



Hypersecretory Hyperplasia of the Breast in a Non-pregnant Woman Showing a Histomorphologic Spectrum of Benign, Atypical, and Malignant Changes: Report of a Case and Brief Review of the Literature

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Abstract

Benign cystic hypersecretory hyperplasia and cystic hypersecretory duct carcinoma of the breast share similar histologic features including formation of cystically dilated ducts containing a homogeneous eosinophilic secretion that resembles thyroid colloid. However, cystic hypersecretory duct carcinoma of the breast is associated with proliferative malignant epithelium. Cystic hypersecretory lesions of the breast present with a varying morphologic features in the same mass. Strict histomorphologic criteria and confirmatory immunohistochemistry studies are essential for definitive diagnosis and appropriate management. We present a case where secretory proliferation of a breast mass displayed spectrum of changes from benign hyperplasia, to atypical hyperplasia, to frank ductal carcinoma in situ. Due to limited reported cases of these entities, little is known about the biological behavior, prognosis and molecular study of these lesions. By reporting more cases, we may reveal the biologic behavior of these uncommon lesions.

Keywords: Hypersecretory; Hyperplasia; Atypical; Malignant; Cystic

Abbreviations

HH: Benign Hypersecretory Hyperplasia; HHA: Combination of Benign and atypical Epithelium; HHM: Combination of Atypical and Frankly Malignant Epithelium; DCIS: Ductal Carcinoma in Situ; CHC: Cystic Hypersecretory Carcinoma; PLH: Pregnancy-like (Pseudolactational) Hyperplasia; IHC: Immunohistochemistry

Introduction

Cystic Hypersecretory Hyperplasia with atypia and cystic hypersecretory carcinoma was first reported in 1984 by Rosen and Scott [1]. Cystic hypersecretory lesions of the breast present with a varying morphologic features ranging from benign hypersecretory hyperplasia, hypersecretory hyperplasia

with atypia, cystic hypersecretory carcinoma to invasive hypersecretory carcinoma [2]. Our case displays the spectrum of hypersecretory hyperplastic lesions of the breast as benign hypersecretory hyperplasia (HH), hypersecretory hyperplasia with a combination of benign and atypical epithelium (HHA) and hypersecretory hyperplasia with a combination of atypical and frankly malignant epithelium (HHM).

HH is defined morphologically by cystically dilated ducts of various sizes with colloid-like material and the ducts are lined by flat, bland columnar, orderly epithelial cells [3]. HH is of rare epidemiology and unknown etiology and is not included in the WHO classification of breast lesions [3]. HH grossly resembles juvenile papillomatosis - large, ill-defined, and firm to rubbery, spongy mass of fibrous tissue containing multiple small cysts.

Ductal Carcinoma In Situ (DCIS) in the background of HH can give rise to a rare, distinct variant of cystic hypersecretory carcinoma (CHC), characterized by micropapillary growth, intermediate-grade to high-grade nucleoli and luminal colloid-like secretion [4]. This is very rare as there are less than a hundred reported cases with a mean age of 55 years at presentation [5]. CHC microscopically looks similar to HH with dilated ducts and cysts containing eosinophilic secretions resembling thyroid colloid, the lining epithelium usually grows as micropapillary DCIS and the secretions may retract the epithelium, causing smooth or scalloped margins [5].

Abnormal lesions detected by breast imaging can be assessed by a core needle sampling or excision biopsy. Breast needle core biopsy performed under stereotactic guidance is the preferred method for evaluation of mammographically or MRI-detected

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microcalcifications if also visible on mammogram [6]. Careful clinical follow-up is recommended for lesions that display atypical features in HH, HHA or HHM. If these lesions are found in a breast needle core biopsy specimen, an excisional biopsy is recommended.

Case Presentation

We report the case of a 42-year-old, non-pregnant woman, who underwent excisional biopsy of 3 irregularly thickened areas in 3 different quadrants of the left breast, some with microcalcifications identified during routine mammogram. Incisional biopsy was performed with histologic examination of one of the three masses showing cystically dilated ducts of various sizes with thyroid colloid-like material. The ducts were lined by flat, orderly, bland columnar epithelial cells. Although, most of the tissue displayed features of HH with focal microcalcifications (Figure 1 A,B), scattered areas showed transition to HHA (Figure 1 C), and other areas even showed transition to frank HHM (Figure 1 D). The carcinoma was identified to be ductal carcinoma in situ stage 2 without necrosis. The other two masses were sampled via core biopsy and showed similar histomorphologic features to the first mass. The patient was consulted of options and decided to perform complete left mastectomy to clear all possible carcinoma of the breast. Post-operative radiation was used and a breast implant was placed. The patient followed up with tamoxifen for four years. There was no evidence of progression or appearance of any new masses. The patient was eventually lost to follow up after 4 years.

Discussion

Cystic hypersecretory hyperplasia lesions have historically been classified into benign HH, HH with atypia, HH carcinoma in situ and invasive carcinoma. Our case supports prior reports suggesting that HH breast lesions encompass a spectrum of pathologic lesions, including HH, HHA and HHM, which can all be present within the same breast lesion. Clinical presentation can vary widely from a palpable mass to an asymptomatic, accidental mammographic finding, as was initially seen in our case [7-9]. We did not identify invasive components, which are rarely reported. HH by itself appears to have a benign outcome without atypia, however it is imperative to exclude concurrent carcinoma through histologic sampling and immunohistochemistry studies [7].

The morphologic spectrum of secretory breast lesions: HH, HHA and HHM are characterized by dilated ducts and cysts containing luminal pink, proteinaceous, colloid-like secretions with varying degrees of cytologic atypia which can range from low-grade to high-grade with frequent papillary formations [8]. CHC is a rare variant of ductal carcinoma, HH and CHC share similar features consisting of the presence of cysts, micropapillae and often are ER+ and HER-, however CHC presents with nuclear atypia and HH does not. [8]

Tawny Hung et al., reported a case with similar histomorphology, but called it "Hypersecretory Thyroid-like Adenosis of the Breast". In their report, they described that this lesion lacks myoepithelial cells and can be misdiagnosed as

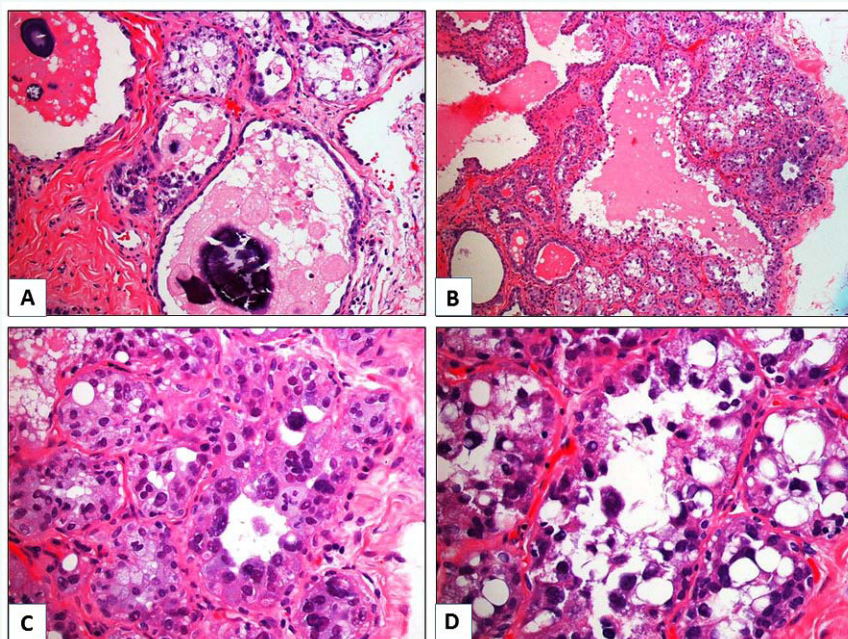


Figure 1 Microscopic examination of left breast masses

- A) Features of benign hypersecretory hyperplasia (HH) with intracystic colloid-like material and focal microcalcification. H&E stain X40 High power
- B) Features of HH with intracystic colloid-like material. H&E stain X20 Low power
- C) Scattered areas showed transition to combination of benign and atypical epithelium (HHA). H&E stain X20 Low power
- D) Other areas showed transition to combination of atypical and frankly malignant epithelium (HHM) in form of in situ carcinoma. H&E stain X100.



invasive ductal carcinoma. They also highlighted the similarity of their described lesion with microglandular adenosis of the breast as both lack the presence of myoepithelial cells and can be potential for diagnostic error as carcinoma. We believe that the case they described is an example of the spectrum of histomorphologic features of breast hypersecretory hyperplasia as we demonstrated in our case [10,11].

Sandra Shin et al., described a lesion they called "Pregnancy-like (pseudolactational) hyperplasia (PLH) of the breast". In their 12 cases they studied, they reported that Cystic hypersecretory hyperplasia (HH) was present in five specimens, and in four of the five specimens, HH merged with PLH (PLH/HH). They suggested that calcifications associated with PLH have a distinctive histologic appearance, and their recognition can aid in the diagnosis of PLH. They concluded that additional cases of combined PLH/HH must be studied to ascertain the clinical significance, if any, of this previously undescribed entity. The precancerous significance of PLH/HH and of PLH with atypia has not been fully determined. In most instances, surgical excision would be prudent if PLH/HH or PLH with atypia is present in a needle core biopsy specimen [12].

Differentiating these lesions is important for appropriate patient management, although HH is usually a benign lesion, HHM and HHA can be present in the same lesion or in other lesions in the breast, therefore thorough sampling is imperative and always indicated to exclude the more potentially serious lesions. One follow-up study showed that two out of eight patients with HH developed subsequent carcinoma, and one of two cancer patients developed fatally invasive ductal carcinoma [10].

Rosen and Scott defined cystic hypersecretory carcinoma (CHC) as a subtype of intraductal carcinoma of the breast and described this entity in a series of 10 cases [1]. Since then, only few case reports described this entity. Among the reported cases of malignant cystic hypersecretory breast lesions, most cases are of in situ CHC (intraductal), with only a few cases of invasive CHC. Invasion is suggested by solid nests structures and is usually poorly differentiated with no secretory characteristic [13]. Our reported case was an in situ carcinoma in the form of an intraductal hypersecretory carcinoma with no evidence of invasion.

Excision biopsy is curative for HH lesions, whereas CHC, invasive or in situ, requires treatment similar to that of other forms of ductal carcinoma [9]. As HH, HHA and HHM can be present in the same mass; studies have suggested that there may be an evolution from a benign hyperplasia to a malignant carcinoma, although convincing evidence is still lacking [9]. This further implores clinicians to perform an excisional biopsy and thoroughly examine the resected mass in order to distinguish HH from CHC [9].

It is our hope that this report raises awareness of pathologists and clinicians of the diagnosis and management of hypersecretory hyperplasia of the breast, and continued investigation drives further development of efficacious diagnosis and safe treatments for improving patient outcomes.

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References

1. Rosen PP, Scott M. Cystic hypersecretory duct carcinoma of the breast. *Am J Surg Pathol.* 1984; 8: 31-41.
2. Jie Sun, Xing Wang, Cuifang Wang. Invasive cystic hypersecretory carcinoma of the breast: a rare variant of breast cancer: a case report and review of the literature. *BMC Cancer.* 2019; 19: 31.
3. Warzecha H. Cystic hypersecretory hyperplasia of breast. 2019.
4. D'Alfonso TM, Ginter PS, Liu YF, Shin SJ. Cystic hypersecretory (in situ) carcinoma of the breast: a clinicopathologic and immunohistochemical characterization of 10 cases with clinical follow-up. *Am J Surg Pathol.* 2014; 38: 45-53.
5. Dina Kandil. Cystic hypersecretory DCIS. 2019.
6. Burbank F. Stereotactic breast biopsy of atypical ductal hyperplasia and ductal carcinoma in situ lesions: improved accuracy with directional, vacuum-assisted biopsy. *Radiology.* 1997; 202: 843-847.
7. Singh K, Falkenberry S, Eklund B, Quddus MR. Cystic Hypersecretory Hyperplasia of Breast. *Int J Surg Pathol.* 2018; 26: 432-433.
8. Toll A, Joneja U, Palazzo J. Pathologic Spectrum of Secretory and Mucinous Breast Lesions. *Arch Pathol Lab Med.* 2016; 140: 644-650.
9. Zhao XF, Deeb G, Tan DF. Pathologic Quiz Case: A Cystic Breast Mass. *Arch Pathol Lab Med.* 2003; 127: 389-390.
10. Moriya T, Ito J, Takasuga H, Okazaki K. Cystic Hypersecretory Duct Carcinoma of the Breast: A Case Report Describing the Cytologic Features Breast Cancer. 1996; 3: 131-134.
11. Tawny Hung William R. Hypersecretory Thyroid-like Adenosis of the Breast: A Distinct Benign Entity. Devoid of Myoepithelial Cells. *J Clin Exp Pathol* 2015; 5: 2.
12. Shin SJ, Rosen PP. Pregnancy-like (pseudolactational) hyperplasia: a primary diagnosis in mammographically detected lesions of the breast and its relationship to cystic hypersecretory hyperplasia. *Am J Surg Pathol.* 2000; 24: 1670-1674.
13. Jie Sun, Xing Wang, Cuifang Wang. Invasive cystic hypersecretory carcinoma of the breast: a rare variant of breast cancer: a case report and review of the literature. *BMC Cancer.* 2019; 19: 31.