### ABSTRACT

**Objective:** The association of tubular carcinoma, columnar cell lesions and lobular carcinoma in situ, also known as the "Rosen Triad", may be encountered in breast biopsies performed for evaluation of mammographically detected microcalcifications.

**Case Report:** A case in which tubular carcinoma and columnar cell hyperplasia were associated with a histologically unusual form of signet ring lobular carcinoma in situ is presented. Signet ring non-invasive lobular carcinoma is classified as high-grade lobular carcinoma in situ, but herein is associated with changes that belong to the molecular pathway of low-grade mammary neoplasia.

**Conclusion:** We reported the case of lobular carcinoma in situ associated with columnar cell hyperplasia and tubular carcinoma, in which the lobular carcinoma in situ was presented in a histologically unexpected form comprised predominantly of signet ring cells.

**Key Words:** Breast, Carcinoma, Signet ring cell, Carcinoma in situ

### INTRODUCTION

The widespread use of mammographic screening has called attention to columnar cell lesions, a histological finding commonly encountered in breast biopsies performed for evaluation of detected microcalcifications. Columnar cell lesions are histologically characterized by dilated terminal duct lobular units lined by epithelium showing columnar cell morphology, ranging from one or two layers of benign epithelium to stratified epithelium with or without atypia (1,2). In the past, many investigators recognized these morphological changes under a variety of terms. Nowadays a practical classification system, which divides columnar cell lesions in three broad categories as columnar cell change (CCC), columnar cell hyperplasia (CCH), and columnar cell change/hyperplasia with cytological atypia has been adopted. The World Health Organization has proposed the term flat epithelial atypia (FEA) for columnar cell change/hyperplasia with atypia, with alternative designation of ductal intraepithelial neoplasia grade 1A (DIN 1A) (1,3).

Rosen first observed frequent histological coexistence of tubular carcinoma (TC) and CCH, with occasional association of lobular carcinoma in situ (LCIS) (4). The histological triad of TC, columnar cell lesions and LCIS is also known as the "Rosen Triad". Here we portray a case of "Rosen Triad" in which TC is associated with CCH and signet ring LCIS.

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CASE REPORT

A 75-year-old woman presented with suspicious microcalcifications in the right breast discovered by mammography, with no palpable abnormalities on physical examination. Ultrasound examination depicted a heterogeneous, hypoechogenic zone of 1 cm in diameter, with dorsal attenuations and ill-defined borders suggestive of carcinoma. Fine needle aspiration cytology showed only epithelial proliferation without atypia. Surgical excision of the lesion was recommended.

Surgical intraoperative biopsy of the detected abnormality was performed. On gross examination the tumor was an ill-defined, grey-white mass measuring 1 x 0.6 cm, with firm consistency. Frozen section analysis rendered a diagnosis of invasive TC. Modified radical mastectomy with an axillary lymph node dissection followed.

Tissue was fixed in neutral buffered formalin and embedded in paraffin for routine histological examination. Slides were stained with hematoxylin and eosin with additional ER, PgR, CD10, p63, E-cadherin, and HER2/neu immunohistochemical analysis.

On histological examination, the tumor was composed of oval, focally angulated glands and few cords haphazardly distributed in fibrous stroma with an occasional microcalcification (Figure 1, 2). A single layer of epithelial cells, with grade 1 nuclei and no mitoses, lined the tumor glands without visible myoepithelial layer on CD10 and p63 immunostains. This description was consistent with diagnosis of TC. In the carcinomatous tissue several dilated acini, lined with two to three layers of columnar cells without atypia, oriented perpendicularly to the basement membrane were seen, representing CCH (Figure 1, 2). Adjacent to TC and foci of CCH a few dilated acini, colonized by small discohesive cells whose cytoplasms were eosinophilic or vacuolated, many with peripherally displaced nuclei, were seen (Figure 1, 3). Cells were immunohistochemically E-cadherin negative, which is consistent with the diagnosis of signet ring type LCIS.

Tubular carcinoma, CCH and LCIS cells were ER and PgR positive and HER2/neu negative. Neither residual breast tissue nor dissected axillary lymph nodes showed additional histological abnormalities.

DISCUSSION

The introduction of screening mammography in the early 1980s has dramatically influenced many aspects of breast surgical pathology. Compared to the pre-screening period, breast biopsies of screened abnormalities contain a greater...

At first glance our signet ring LCIS finding associated with premalignant and low grade malignant changes may look controversial. Lobular carcinoma in situ, composed predominantly of signet ring cells, is classified as high-grade LCIS (LIN 3) because of its higher frequency of associated invasive carcinoma at presentation, particularly lobular invasive carcinoma (10). However, we feel that designation of high-grade LCIS (LIN 3) in aforementioned context is predominantly based on the frequent association with invasive breast carcinoma, and not on the cell morphology itself. Tumor cells in presented case of LCIS resemble classic LCIS cells, but with prominent intracytoplasmic vacuoles and consecutive signet ring appearance. Pleomorphic LCIS (high grade LCIS, LIN 3), which may also be composed of signet ring cells, differs from classic LCIS. Pleomorphic LCIS shows significant nuclear atypia, cellular pleomorphism, presence of macro nucleoli, and occasional central necrosis (11,12). None of these features were presented in our case of signet ring LCIS.

In conclusion, we reported the case of TC associated with CCH and LCIS, in which the later presented in a histologically unexpected form comprised predominantly of signet ring cells.

REFERENCES


