Invasive Pure Mucinous Carcinoma of Breast: A Rare Case Report.

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Abstract:
Breast Carcinomas is a heterogeneous disease that encompasses several distinct entities with remarkably different characteristics. Mucinous carcinoma is a rare variety accounting for 2% of the invasive duct carcinomas. It has a favorable prognosis due to low incidence of axillary lymph node metastasis and adherence to overlying skin and bottom fascia with high incidence of ER & PR positivity. The incidence of Mucinous carcinoma in females under 35 years of age is only 1%. 10 year survival rate ranges from 80-100%, in noninvasive carcinomas. We report a case of 58 yr old female with locally advanced mucinous carcinoma of the breast showing tumor size of >15 cm, involving skin, underlying tissue with axillary lymph node metastasis.

Keywords: Mucinous, Carcinoma, Breast, Invasive etc

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Introduction:
Mucinous carcinoma (MC) of the breast is a distinctive, well differentiated type of adenocarcinoma, constituting 2% - 5% of breast cancers and occurs in old age [3]. Breast cancer is a heterogeneous disease with different tumors possessing different biology and natural history. The identification of patients with indolent and low-risk tumors is important and would have significant implications for clinical management, with the possibility of sparing patients medically unnecessary and potentially harmful interventions [1]. Pure MC of breast has been reported to have a more favorable prognosis than other well differentiated adenocarcinomas of breast, with a lower frequency of axillary node metastasis and excellent short-term prognosis, especially when the tumor measures less than 5 cm in diameter [3].

Observations: Frequency of lymph node metastasis depends on the form, only 3-15% of pure variety shows node positivity. Rarity of the tumor and unique pathological features are the purpose of the presentation of this case.

Case History: 58 yrs old female presented with lump in breast with history of one year. On examination it measured approx. 20 x 10 x 08 cm. It was ill defined, hard in consistency at cystic at places. Overlying skin was ulcerated with retracted areola and nipple. Axillary lymph nodes were palpable. Opposite breast looked normal. FNAC was done and diagnosed as positive for malignancy. Modified radical mastectomy (MRM) with axillary tail and lymph node resection was done. MRM was followed by chemotherapy and radiotherapy.

Pathological findings: Gross: Modified radical mastectomy specimen with apex lymph nodes was received. Specimen of the breast (Fig 1) was of size 18 x 20 x 6 cm covered with ulcerated skin and retracted nipple and areola. Cut section showed large cavities with necrotic and hemorrhagic areas of size 15x7 cm and small grayish white areas approx 5 x 4 x 3 cm. Tumor was extending up to the skin. Axillary fat of length
15 cm attached to the breast was noted. Total 19 lymph nodes were identified, larger of size 4 x 2 x 1 cm, cut section revealed gray white areas with necrosis.

Fig 1 shows specimen of the breast covered with ulcerated skin and retracted nipple and areola. Cut section shows tumor area.

**Microscopic examination:**
Initial sections from different areas showed hemorrhagic and necrotic areas with mucinous material only and no tumor cells were identified. The specimen was regrossed. Subsequent sections studied showed clusters of tumor cells. (Fig.2A) The clusters show acinar formations and micro papillary structures. The cells are round to polyhedral with pleomorphic, hyperchromatic nuclei with plenty of cytoplasm. (Fig.2B) A lot of extracellular mucin was seen. Surrounding areas showed necrosis and plenty of inflammatory cells. Section studied from overlying skin, nipple, areola and superior border showed tumor infiltration. Rest i.e. both lateral margins, posterior margin or base and inferior margin were free from tumor infiltration. Sections studied from lymph nodes shows twelve lymph nodes positive for metastasis. Tumor tissue shows plenty of mucin with hyperchromatic tumor cells floating in it. (Fig. 3) Out of 12 positive lymph nodes 6 were showing paranodal extension and no sub capsular extension. Rest lymph nodes were showing reactive lymphadenitis.

Clinical staging: T₄N₂Mₓ

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**Fig 2A:** (10x H&E) sections studied showed clusters of tumor cells. The clusters show acinar formations and micro papillary structures.

**Fig. 2B:** (40x H&E) Section from tumor shows the cells are round to polyhedral with pleomorphic, hyperchromatic nuclei with plenty of cytoplasm.

**Fig. 3A:** shows (10 X) H & E stained preparation of lymph node. It shows mucin with tumor cells.
Fig 3B: shows (40 X) H & E stained preparation of lymph node. It shows pools of mucin with hyperchromatic, pleomorphic tumor cells.

**Discussion:**

Invasive mucinous (colloid) carcinoma represents a distinctive morphologic pattern that may manifest in breast carcinoma, as well as carcinomas of other organs (colon, stomach, etc). Mucinous breast carcinoma is characterized by a relatively large volume of extracellular mucin, in which malignant epithelial cells are floating [2]. Mucinous carcinoma of the breast is a rare malignancy in postmenopausal females, accounting for only 2% of all breast carcinomas. Mucinous carcinomas can be classified as pure and mixed forms. The pure form shows variable amount of extracellular mucin surrounding the tumor cells which was seen in this case. Mucinous carcinoma with invasive areas not surrounded by mucin is considered as a mixed mucinous carcinoma.

The prognosis of pure mucinous carcinoma is much better than that of mixed one. The pure mucinous carcinomas are further subdivided into cellular and hypo cellular variants. The most common admixture is with regular invasive duct carcinoma. Two lesions most likely to be confused with mucinous carcinoma are mucoid fibroadenoma and a mucocele-like lesion [3]. The incidence of axillary lymph node involvement was 41% in NOS carcinomas and mucinous carcinoma (14%) [1].

Pure mucinous carcinoma generally has a less aggressive growth pattern as defined by tumor size, adherence to the overlying skin / bottom fasciae, estrogen and progesterone receptor positivity and primary axillary lymph node metastasis.

In this case, the tumor size was >15 cm, skin was involved, nipple and areola were free and 9/19 lymph nodes were positive for tumor metastatic deposits. The 5-year overall survival (OS) was 80% for mucinous and 77% for NOS carcinomas [1]. Only 3-15% of the pure variety show axillary lymph node metastasis compared to 33-46% of the mixed type. Both components of mixed mucinous tumors are remarkably similar at the molecular level to pure mucinous cancers, suggesting that mixed mucinous carcinomas may be best classified as variants of mucinous cancers rather than of IDC-NSTs [4].

Disease Free Survival (DFS) is significantly better for mucinous carcinomas compared with NOS carcinomas, with a 5-year DFS of 90% for mucinous and only 80% for NOS carcinomas [1].

However, node positivity for mucinous carcinomas conferred a substantially worse prognosis, with a 5-year DFS of 76%, similar to the prognosis for node-positive NOS carcinoma patients. The 5-year OS for node-positive patients was 81% for mucinous and 69% for NOS carcinomas [1]. The tumor cells have been described as being generally small and fairly uniform with minimal atypia, and this may give a false impression of “benignancy”, a term used to describe this uncommon condition [3].

It is mucin rather than the tumor cells that is invading the stroma which explains the good prognosis of pure mucinous carcinoma. The mucin production is typically extracellular [6]. In this specimen, mucin formed nests where tumor cells were degraded or had already disappeared, i.e., a ‘muconodular pattern’. This is a phenomenon that is seen when cells produce a large amount of mucin rapidly. Although it is unknown what triggered the sudden growth of this tumor, rapid enlargement of the tumor by mucin production developed the extremely locally advanced breast tumor with deep ulcer formation [5].

Papillary Carcinomas, papillomas and ductal hyperplasia or florid ductal hyperplasia can accompany with abundant mucin secretion [6].
Conclusion:
Repeat sections were taken in view of hypocellular variant of mucinous carcinoma found in this case. The previous sections were negative for tumor cells and only after thorough sampling, the tumor cells were identified on microscopy. Thus, it is necessary to adequately sample the tissue in case of extracellular mucin producing breast lesion to avoid discrepancies and negligence in the diagnosis of this rare tumor.

References:
2] Elizabeth L. Kehr, Julie M. Jorns, Daphne Ang, Andrea Warrick, Tanaya Neff, Michelle Degnin, Rebecca Lewis, Carol Beadling, Christopher L. Corless, Megan L. Troxell. Mucinous breast carcinomas lack PIK3CA and AKT1 mutations.