Mucocele-Like Tumor of the Breast: A Pathological Continuum of Mucinous Breast Lesions. Report of a Case

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Abstract

Mucocele like Tumor (MLT) of the breast is a rare neoplasm, initially considered as a benign lesion by Rosen, who first described it in 1986. However, subsequent studies showed as MLTs were related to Atypical Ductal Hyperplasia (ADH), Ductal Carcinoma In Situ (DCIS) and mucinous carcinoma, so these lesions are now believed to be framed within a pathologic continuum from benign to malignant.

Here we report a case of a woman with a palpable mass in the right breast, which was initially seen as a fibroadenoma at the ecography. Histological examination revealed the presence of a MLT containing areas of ADH, DCIS and a focus of mucinous carcinoma, noted at the periphery of the lesion. Immunohistochemical studies supported the morphological evidence of malignancy in the context of MLT. Our case confirms the concept of a spectrum of mucinous breast lesions and affirms the importance of an accurate histological examination of Mucocele-like Lesions (MLLs), due to the risk of malignancy.

Keywords: Breast; Mucocele-like Tumor; Mucin; Pathological continuum; Invasive mucinous carcinoma

Introduction

A Mucocele-like Tumor (MLT) of the breast is an unusual lesion, first described in 1986 by Rosen as a benign lesion, similar to mucocele of the salivary gland [1]. Since the early 1990s, there have been several studies on mucocele-like tumors associated with Atypical Ductal Hyperplasia (ADH) or carcinoma (in situ and invasive), and a pathologic spectrum of mucinous breast lesions has been suggested [2-6]; Ro et al. first described MLTs that contained areas of ADH, intraductal carcinoma and focal invasive mucinous carcinoma [4].

A mucocele-like tumor consists of mucin-containing cysts, which tend to rupture and dump the secretion into the adjacent stroma; pathogenesis seems to be linked to an overproduction of mucous and the obstruction of ducts. The association between Mucocele-like Lesions (MLL) and invasive carcinomas has prompted some to consider them as a precursor to breast cancer, so MLLs recognized on needle core biopsies are considered “high-risk” lesions and excisional biopsy is recommended in order to rule out malignancy [7]. Here we present a case of mucocele-like tumor of the breast with atypical ductal hyperplasia, Ductal Carcinoma in Situ (DCIS) and focal areas of invasive mucinous carcinoma in a 34-year-old Italian woman.
Material and Methods

A 34-year-old female patient was admitted to the Endocrine Surgery Unit “Policlinico G. Rodolico” hospital of Catania, with the complaint of a palpable round and elastic mass without pain in the right breast. No family history for breast cancer was reported. There was no history of previous breast surgery or use of exogenous hormones. No nipple discharge was present at the clinical exam. The mass was not attached to the overlying skin. Considering these findings, breast ultrasound was made and the patient underwent to surgical removal of the breast lesion.

The surgical specimen was submitted for histological examination in neutral-buffered 10% formalin, dehydrated using standard techniques, embedded in paraffin, cut to 5 μm, and stained with hematoxylin and eosin (H&E). Immunohistochemical studies were performed with the labeled streptavidin-biotin peroxidase detection system using the Ventana automated immunostainer (Ventana Medical Systems, Tucson, AZ). Following antibodies were tested: anti-Estrogen receptor antibody (1D5; Dako Corporation, Glostrup, Denmark), diluted 1:50 in PBS (Sigma, Milan, Italy), anti-Progesterone receptor antibody (PGR636; Dako Corporation, Glostrup, Denmark), diluted 1:100 in PBS (Sigma, Milan, Italy), anti-c-erbB-2 polyclonal rabbit antibody (Dako Corporation, Glostrup, Denmark), diluted 1:500 in PBS (Sigma, Milan, Italy), anti-p63 antibody (DAK-p63; Dako Corporation, Glostrup, Denmark), diluted 1:75 in PBS (Sigma, Milan, Italy), anti-c-erbB-2 polyclonal rabbit antibody (Dako Corporation, Glostrup, Denmark), diluted 1:500 in PBS (Sigma, Milan, Italy), anti-Estrogen receptor antibody (anti-PgR), showed a low expression (score 0) of c-erbB-2 (luminal A immunophenotype). Based on both morphological and immunohistochemical features, the diagnosis of “Mucocoe-like tumor with areas of atypical ductal hyperplasia, micropapillary intraductal carcinoma and a minor component of invasive mucinous carcinoma” was rendered.

Discussion

MLT was first reported by Rosen [1] to describe mucin-filled dilated cysts lined by flattened or low columnar epithelium with focal areas of hyperplasia, sometimes producing a papillary pattern. There was no association with malignancies in the cases reported by Rosen. Later, Ro et al. [4] reported seven cases of mucocoe-like tumor associated with atypical ductal hyperplasia or foci of mucinous carcinoma, so they suggested that some MLTs may be the early form of mucinous carcinoma of the breast.

Weaver et al. [2] suggested that MLT and mucinous carcinoma may represent the two ends of pathological continuum of mucinous lesions of the breast. Also Yeoh et al. [8] in 1999 confirmed the possibility of a spectrum of pathologic lesions including benign tumor, atypical hyperplasia, ductal carcinoma in situ and mucinous carcinoma. It is difficult to detect the malignancy of a MLT if it is localized in very small areas within the tumor, so detailed pathological examination of excised material is recommended for a correct diagnosis. Liebman et al. [9] reported that intraductal carcinoma was found by excisional biopsy in 25% of patients with benign MLT and in 75% with an atypical MLT diagnosed by core-needle biopsy. On the other hand, Rakha et al. [10] reviewed the course of pure mucocoe-like lesions (without atypia) diagnosed with core biopsy in literature and claimed that DCIS was present in two of the 54 patients (4%) in the excision tissue; they also stated that in case of atypia in core biopsy in the previous studies [11,12], the frequency of malignancies were higher (21%).

Very interesting results were obtained by a recent review of 102 cases of MLTs [13]: despite an association with atypical hyperplasia, in women older than 45 years, MLTs did not convey an additional risk of breast cancer beyond that associated with the presence of proliferative disease; additionally, in younger patients (younger than 45 years) with these lesions, there was a non significant increase in risk of breast cancer compared with the general population. Clinical features of benign and malignant MLTs were compared by Hamele-Bena et al. [14] and no appreciable differences in age, tumor size or laterality were detected, even if malignant MLT had coarse calcification more often than benign one.
Figure 1: a) Ecographic evidence of a homogeneous, rounded mass with well bounded margins in the right breast; b) no lesions were detected in the left breast of the same patient.

Figure 2: Low magnification showing a well circumscribed area, consisting of mucin-containing cistically dilated ducts and acini, in the context of a mastopathy (H&E staining; original magnification 25x).
Figure 3: Mucin results diffusely positive to the histochemical coloration with Alcian blue at pH 2.7. At low magnification it’s already possible to note the presence of extravasated mucin (arrows) in the stroma (H&E staining; original magnification 50x).

Figure 4a,b: In the context of mucin-filled cysts lined by low columnar and papillary epithelium, areas of ADH and micropapillary DCIS are also detected (H&E staining; original magnification 100x (a,b)).
Figure 5: low (a) and higher (b,c) magnification of the periphery of the tumor, showing the presence of ducts of small size, lined by atypical epithelium, which tend to rupture and discharge the mucinous secretion into the adjacent stroma. These findings are highly suggestive of invasive cancer. (H&E staining; original magnification 100x (a); 200x (b,c)).

Figure 6: high magnifications showing the total absence of myoepithelial cells in the highly suspicious for malignancy areas; immunohistochemical stainings for myoepithelial markers p63 and calponin are totally negative (a,c,d); note p63 nuclear staining (b) and calponin cell membrane one (e) in a benign mammary adenosis area at high magnification (Immunoperoxidase staining; original magnification 200x (a-e)).
MLTs have non-specific mammographic findings and the sonographic findings are similar to those of low internal echolar and multiple, well-margined, hypoechoic structures and complex cysts [9,15]; MLTs associated with ADH or malignancy are more frequently seen as clustered cyst or cyst with thick septations [16]. Clear distinction between atypical ductal hyperplasia, ductal carcinoma in situ and invasive carcinoma involving a mucocele-like tumor can sometimes be challenging; ADH and low grade DCIS are quite similar lesions and the separation of these lesions is pretty subjective. In a background of MLT, the diagnosis of ADH and DCIS is based on conventional cytoarchitectural criteria; for ADH, guidelines describe partial involvement of ductal spaces by an uniform population of evenly spaced cells resembling low grade non comedo DCIS, sometimes merging with usual epithelial hyperplasia. Lesions with these features, but measuring less than 2 mm or involving a single duct space, are categorized as ADH. In a MLT with dilated duct spaces, when the assessment of the true extent of involvement becomes difficult, a diagnosis of DCIS should be rendered only when there are two or more duct spaces/lobules disclosing completely fulfilled cytoarchitectural patterns of DCIS [17].

Rupture of mucin-filled cystically dilated ducts is very common in MLT, so it is not infrequent that small flap of epithelium become displaced into extracellular mucin pools, which may mimic an invasive mucinous carcinoma; this is very challenging when there is already DCIS associated with MLT, so the concern for focal invasion is a real problem. If a MLT is devoid of any atypical or in situ malignant changes, or, also, if there are simply focal ADH alterations, it is unlikely that small epithelial flaps floating within mucin would represent anything malignant. In a background of MLT with established DCIS, however, a conclusion of dislodged epithelium, is likely when floating epithelial nests are few and focal, or when there is the evidence of associated identifiable myoepithelial cells, or also when epithelial limbs are seen in contiguity with the duct wall. Immunohistochemistry may be useful to evaluate the myoepithelial cell component in these areas and the absence of myoepithelial markers is a great support to the diagnosis of malignancy [18].

Differential diagnosis of MLT includes cystic hypersecretory hyperplasia and cystic hypersecretory duct carcinoma of the breast; these lesions show cystically dilated ducts as well as MLLs, but are characterized by a luminal pink, proteinaceous, thyroid colloid like material and are not associated with extravasated mucin material into the stroma, which is a typical feature of mucinous lesions [17,19]. As regards treatment, surgical resection is the gold-standard for MLLs and breast-conserving surgery is recommended, even for MLTs with malignancies. Axillary lymph node dissection may be avoided as lymph node metatasis is rare; however, for patients with malignant lesions, sentinel lymph node biopsy, using the indocyanine green fluorescent imaging system [20], could be appropriate [21,22].

Conclusions

Data from published literature demonstrate MLT is an uncommon and still not clearly defined pathologic entity and making a correct diagnosis can be often challenging. Since ADH, DCIS and invasive cancer features may coexist in it and, as previous mentioned, presence of extravased mucin pools is a relatively common finding and does not represent a histologic “gold standard” of malignancy, an accurate and detailed pathological examination is highly recommended. Immunohistochemical evaluation of myoepithelial markers often turns out to be the most reliable indicator of invasive cancer. Our case emphasizes the concept that mucocele-like tumors of the breast have to be considered as a pathological continuum from benign, to atypical, to malignant and proves that small malignant foci may hide in largely benign lesion.

References


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