patient had ipsilateral local recurrence. The details of the clinical presentation of the cases are summarized in Table 1.

### Morphological characteristics

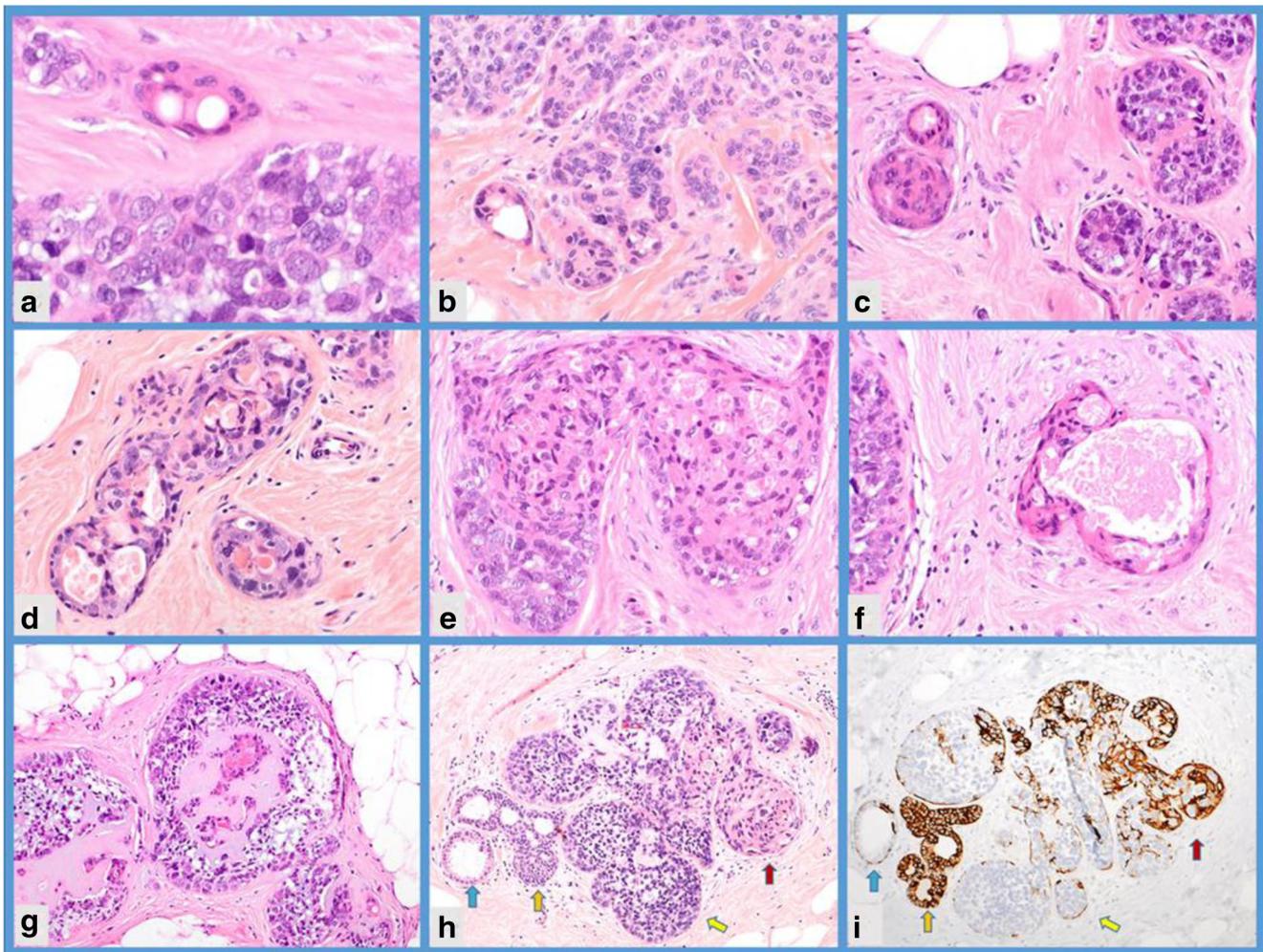
Eccrine ductal and acrosyringal metaplasia may be observed in both the in situ and/or invasive components of breast carcinomas. This metaplasia results in luminate structures built up of eosinophilic cells (Fig. 1). The structures may have a single lumen or multiple lumina (Fig. 1a–f). The lumen may be empty (Fig. 1a, b) or contain a cuticle-like substance (Fig. 1c–f). The structures may resemble glands (Fig. 1a, b), squamous pearls (Fig. 1c), or be irregular (Fig. 1d–h). The metaplastic structures may become deformed upon interaction with the tumor stroma (Fig. 1e, f), although they may be of bizarre shapes even without a conspicuous stromal reaction (Fig. 1d). In some areas, the presence of hyalinized, slightly basophilic stroma within and around the metaplastic epithelial structures resulted to some extent in an “adenoid cystic appearance” of these structures (Fig. 1g).

The percentage of the cut surface of the tumor showing acrosyringal and/or eccrine ductal metaplasia in histological slides varied between 1 and 80%. Most cases showed such area in > 30% of the tumor and were classified as metaplastic cancer. A single case with 3% metaplastic area was classified as breast cancer NST. One of the tumors fulfilled the WHO criteria for squamous cell carcinoma (acantholytic variant), another one for low-grade adenosquamous carcinoma. A single case showed in situ carcinoma only, while five invasive carcinomas were associated with an in situ component. The in situ component of the tumors was extensive (extent > 40 mm) in three cases, while the invasive component was multifocal in three. The tumors were

**Table 1** Clinical and radiological characteristics of the cases showing eccrine ductal and acrosyringal metaplasia

	Patient age	Detection mode	Localization	Clinical signs	Radiologic findings	Neoadjuvant therapy	Follow-up
Case 1	42	Interval cancer, 18 months	Right breast, upper lateral quadrant	Palpable	Circular mass	No	126 months, no events
Case 2	46	Interval cancer, 6 months	Right breast, upper lateral quadrant	Palpable	Architectural distortion	Yes	18 months, died of the disease
Case 3	49	Outside screening, preventive mastectomy in BRCA1 carrier	Right breast, lower lateral quadrant	None	Only seen on MRI	No	66 months, no events
Case 4	68	Mammography screening	Right breast, upper lateral quadrant	None	Microcalcifications (casting type)	No	34 months, no events
Case 5	70	Mammography screening	Right breast, upper lateral quadrant	None	Microcalcifications (casting type)	No	4 months, no events
Case 6	60	Mammography screening	Right breast, upper lateral quadrant	Palpable	Circular mass	No	x
Case 7*	62	Follow-up (local recurrence 12 years after primary surgery)	Right breast, upper lateral quadrant	Palpable	Microcalcifications	No	x
Case 8*	64	Interval cancer	Right breast, upper lateral quadrant	Palpable	Circular mass	No	Local recurrence 26 months, alive

\* Previously published cases in reference [1]



**Fig. 1** Invasive breast carcinomas showing eccrine ductal and acrosyringal metaplasia. Metaplastic structures with empty lumina (**a**, **b**); metaplastic structure with a single lumen containing a cuticle-like substance and metaplastic structure resembling a squamous pearl with a minimal lumen (**c**); deformed and bizarre gland-like structures with multiple lumina containing a cuticle-like substance; note the eosinophilic cytoplasm of the cells (**d–f**); metaplastic structures

resembling adenoid cystic cancer (**g**); the same terminal ductal–lobular unit stained with hematoxylin and eosin and with CK5/6 staining: a normal acinus showing partial CK5/6 positivity (blue arrow), hyperplastic epithelial structures showing strong CK5/6 positivity (orange arrow), cancer in situ with basaloid cells, negative reaction with CK5/6 staining (yellow arrow), and eccrine ductal/acrosyringal metaplastic structures showing positive CK5/6 staining (red arrow) (**h**, **i**)

invariably negative for the estrogen and progesterone receptors and HER2, and showed a positive reaction with at least one of the applied basal markers (Table 2). Figure 1h and i demonstrates a terminal unit with in situ carcinoma, showing eccrine ductal metaplasia in both hematoxylin–eosin–stained slides and the corresponding slide stained for cytokeratin 5/6.

## Discussion

The small series of breast carcinomas with eccrine ductal and acrosyringal metaplasia presented here constitutes 0.002% (5/2244) of the entire 10-year series at our institution, indicating that these changes are extremely rare. Even if we accept a considerable level of underdiagnosis of these metaplasias in

breast cancer, the incidence is expected to be far less than 1%. On the other hand, although the lesions may be focal and hardly detectable, they were already conspicuous in hematoxylin–eosin–stained slides in most of our cases. We believe that in everyday routine, these metaplasias are either ignored by pathologists or reported as squamous metaplasia, despite their typical histological appearance.

Unlike squamous metaplasia, acrosyringal and eccrine duct metaplasias are luminate structures. Similar to the normal skin eccrine ducts and acrosyringium, the metaplastic structures in our cases expressed high molecular weight cytokeratins, and invariably lacked expression of the estrogen, progesterone, and HER2 receptors. As we previously reported, these structures express maspin, but not low molecular weight cytokeratins which may help in diagnosing this type

**Table 2** Morphological and phenotypic characteristics of the cases showing eccrine ductal and acrosyringal metaplasia

	Invasive component	In situ component	Invasive tumor type	Percentage of metaplastic area	Phenotype	Basal markers	ki67	Lymph node metastasis
Case 1	Unifocal 18 mm, grade 3	Unifocal 18 mm, grade 3	NST	3%	Triple negative	CK14+, CK5/6+, EGFR+	50%	No (0/2)
Case 2	Multifocal, 23 mm grade 3	Diffuse, 102 × 45 mm, grade 3	Metaplastic	40%	Triple negative	CK14+, CK5/6+, EGFR+	90%	Yes (6/7)
Case 3	None	Unifocal, 8 × 7 mm, grade 2	None	30%	N.a.	N.a.	N.a.	No (0/0)
Case 4	Unifocal 7 mm, grade 3	Diffuse, 32 × 16 mm, grade 3	Metaplastic	70%	Triple negative	CK14+, CK5/6+, EGFR+	70%	No (0/1)
Case 5	Unifocal, 3 mm, grade 3	Diffuse, 40 × 20 mm, grade 3	Metaplastic	80%	Triple negative	CK14+, CK5/6+, EGFR+	30%	No (0/2)
Case 6	Unifocal, 16 mm, grade 2	None	Squamous cell carcinoma, acantholytic	1%	Triple negative	CK14+, CK5/6+, EGFR	14%	No (0/1)
Case 7*	Multifocal, 25 mm grade 1	None	Low-grade adenosquamous	Mostly peritumoral	Triple negative	CK14+, CK5/6+, EGFR	N.a.	No data
Case 8*	Unifocal, 13 mm, grade 3	Diffuse, 70 × 30 mm, grade 3	Metaplastic	70%	Triple negative	CK14+, CK5/6+, EGFR	N.a.	No data

NST no special type; N.a. not analyzed

\* Previously published cases in reference [1]

of metaplasia but is not obligatory as the morphology of the lesions is diagnostic itself [1].

In his publication in 2014, Wilsher indicated that eccrine ductal metaplasia is part of the histological picture of low-grade adenosquamous carcinoma and is not an independent phenomenon. Our series included only one case of low-grade adenosquamous carcinoma, while all the other tumors showing eccrine ductal and acrosyringal metaplasia were neither low-grade nor adenosquamous. Although Wilsher's suggestion may be correct in relation to low-grade adenosquamous carcinoma, the metaplasia discussed here is not restricted to this tumor type and obviously represents an independent phenomenon. As we show here, tumors demonstrating eccrine ductal and acrosyringal metaplasia vary widely in their clinical, radiological, and morphological manifestations.

## Conclusions

We report a series of breast carcinomas showing eccrine ductal and acrosyringal metaplasia. These rare lesions are easily recognized histologically based on their luminated character and the eosinophilic cytoplasm in the cells. These lesions invariably appeared in triple-negative carcinomas, but the cases varied in their clinical, radiological, and histological manifestations. Correct interpretation of these changes may facilitate identification of some metaplastic carcinomas.

## Compliance with ethical standards

This manuscript has not been published or submitted to another journal. Informed consent was obtained from all the patients operated on in our institution.

**Conflict of interest** The author declares that he has no conflict of interest.

## References

- Tot T (2006) Eccrine ductal and acrosyringal differentiation of the breast epithelium—a lesion associated with some metaplastic breast carcinomas. *Virchows Arch* 449:565–571. <https://doi.org/10.1007/s00428-006-0281-7>
- Wilsher MJ (2014) Adenosquamous proliferation of the breast and low grade adenosquamous carcinoma: a common precursor of an uncommon cancer? *Pathology (Australia)* 46:402–410. <https://doi.org/10.1097/PAT.0000000000000115>
- Tot T (2008) Metaplastic breast carcinoma: detection using histology and immunohistochemistry. In: Hayat MA (ed) *Methods of cancer diagnosis, therapy and prognosis*, vol 1. Springer, Dordrecht, pp 275–290. [https://doi.org/10.1007/978-1-4020-8369-3\\_21](https://doi.org/10.1007/978-1-4020-8369-3_21)

4. Lee SA, Lee KE, Moon BI, Han WS, Sung SH (2009) Metaplastic squamous carcinoma of the breast: clinicopathologic analysis of 17 cases. *Korean J Pathol* 43:20–25. <https://doi.org/10.4132/KoreanJPathol.2009.43.1.20>
5. Tot T (2012) The role of large-format histopathology in assessing subgross morphological prognostic parameters: a single institution report of 1000 consecutive breast cancer cases. *Int J Breast Cancer* 2012:395415. <https://doi.org/10.1155/2012/395415>