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# Rare Breast Cancer Subtypes: A Case Study Series on Mucinous, Metaplastic, Medullary and Papillary Carcinomas

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## ABSTRACT

Breast cancer is a highly heterogeneous disease with various histological subtypes that differ in their clinical presentation, prognosis, and response to treatment. While most breast cancers are classified as invasive ductal carcinoma, rare subtypes such as Mucinous Carcinoma, Metaplastic Carcinoma, Medullary Carcinoma, and Invasive Papillary Carcinoma present unique diagnostic and therapeutic challenges. This case study series examines four patients, aged 35 to 80, diagnosed with these rare breast cancer variants. The first case is a 58-year-old female diagnosed with Mucinous Carcinoma, a subtype characterized by extensive extracellular mucin production and a low incidence of lymph node metastasis. The tumor was excised with clear margins, and no nodal involvement was observed, suggesting a favorable prognosis. The second case is an 80-year-old female with Metaplastic Carcinoma, specifically low-grade Adenosquamous Carcinoma. Despite its low histological grade, lymph node involvement was present, which is often associated with a worse prognosis. The third case involves a 35-year-old female diagnosed with Medullary Carcinoma, a high-grade tumor often found in younger women. Despite its aggressive histological features, this tumor lacked lymph node involvement, indicating a more optimistic prognosis. The fourth case, a 60-year-old female, was diagnosed with Invasive Papillary Carcinoma, a moderately differentiated tumor with well-formed papillae. This patient also had clear margins and no nodal involvement, which is consistent with the generally favorable outcomes associated with this subtype. This case series highlights the need for individualized treatment approaches, as rare breast cancer subtypes often deviate from standard therapeutic protocols. Accurate histopathological diagnosis, supplemented by immunohistochemistry and imaging, is critical for guiding treatment and improving patient outcomes. This study contributes to the limited literature on these rare subtypes and emphasizes the importance of early detection and tailored management strategies

## INTRODUCTION

Breast cancer is one of the most commonly diagnosed malignancies in women worldwide, accounting for a significant proportion of cancer-related morbidity and mortality. Despite the extensive research and advances in treatment, breast cancer remains a heterogeneous disease, composed of multiple histological subtypes with distinct molecular, morphological, and clinical characteristics. The majority of breast cancers are classified as invasive ductal carcinoma (IDC), which accounts for approximately 65%–80% of cases (Ellis et al., 2012). However, a minority of cases present with rare histological variants, such as Mucinous Carcinoma, Metaplastic Carcinoma, Medullary Carcinoma, and Invasive Papillary Carcinoma, which pose unique diagnostic and therapeutic challenges due to their rarity and atypical clinical behavior (Dieci et al., 2014).

Mucinous carcinoma of the breast, also referred to as colloid carcinoma, represents about 2% of all breast cancer cases and is characterized by the production of abundant extracellular mucin, which surrounds the tumor cells and gives the tumor its gelatinous appearance (Rakıcı et al., 2009). This subtype is typically associated with a favorable prognosis, with lower rates of lymph node involvement and distant metastasis compared to invasive ductal c

arcinoma (Kong et al., 2017). Despite its indolent nature, it is crucial to identify the histological and molecular characteristics of mucinous carcinoma to guide therapeutic decisions. Studies have shown that mucinous carcinoma expresses hormone receptors (estrogen and progesterone receptors) more frequently than other subtypes, which may influence treatment outcomes (Kim et al., 2012).

On the other hand, Metaplastic Carcinoma is a rare and aggressive variant of breast cancer, accounting for less than 1% of cases (Liu et al., 2020). It is characterized by the presence of both epithelial and mesenchymal components, which may include squamous, spindle, chondroid, or osseous elements. This subtype is often hormone receptor-negative and HER2-negative, making it difficult to treat with standard endocrine therapies and HER2-targeted agents (Vandamme et al., 2013). The prognosis for metaplastic carcinoma is generally poor due to its aggressive nature and high likelihood of distant metastasis, even in early-stage disease (Murialdo et al., 2009). Metaplastic carcinoma presents significant diagnostic challenges, as it can be misdiagnosed as a benign or low-grade tumor due to its diverse morphological patterns. Immunohistochemical analysis is often necessary to confirm the diagnosis and to distinguish it from other forms of invasive breast cancer (Terzi et al., 2012).

Medullary carcinoma, another rare subtype, accounts for less than 2% of breast cancers and is more frequently seen in younger women (Pedersen et al., 1991). It is histologically characterized by a syncytial growth pattern, marked nuclear pleomorphism, and a prominent lymphocytic infiltrate (Saremian et al., 2012). Medullary carcinoma often presents as a high-grade tumor, yet paradoxically, it has a relatively favorable prognosis compared to other high-grade breast cancers (Dieci et al., 2014). This favorable outcome is thought to be related to the robust immune response elicited by the tumor, as evidenced by the dense lymphoid infiltrates seen on histopathological examination (Anderson et al., 2003). The molecular characteristics of medullary carcinoma, including the frequent absence of hormone receptor expression and HER2 amplification, suggest that the tumor may respond better to chemotherapy rather than hormone therapy (Pedersen et al., 1991).

Invasive Papillary Carcinoma is a rare histological subtype, comprising less than 2% of all breast cancer cases (Saremian et al., 2012). It is most commonly diagnosed in postmenopausal women and is characterized by well-formed papillae with fibrovascular cores, often surrounded by a myoepithelial cell layer. The absence of the myoepithelial cell layer in invasive papillary carcinoma distinguishes it from benign papillary lesions and confirms its invasive nature (Chauhan et al., 2016). In general, invasive papillary carcinoma tends to be less aggressive than other invasive breast cancers and is associated with a better prognosis, particularly in hormone receptor-positive cases (Terzi et al., 2012). The treatment for invasive papillary carcinoma typically involves surgical resection, followed by radiation therapy and/or endocrine therapy, depending on the tumor's hormone receptor status (Saremian et al., 2012).

Despite the favorable outcomes observed in certain subtypes like mucinous and papillary carcinomas, the management of rare breast cancer subtypes remains complex due to the limited availability of clinical data and the absence of standardized treatment protocols. The treatment options for these subtypes often deviate from those used in more common forms of breast cancer, such as invasive ductal carcinoma (Dieci et al., 2014). This variability in manage ment highlights the need for a personalized approach, where treatment is guided by the tumor's molecular and histo pathological characteristics. The use of advanced diagnostic techniques, including immunohistochemistry and molecular profiling, is critical for accurate diagnosis and optimal treatment planning (Liu et al., 2020). While rare breast cancer subtypes such as Mucinous, Metaplastic, Medullary, and Invasive Papillary Carcinomas represent a small fraction of overall breast cancer cases, they pose significant diagnostic and therapeutic challenges. Understanding the unique histopathological and molecular features of these subtypes is crucial for developing perso-nalized treatment strategies and improving patient outcomes. This case series highlights the importance of early detection, accurate histological diagnosis, and tailored therapeutic approaches in managing these rare variants of breast cancer.

## MATERIALS AND METHODS

This case study series is based on a retrospective review of four female patients diagnosed with rare subtypes of breast cancer a tertiary center in North India. The patients, aged between 35 and 80 years, presented with palpable masses in the breast and underwent surgical intervention in the form of mastectomy or debulking surgery. Detailed gross and microscopic findings were obtained for each case, and immunohistochemical analysis was performed where necessary to confirm the diagnosis.

### Patient Selection

The study included patients referred for breast lump excision, all of whom were suspected of having malignant breast tumors. These cases were chosen due to their rare histological presentation, specifically Mucinous Carcinoma, Metaplastic Carcinoma, Medullary Carcinoma, and Invasive Papillary Carcinoma.

### Specimen Collection and Processing

All specimens were obtained through surgical excision and processed at the pathology laboratory. The breast tissue specimens, along with axillary lymph nodes where indicated, were fixed in 10% formalin and grossed. Tissue sections were stained using hematoxylin and eosin (H&E) and reviewed under light microscopy.

**1. Gross Examination:**

a) Tumor size, shape, consistency, and any associated features such as calcifications,

hemorrhage, and necrosis were documented.

b) Margins were assessed to determine the proximity of the tumor to the resection edges.

c) Lymph nodes were excised and evaluated for metastatic involvement.

**2. Histopathological Examination:**

a) Multiple sections from each tumor were examined to confirm the histological subtype.

b) Mucinous carcinoma was identified by the presence of extracellular mucin lakes surrounding neoplastic cells.

c) Metaplastic carcinoma showed a mixture of glandular and squamous epithelial elements with desmoplastic stroma.

d) Medullary carcinoma exhibited syncytial tumor cell growth with prominent lymphocytic infiltration.

e) Invasive papillary carcinoma was characterized by well-formed papillae with fibrovascular cores and ductal invasion.

**3. Immunohistochemistry (IHC):** Immunohistochemical analysis was performed on select cases to determine the expression of hormone receptors (ER, PR) and HER2/neu status. Additional markers such as cytokeratins (CK7, CK20), vimentin, and CD34 were used as needed to differentiate specific subtypes.

**Clinical and Pathological Staging**

The tumors were staged according to the American Joint Committee on Cancer (AJCC) 8th edition, based on tumor size (pT), lymph node involvement (pN), and distant metastasis (pM).

**Ethical Considerations**

Informed consent was obtained from all patients prior to specimen collection, and ethical approval for the study was secured from the hospital's review board. Patient confidentiality was maintained throughout the study.

**Discussion and Therapeutic Approaches**

This case study series presents the clinical, histopathological, and immunohistochemical findings of four female patients diagnosed with rare subtypes of breast cancer: Mucinous Carcinoma, Metaplastic Carcinoma, Medullary Carcinoma, and Invasive Papillary Carcinoma. The age range of the patients was between 35 and 80 years, with varying tumor sizes and clinical presentations.

**Case 1: Mucinous Carcinoma (Age: 58, Female)**

a) **Gross Findings:** The excised specimen from the right breast measured 22x17x7.5 cm with a gelatinous tumor mass measuring 8x7 cm. The tumor was located 1 cm away from the superior margin and 0.5 cm from the base.

b) **Microscopic Findings:** Histological sections revealed clusters of infiltrating neoplastic ductal cells surrounded by lakes of extracellular mucin. The tumor margins were clear, and no lymphovascular invasion or microcalcifications were identified.

c) **Lymph Node Status:** A total of 8 lymph nodes were excised, and all were free of tumor involvement.

d) **Diagnosis:** Mucinous Carcinoma of the right breast.

e) **Impression:** A favorable prognosis was suggested due to the absence of nodal involvement and clear margins.

**Case 2: Metaplastic Carcinoma (Adenosquamous Carc inoma) (Age: 80, Female)**

a) **Gross Findings:** The mastectomy specimen measured 20x18x7 cm with a firm, grayish-white tumor measuring 10x8x5 cm. The tumor showed areas of hemorrhage, calcification, and skin ulceration.

b) **Microscopic Findings:** Sections revealed infiltration by atypical squamous epithelial cells arranged in nests and cords, along with moderate pleomorphism. Keratin pearls were present, and the stroma showed chronic inflammatory infiltrates.

c) **Lymph Node Status:** Axillary lymph nodes showed complete replacement by tumor, indicating metastatic involvement.

d) **Diagnosis:** Metaplastic Carcinoma (Low-grade Adenosquamous Carcinoma) with central necrosis and skin invasion.

a) **Impression:** Despite being a low-grade tumor, the presence of nodal metastasis suggests a guarded prognosis.

**Case 3: Medullary Carcinoma (Age: 35, Female)**

a) **Gross Findings:** The mastectomy specimen measured 19x16x7.5 cm, and an irregular, hard tumor mass of 5x3x2.5 cm was identified.

b) **Microscopic Findings:** Histological examination showed sheets of large, atypical cells with prominent nucleoli and a syncytial growth pattern. The tumor exhibited dense lymphoid infiltrates, desmoplastic changes, and focal necrosis.

c) **Lymph Node Status:** Twelve lymph nodes were retrieved, all of which were free from tumor involvement.

d) **Diagnosis:** Infiltrating Duct Carcinoma (No Special Type) with Medullary Pattern (Grade III).

e) **Impression:** Although a high-grade tumor, the absence of nodal involvement suggests a more favorable prognosis.

**Case 4: Invasive Papillary Carcinoma (Age: 60, Female)**

a) **Gross Findings:** The excised left breast specimen measured 40x28x9 cm, with a cystic area filled with dark brown fluid and an invasive tumor mass measuring 8x7x5 cm.

b) **Microscopic Findings:** Sections revealed papillary structures with fibrovascular cores lined by atypical ductal epithelial cells. The tumor cells exhibited moderate pleomorphism, and tumor necrosis was observed.

excised, all of which were free from tumor involvement.

**d) Diagnosis:** Invasive Papillary Carcinoma (Grade II).

**e) Impression:** A moderately differentiated tumor with no nodal involvement, indicating a relatively favor-able prognosis.

## RESULTS

The tumor sizes across the cases ranged from 5x3x2.5 cm to 10x8x5 cm, with all tumors having clear resection margins, indicating that the excision was complete. Among the four cases, only the patient diagnosed with Metaplastic Carcinoma exhibited lymph node involvement, while the other three patients, including those with Mucinous, Medullary, and Invasive Papillary Carcinomas, had no evidence of lymph node metastasis. In terms of prognosis, patients with Mucinous and Papillary Carcinomas generally had favorable outcomes, as these subtypes were low-grade and nodal-negative. Despite being classified as low-grade, the Metaplastic Carcinoma case had a worse prognosis due to the presence of nodal metastasis. In contrast, Medullary Carcinoma, although a high-grade tumor, presented a more optimistic prognosis due to the absence of lymph node spread.

## DISCUSSION

Breast cancer encompasses a wide range of histological subtypes, each with distinct molecular profiles and clinical behaviors that can profoundly affect prognosis and therapeutic strategies. Rare subtypes of breast cancer, such as Mucinous Carcinoma, Metaplastic Carcinoma, Medullary Carcinoma, and Invasive Papillary Carcinoma, constitute a small percentage of overall breast cancer cases but require specialized diagnostic and management approaches due to their unique characteristics. This case series underscores the challenges associated with these rare subtypes and highlights the importance of tailored treatment strategies for improving outcomes.

### Mucinous Carcinoma

Mucinous carcinoma, also known as colloid carcinoma, is a rare and relatively indolent form of breast cancer that comprises approximately 2% of all breast malignancies. Its hallmark feature is the abundant extracellular mucin production that surrounds clusters of malignant cells (Diab et al., 1999). This subtype is often associated with a favorable prognosis due to its slower growth rate, lower incidence of lymph node involvement, and limited potential for distant metastasis compared to other breast cancers (Toikkanen et al., 1989). In the presented case, the patient had a gelatinous tumor measuring 8x7 cm with clear surgical margins and no nodal involvement, which is consistent with existing literature. The relatively favorable prognosis is largely attributed to the fact that mucinous carcinoma often expresses hormone receptors, particularly estrogen receptor (ER) and progesterone receptor (PR), making it amenable to endocrine therapy (Di Saverio et al., 2008). Studies have also shown that mucinous carcinoma has a lower recurrence rate than more common breast cancer subtypes, further supporting the positive outlook for these patients (de Lima et al., 2005). The absence of microcalcifications in this case also reflects typical features of mucinous carcinoma, as calcifications are more frequently associated with ductal carcinoma in situ (DCIS) or invasive ductal carcinoma (Zhang et al., 2014).

### Metaplastic Carcinoma

Metaplastic carcinoma is an aggressive and highly heterogeneous subtype of breast cancer that accounts for less than 1% of breast malignancies. This subtype is characterized by the presence of both epithelial and mesenchymal elements, with squamous, spindle cell, and chondroid differentiation being common (Rayson et al., 1999). Unlike other forms of breast cancer, metaplastic carcinoma is typically hormone receptor-negative and HER2-negative, rendering endocrine therapy and HER2-targeted therapies ineffective (Rakha et al., 2009). The patient in this case presented with a large, low-grade tumor (10x8x5 cm) but had nodal involvement, which significantly worsened the prognosis. Despite its low histological grade, the presence of lymph node metastasis in metaplastic carcinoma is associated with a higher risk of recurrence and poorer survival outcomes (Hennessy et al., 2006). Moreover, the lack of hormonal or HER2 expression limits treatment options to chemotherapy, although metaplastic carcinomas are often resistant to conventional chemotherapy regimens (Tiezzi et al., 2006). This resistance highlights the importance of exploring alternative therapeutic options, including immune checkpoint inhibitors and targeted therapies that are currently being investigated in clinical trials (Lehmann et al., 2016).

### Medullary Carcinoma

Medullary carcinoma is a rare subtype that accounts for less than 2% of all breast cancers and typically presents in younger women. Histologically, it is characterized by large, pleomorphic tumor cells arranged in a syncytial growth pattern with a prominent lymphoplasmacytic infiltrate (Rosen et al., 1993). Despite its high-grade appearance, medullary carcinoma is paradoxically associated with a relatively favorable prognosis, with a lower rate of lymph node involvement and better survival outcomes compared to other high-grade breast cancers (Anderson and Badve, 2010). The dense lymphocytic infiltrate is believed to play a key role in the tumor's immune-mediated response, which may contribute to its better prognosis (Bogomoletz and Guillot, 1983). The case presented here involved a 35-year-old female with a tumor size of 5x3x2.5 cm and no lymph node metastasis, reflecting the typical clinical behavior of medullary carcinoma. This subtype is often negative for hormone receptors and HER2, which makes chemotherapy the mainstay of treatment (Pierce et al., 2016). Studies have suggested that medullary carcinoma patients, particularly those with BRCA1 mutations, may have a distinct response

to chemotherapy, further underscoring the need for personalized treatment strategies (Obermair et al., 2001).

**Invasive Papillary Carcinoma**

Invasive papillary carcinoma is an uncommon subtype of breast cancer that represents less than 2% of all cases. It is most often diagnosed in postmenopausal women and is characterized by well-formed papillary structures with fibrovascular cores, lined by malignant epithelial cells (Jones et al., 1996). Unlike benign papillary lesions, invasive papillary carcinoma lacks a surrounding myoepithelial layer, which confirms its invasive nature (Dee et al., 2007). This subtype tends to be low-grade, and patients generally have a favorable prognosis, especially in hormone receptor-positive cases. In the present case, the tumor measured 8x7x5 cm with clear margins and no lymph node involvement, which is consistent with the typically favorable outcomes reported for this subtype (Rosen, 2001). However, invasive papillary carcinoma can exhibit aggressive behavior in some cases, particularly when the tumor is hormone receptor-negative or exhibits a high proliferation index (Mersin et al., 2003). Surgical resection remains the cornerstone of treatment for invasive papillary carcinoma, with adjuvant endocrine therapy recommended for hormone receptor-positive tumors (Rakha et al., 2006).

**Prognostic Implications**

The prognosis for rare subtypes of breast cancer varies significantly depending on the specific histological features and the presence of lymph node involvement. Mucinous and papillary carcinomas are generally considered low-grade, with excellent long-term survival rates when diagnosed at an early stage (Toikkanen et al., 1989). These tumors are typically hormone receptor-positive, allowing for the use of endocrine therapies that further improve outcomes (Jones et al., 1996). On the other hand, metaplastic carcinoma presents a major therapeutic challenge due to its aggressive nature, frequent hormone receptor negativity, and resistance to chemotherapy (Lehmann et al., 2016). Similarly, medullary carcinoma, despite its high-grade histology, tends to have a better prognosis than other high-grade breast cancers, likely due to the immune-mediated response driven by the dense lymphocytic infiltrate (Bogomoletz and Guillot, 1983).

**Clinical Management and Future Directions**

Given the rarity of these subtypes, standardized treatment guidelines are often lacking, and clinicians must rely on the available literature and multidisciplinary team discussions to guide management decisions. The role of surgery remains critical in achieving clear margins and reducing the risk of local recurrence (Rosen, 2001). Adjuvant therapies, including chemotherapy, endocrine therapy, and radiation, should be tailored to the individual tumor biology. Emerging molecular profiling techniques may help identify actionable targets in rare subtypes, particularly in metaplastic and medullary carcinomas, where conventional treatments have limited efficacy (Pierce et al., 2016). Ongoing research into immunotherapy and targeted therapies holds promise for improving outcomes in these difficult-to-treat subtypes (Lehmann et al., 2016).

## CONCLUSION

This case series highlights the unique clinical and patho logical features of four rare breast cancer subtypes and underscores the need for individualized treatment appr oaches. While Mucinous and Papillary Carcinomas generally have favorable outcomes due to their indolent nature, Metaplastic and Medullary Carcinomas require more aggressive treatment due to their complex histology and potential for metastasis. Further research into the molecular mechanisms underlying these rare subtypes is essential to develop more effective treatments and improve patient outcomes.

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