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Cystic Hypersecretoric Carcinoma of Breast: A Case Report

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Abstract: ***Introduction: Cystic hypersecretory carcinoma is a very rare subtype variant of breast cancer, it is one of special variants of ductal carcinoma. Having different pathologies, cystic hypersecretory carcinoma may be in form of a benign or malignant lesion. The average incidence for this breast cancer is 56 years old and all in females by age and gender respectively. At December 2018, this case is reported only 19 cases so far. Therefore, the rare occurrence of this type of malignancy makes it valuable for case reports. Case description: A sliced specimen of 4, 5x3x2 cm of excision biopsy tissue is sent to our anatomical pathology department to be analyzed. Results: Specimen shows multiple cystic lesions with diameters of 0, 5 – 1 cm. Some part contains colloid - gelatinous substance, and other part contain blood clots. Cystic spaces lined with atypical epithelial cells with dominant micropapillary pattern and complex papillary branching frond as others. Constituent epithelial cell is composed as column with crowding and overlapping, pleomorphic - hyperchromatic to vesicular oval nuclei with prominent nucleoli. Part of nuclei is visible hobnail like appearance. Particular microscopic focuses of invaded areas on conventional HE staining shows desmoplastic response and lymphocyte inflammation infiltrates with moderate to high density with hemosiderin pigment surroundings. These area shows solid islands with centers resembling cystic area. Part of nuclei cells at this area shows angulated grooves and ground - glass appearance. Mitotic is founded 13 - 16/ 10 Hpf. limfovaskuler invasion (LVI) is negative. Conclusion: Pathological specimen shows invasive cystic hypersecretory carcinoma marked by cystic secretory activity of thyroid colloid - like substance, also micropapillary and pseudostratified - arranged cyst with focus of invasion.***

Keywords: Cystic hypersecretory carcinoma, hypersecretory cystic lesion, invasive breast carcinoma

1. Introduction

Cystic hypersecretory carcinoma is a very rare subtype variant of breast cancer. Therefore, reports, publications ad discussions are essential. This type of carcinoma is a part of cystic hypersecretory lesion group. The benign pattern of this lesion is called cystic hypersecretory hyperplasia. Due to the lack of reported cases, the biological behavior, prognosis, and molecular study of this cystic hypersecretory carcinoma are difficult and less understood.

In one of the journals published in December 2018, stated that there are only 19 reported cases of cystic hypersecretory carcinoma. The authors of this paper decided this case of cystic hypersecretory breast carcinoma in a 48 - year - old female is too valuable to be missed considering the lack of case reports around the time.

2. Case Description

A 48 - year - old female with a complaint of a palpable lump in her right breast in the last month. According to the patient, the lump gradually progressive in size along with local tenderness. On physical exam, a palpable lump on right breast with diameters around 5cm with solid consistency.

Ultrasound examination reveals a solid nodule with cystic part on lower lateral quadrant of the right breast extending to upper lateral quadrant, multi lobulated, with increased vascular markings on solid part with cancerous tendency. This result was obtained before fine needle aspiration biopsy sample was performed.

Fine needle aspiration biopsy (FNAB) was performed before excision biopsy with result coming as atypical high grade nuclear epithelial cell hyperplasia with background observed by conventional stain, DD/ carcinoma with high grade nuclear feature with mucinous substance as the background.

On August 10th, 2020, excision biopsy was performed on the patient. The tissue obtained from the biopsy was sent to our anatomic pathology laboratory for further analysis. A preparation of sliced specimen submerged in 10% NBF (neutral buffered formalin) with patient's identities label was received in our laboratory.

The specimen's dimension is 4, 5 x 3 x 2 cm. The sliced specimen shows multiple cystic lesions with diameter of 0, 5 – 1 cm, some part contains colloid - gelatinous substance with the other part contain blood clots with white - yellowish necrotic areas. Histological examination was further performed with hematoxylin and eosin staining. (Figure 1)

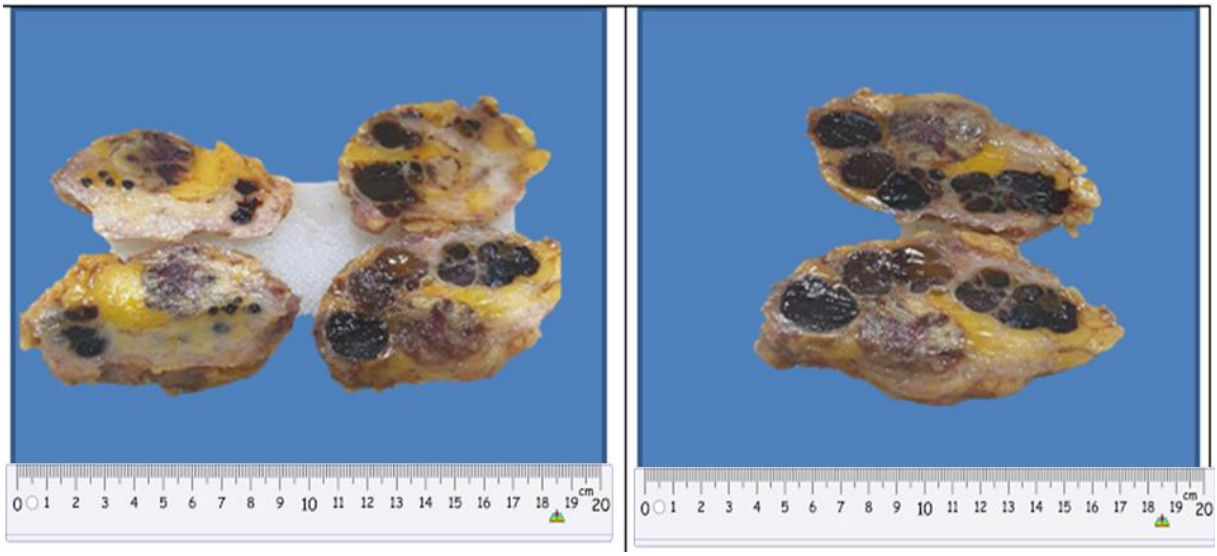
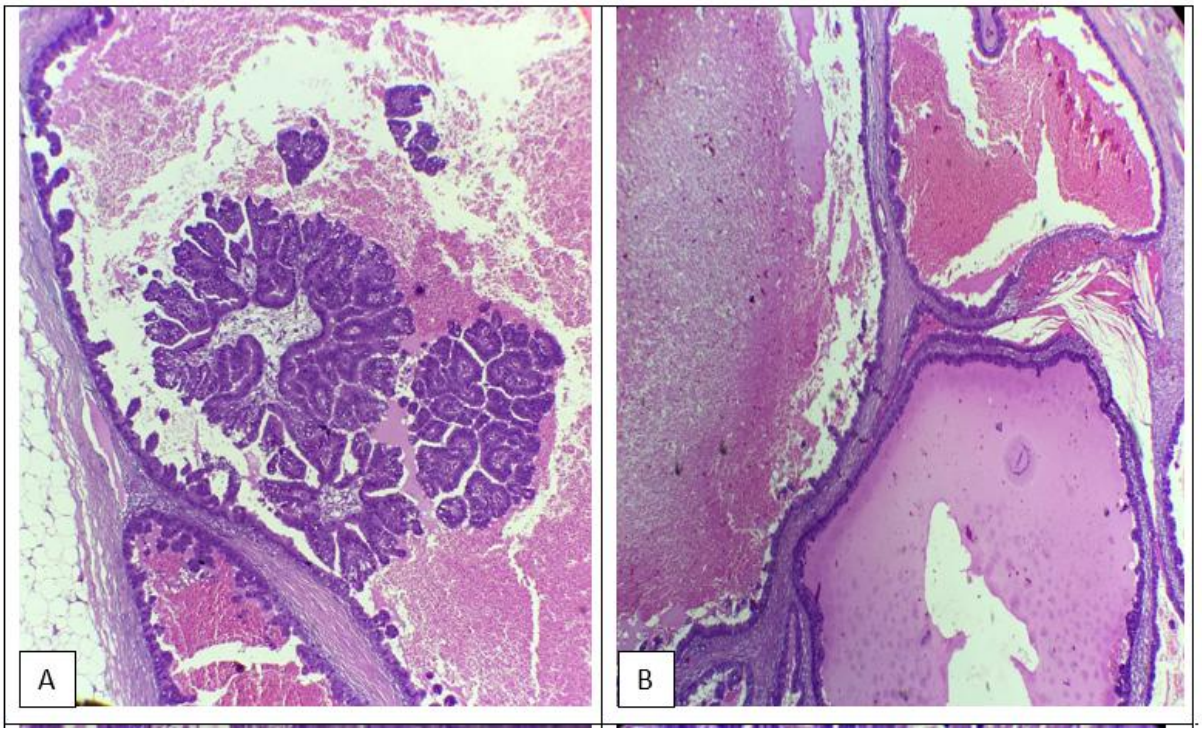


Figure 1: Sliced tissue specimen of cystic mass obtained from incision biopsy sent to pathology anatomy laboratory

Microscopic inspection of the tissue of the right breast tumor showed general pushing margin. The mass of the tumor consists of multiple cystic formations in various sizes, some part consists of amorph - intra - cystic substance resembling pale eosinophilic - dyed colloid - like substance, and the other part accompanied with absorbed vacuole - like appearance.

The cystic spaces were lined with atypical epithelial cells with dominant micropapillary pattern, with the others as complex papillary branching frond. Constituent epithelial cells are composed as columnar structure, arranged in crowding, and overlapping pattern, with pleomorphic oval nuclei, hyperchromatic to vesicular with prominent single to multiple nucleoli. Some part of the nuclei showed hobnail like appearance. Foci of atypical epithelial cells with dilated intraluminal coagulative necrosis were observed. Mitoses were found to be 13 - 16 / 10 of large viewing area.

On certain microscopic foci, invasive process along with desmoplastic response and lymphocyte inflammation infiltration of moderate – high density with surrounding hemosiderin pigment were observed. These areas showed solid islands with centers resembling cystic area. Part of the nucleoli in this area showed angulated grooves and ground - glass appearance. Lympho - vascular invasion (LVI) was not evident. (Figure 2)



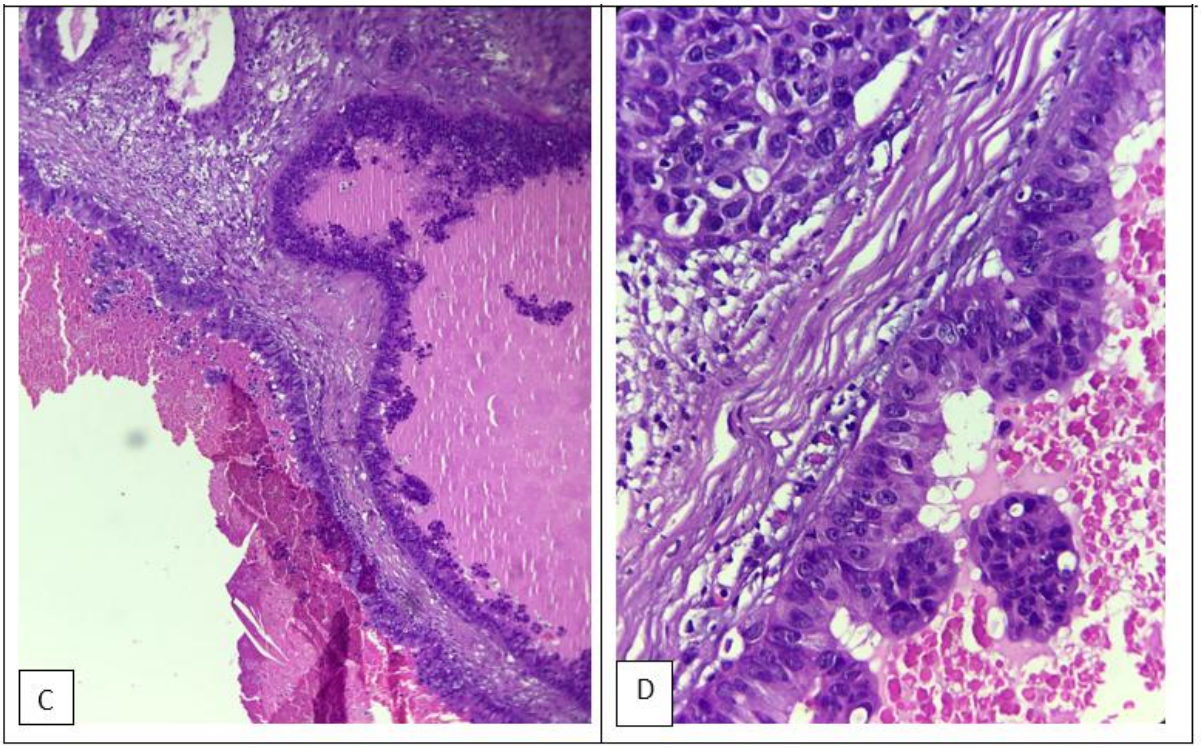


Figure 2: Microscopic features with H&E staining show multiple cysts with lumen filed with eosinophilic and homogenous colloid - like secretion. A) Focus of in situ ductal micropapillary carcinoma is observed (40x magnification), B) Cystic spaces with Hobnail like appearance, C) Cystic spaces lined with crowding and overlapping columnar epithelial cell (100x magnification), D) Crowding overlapping columnar epithelial cells with solid nest focus (400x magnification).

After the histopathologic image of cystic hypersecretory carcinoma with microscopic focus area with microinvasive tendency was obtained, further immunohistochemical examination was required to ascertain the malignancy.

3. Results

From immunohistochemical examination was found:
ER: 80% positive staining on tumor cell nuclei with strong intensity
PR: 60% positive staining on tumor cell nuclei with strong intensity
HER - 2: Negative
Ki - 67: 25 - 30% positive staining on tumor cell.

4. Discussion

Cystic hypersecretory carcinoma is a rarely occurring subtype variant of ductal carcinoma and it is considered as a special variant of ductal carcinoma. First discovered by Rosen P and Scott in 1984, due to its unusual pathological features this variant is better discussed separately to avoid any confusion. Cystic hypersecretory carcinoma is included in hypersecretory cystic lesion group, there are some features of cystic hypersecretory lesion, from benign to malignant which as follows; benign pattern of Cystic Hypersecretory Carcinoma (CHC), to malignant CHC with atypia, Cystic Hypersecretory Carcinoma (CHC) to invasive CHC.[1, 2]

Information about the incidence of this malignancy is very limited due to the rarity of the case, some of the cases presumptively not reported or may be misdiagnosed as benign lesion or non - special type of in situ ductal carcinoma. The age distribution of this case is generally similar to other breast malignancies in the third decade (34 - year - old), and seventh decade (79 - year - old) being the youngest and oldest age respectively. The mean occurrence for this cancer is around 56 years old, every single case is found only in the female sex. There are no reported cases of cystic hypersecretory carcinoma correspond to familial genetics alteration, and there are no evidence stating the connection with oral contraception or hormone replacement therapies.[1, 3, 5]

Clinical features often found in cases of CHC are palpable lumps on breast with local tenderness, and rarely accompanied with nipple discharge, and if it were to be accompanied, blood is usually found. In our case, the patient has similar symptoms of which a palpable lump on breast with local tenderness around the lump.[1]

FNAB examination on patients with CHC usually shows most cells in small dense groups with mucinous material background. Some areas also show histiocyte layers with colloid - like background. There are similarities in our cases of which the result of the FNAB specimen as “Atypical hi grade nuclear epithelial cell hyperplasia with background observed by conventional stain, DD/ Carcinoma with high grade nuclear feature with mucinous material background” supported the diagnosis. Hypersecretory cystic lesion can be diagnosed with FNAB specimen if the secretory characteristics were identified. Epithelial cells may form in groups or as individuals and could be found between secretory materials. Lesions with in situ ductal carcinoma usually produces papillary clusters of tumor cells on FNAB

specimen. Differential diagnoses are mucinous carcinoma and or mucocele - like lesion.2[, 3, 4]

The gross appearance of this tumor is reported by Rosen et al may vary in size between 1 - 10 cm in diameter. Generally, the lesion has prominent border, supple to the touch, and can be differentiated with breast tissue surrounding it. On gross examination, dilated ducts and multiple cysts in lesion are commonly found. The prominent gross feature is usually brown or grey brown in color which indicate the embedded cyst. The size also comes in variations with mean of 1, 5cm in diameter. Intra - cyst secretion, as explained, may be as mucinous, gelatinous, or thyroid colloid - like substance. This obvious gross pattern also supports the diagnosis of CHC which we report, as explained by gross examination and figure 1.1[, 3, 4, 5]

On microscopic examination, all secretory cyst lesion is a cyst containing eosinophilic secretion which have a striking similarity to thyroid colloid - like substance, which is homogenic and acellular. The secretion content in this cyst is often absorbed by the surrounding epithelia, causing the margin to fade, or scalloped indicating the epithelial proliferation rate. Necrosis and calcification are generally not visible, but histiocytes sometimes found inside the secretion. There are no differences in secretion materials between cystic hypersecretory carcinoma and cystic hypersecretory hyperplasia.1[, 2, 3]

In connection with invasive carcinoma, in situ ductal hypersecretory cystic carcinoma can also give a hypersecretory overview, although there is rarely a difference in cytomorphological examination. So far, almost every carcinoma has poor differentiation such in ductal type with solid growth pattern. The nuclei of invasive carcinoma exhibit clear vacuolated appearance, similar to nuclei in thyroid papillary carcinoma.1[, 3, 4]

The differential diagnosis of invasive CHC including ductal carcinoma in situ (DCIS) with comedo necrosis, secretory carcinoma, Mucocele - like lesion (MLL) and metastatic thyroid carcinoma.3[, 4, 5]

1) DCS with comedo necrosis: as general, DICS with comedo necrosis shows yellow - whitish ill - defined border granulation. Comedo necrosis can be seen in surface of pathologic slices. Microscopically, dilated ducts are filled with necrotic materials, unlike eosinophilic secretions as in thyroid colloid - like substance.
2) Secretory carcinoma: Secretory carcinoma is also known as teenage secretory carcinoma. This type of malignancy frequently occurs in women of reproductive age with mean age onset of 25. Secretory carcinomas exhibit microcytic honeycomb appearance, vacuolated cytoplasm, whereas CHC is indicated by marked dilation of cyst structure.
3) Mucocele - like lesion: Roughly similar to CHC. This lesion also shows marked dilation containing gelatinous and mucinous substance. On microscopic examination, the secretion is pale blue, basophilic, and often accompanied with calcification, which is not a feature of CHC.
4) Metastatic thyroid carcinoma: metastatic follicular thyroid cancer can resemble CHC. Histological differences of this lesion may need thyroglobulin immunohistochemical staining.

Immunohistochemical examination related to cystic hypersecretory carcinoma varies in results. Rose et al reported that the expression of ER (estrogen receptor) and PR (progesterone receptor) antibodies in in situ cystic hypersecretory ductal carcinoma with invasive carcinoma gave different results. Ten cases of in situ ductal carcinoma researched by D'alfonso et al, four of which gave positive ER and PR results, the other four gave positive ER and negative PR, the last two gave negative ER and PR results. Every HER - 2 (human epidermal growth factor receptor) examination performed on patients with ductal carcinoma in situ gave negative results. Yet, examinations conducted by Skalova et al showed different results with three out of five cases of ductal carcinoma in situ gave positive HER - 2. On the same case, four out of five cases tested positive for androgen receptor (AR). Due to variations of results on IHC examinations, delicate considerations of pathologists and hospital policy is essential for IHC examination.1

5. Conclusion

Invasive type of cystic hypersecretory carcinoma is a subtype of breast cancer rarely found in everyday practice, it is marked by cystic secretory activity with colloid thyroid - like substance along with cystic spaces lined with neoplastic cells of pseudostratified arrangement to micropapillary with focus of invasive area. There has only been one reported case of cystic hypersecretory carcinoma. Due to rarity of the disease or the reports, further investigations are still required to understand the biological behavior, prognosis, and molecular study for cystic hypersecretory carcinoma.

6. Acknowledgements

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