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Case report

Mucinous carcinoma in an octogenarian: Treatment and management of breast cancer in the elderly ☆,☆☆

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ABSTRACT

Age is a risk factor for breast cancer in females, and over 60% of female breast cancer deaths occur in those aged 65 and older. As the population in the United States continues to age, it is expected that there will be a commensurate increase in the number of women diagnosed with breast cancer, making understanding of effective treatment and management of breast cancer in the elderly essential.

Here, we review the treatment and management of early breast cancer in the elderly. We report a case of invasive mucinous carcinoma in an 80-year-old female detected on routine clinical breast exam by her primary care physician. Mucinous carcinoma of the breast is a type of rare invasive neoplasm that generally carries an excellent prognosis. Following an ultrasound-guided core needle biopsy, a right breast needle localized segmental mastectomy was performed and the patient was prescribed an aromatase inhibitor for hormone-receptor positive tumor. After a follow-up of 8 years, the patient remains free of recurrence or metastasis and vibrantly living meaningful daily life.

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Introduction

Though a rare epithelial tumor of the breast, mucinous carcinoma of the breast (MCB) nonetheless exemplifies diagnosis and outcomes for many of the so-called specialized types of breast cancer [1,2]. As defined by the World Health Organiza-

tion (WHO), specialized types of epithelial breast carcinomas contain no less than 90% of the specific tumor type, in contradistinction to the common invasive breast carcinoma of no special type [2]. Pure type MCB is comprised of tumor tissue with extracellular mucin production in over 90% of the tumor (Fig. 1), with an excellent prognosis.³ MCB accounts for 2%–4% of malignant neoplasms of the breast and typically occurs in

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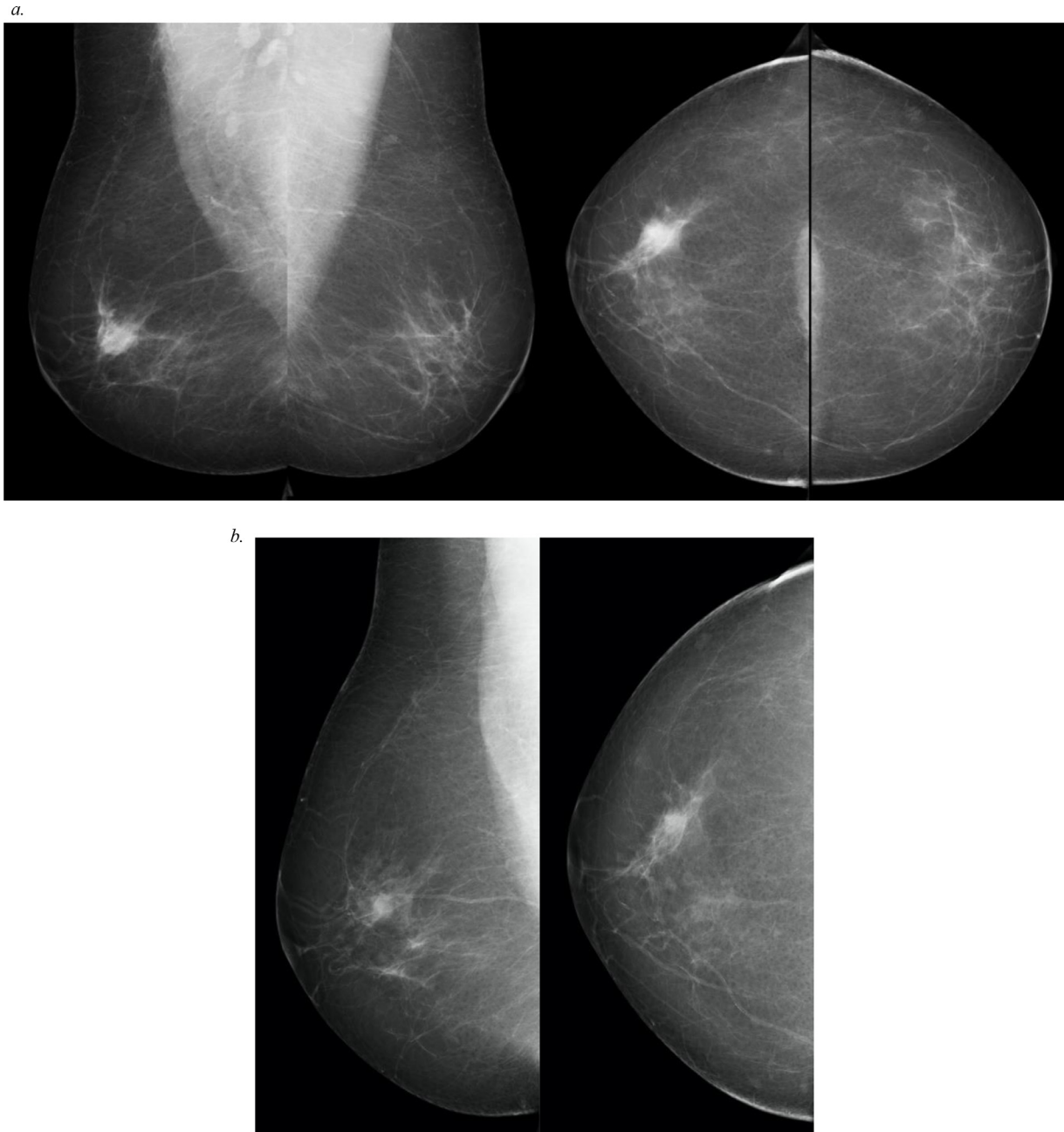


Fig. 1 – (A) Bilateral MLO and CC and compression magnification diagnostic mammograms at presentation demonstrate a 1.2 cm irregular high density spiculated mass in the right breast 9:00 at the junction of the anterior and middle depths. (B) Unilateral right comparison MLO and CC mammograms from two years earlier demonstrates a 1 cm irregular mass.

postmenopausal elderly patients, only very rarely occurring in men [1,4]. MCB is most frequently of the luminal A molecular subtype, low grade, estrogen receptor (ER) positive, progesterone receptor (PR) positive and human epidermoid receptor (HER-2 neu) negative, with very low rates of lymph node metastases [2,5,6] MCB has an excellent prognosis, with the 5-year overall survival rates estimated to be 95-99% [7,8]. Most patients present with abnormal mammogram, in the setting of high breast cancer screening rates [9]. On mammography, MCB often presents as an oval or lobulated, at least partially

circumscribed mass [10]. Occasionally, MCB lesions cannot be detected on mammography [10]. Sonographically, MCB tumors are typically not circumscribed, with microlobulated margins, and may be mixed with isoechoic hypoechoic, or hyperechoic based on portions that correlate with the mucin-producing pathologic cells [11] Appearance can vary greatly on ultrasound (US), especially in MCB tumors that are mixed in cellularity which may tend to be more hypoechoic and heterogeneous [12]. A recent review of the literature identified surgery as the primary treatment [13]. Here, we report a case of an



Fig. 2 – (A–C) Targeted ultrasound in transverse and longitudinal planes demonstrates a 1.2 × 1.0 cm right breast mass in the 9 o'clock middle depth position that is hypoechoic, not parallel, and not circumscribed.

80-year-old female with diagnosis of invasive mucinous carcinoma of the right breast.

Case report

An 80-year-old female presented in 2012 with a palpable 2 cm mass lateral to the right areola at the 9 o'clock position, originally felt by her primary physician on routine physical exam. On mammogram, the mass was found to be a 1.2 cm irregular high-density mass laterally in the backdrop of scattered fibroglandular densities. The patient had previously undergone benign ultrasound-guided right breast core needle biopsies 4 and 6 years earlier. The present mass had increased in size over earlier mammograms (Figs. 1A and B). On ultrasound (US), there was a 1.2 × 1.0 cm right breast mass in the 9 o'clock position, hypoechoic not parallel and not circumscribed (Fig. 2). There was no right axillary lymphadenopathy. The patient underwent US-guided core needle biopsy that yielded invasive ductal carcinoma with mucinous features. The mass was Nottingham combined histologic grade 1 based on tubule formation score of 2, nuclear pleomorphism score of 2, and mitotic activity score of 1. The mass was ER+ (98%, 3+), PR+ (45%, 1-3+), and HER2/neu negative for overexpression (1+). The patient was scheduled for right needle localized lumpectomy (Fig. 3) without sentinel node biopsy based on the CALGB elderly trial having indicated no difference in survival between node positive and node negative elderly patients [14]. The hematology/oncology care team recommended anastrozole (Arimidex, ANI Pharmaceuticals, Baudette, Min), an aromatase inhibitor, for the treatment of postmenopausal hormone receptor positive breast cancer.

The patient underwent mammographic-guided needle localization and final surgical pathology from the right breast segmental mastectomy yielded grade 1 invasive mucinous adenocarcinoma, an adjustment to the earlier diagnosis of invasive ductal carcinoma with mucinous features (Fig. 4). The apparent discrepancy between the core needle biopsy specimen (invasive ductal carcinoma) and the final surgical specimen (invasive mucinous carcinoma) illustrates WHO tenets;

90% of the tumor must meet cellularity criteria that define each specialized type of epithelial breast carcinomas [2,5]. Thus, the core needle biopsy results often provide advance indication of a specialized type but the resected surgical specimen in toto is needed to assign the final diagnosis as a specialized type of breast cancer. At its greatest dimension, the excision measured 14 mm. Ductal carcinoma in situ comprised approximately 10% of total tumor volume. Ductal carcinoma in situ was described as grade 2, solid, cribriform, micropapillary, and without necrosis. All margins were negative by at least 3 mm. The tumor was staged as AJCC pathologic TNM stage of pT1c pNx and breast stage grouping of IA. In consultation with the radiation oncologist, it was decided that the patient did not require radiation therapy given the low grade of the tumor. The patient, very active in her care algorithm and concerned about the side effects of anastrozole, nonetheless elected to take long term anastrozole based on its recurrence risk reduction profile. Over the years, the patient reported mild symptoms potentially associated with anastrozole therapy, including occasional musculoskeletal pain, headaches, and "spells of feeling hot and cold" but has continued PO therapy to current date. The patient has undergone annual mammography surveillance since 2015 (following closer surveillance 2013-2015). The post-lumpectomy site remains stable, and the results continue to be categorized as BIRADS category 2 (Fig. 5). Most importantly, in her daily life she is a voracious reader and talented pianist who is passionate about lifelong learning, attends strength-training and yoga classes, and continues to care for family members.

Discussion

Every year in the United States, approximately 300,000 women are diagnosed with breast cancer, of which over half are aged 60 and up [15]. Age is a risk factor for breast cancer in females, with the median age at diagnosis at 63 and peak incidence rate occurring between 65-74 [15,16]. Furthermore, over 60% of female breast cancer deaths occur in those aged 65 and up [16]. Though elderly females tend to have lower grade hormone receptor positive tumors without nodal involvement,

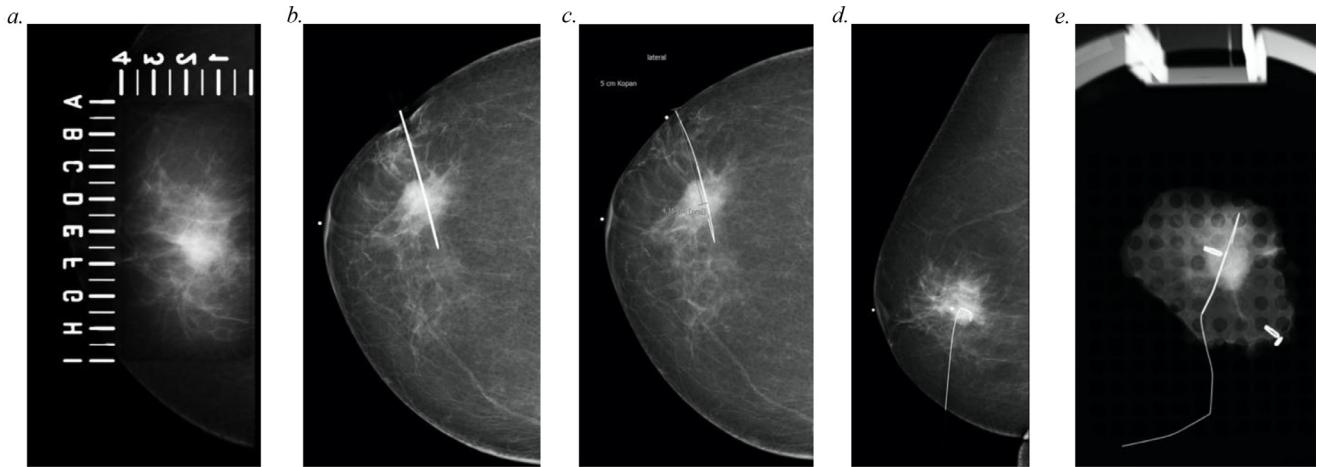


Fig. 3 – (A–E) Five films from the successful mammographic-guided needle localization demonstrate the mass centered in the alphanumeric grid in a true lateral approach (A), post needle placement in the orthogonal CC approach showing the needle traversing the mass (B), exchange of the needle for the localization wire traversing the mass in CC and true lateral projections (C and D), and radiograph of the excised surgical specimen confirming excision of the mass along with biopsy clip and intact localization wire (E).

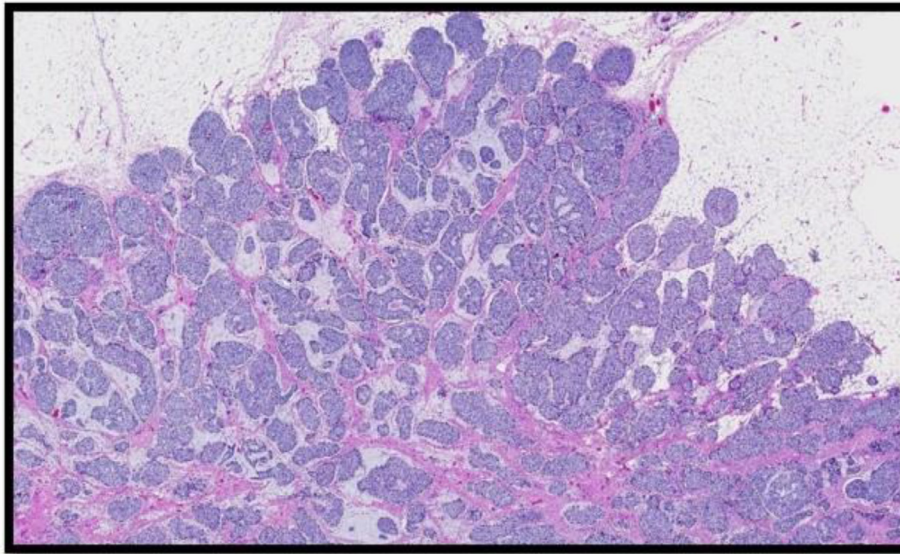


Fig. 4 – 20x magnification of H&E-stained sample collected from lumpectomy; nests of cells floating in lakes of mucin partitioned by delicate fibrous bands.

they have worse survival outcomes than their younger counterparts [17]. As the population in the United States continues to age, it is expected that there will be a commensurate increase in the number of women diagnosed with breast cancer, making understanding of effective treatment and management of breast cancer in the elderly essential. Breast cancer rates overall will rise in the United States through 2030, with yearly incidence predicted to rise to 441,000 by 2030 [18]. By 2030, it is estimated that the proportion of new breast cancer diagnoses in those aged 70-84 will increase from 24.3% in 2011 to 34.8% in 2030 [18]. Given the current trends toward increased screening and effectiveness of endocrine therapies,

deaths from breast cancer are predicted to decline despite the incidence increase [19]. The predicted trend toward greater breast cancer incidences in the elderly, with more ER-positive cancers and better survivability, emphasizes the importance of knowing the types of breast cancers more likely to occur in elderly populations and effective treatment options. The goals are to pursue effective treatment options in this population that improve survivability without the unwanted adverse side effects that more aggressive cancer therapies entail and, at the same time, to ensure the elderly population receives adequate treatment without having to compromise quality of life.

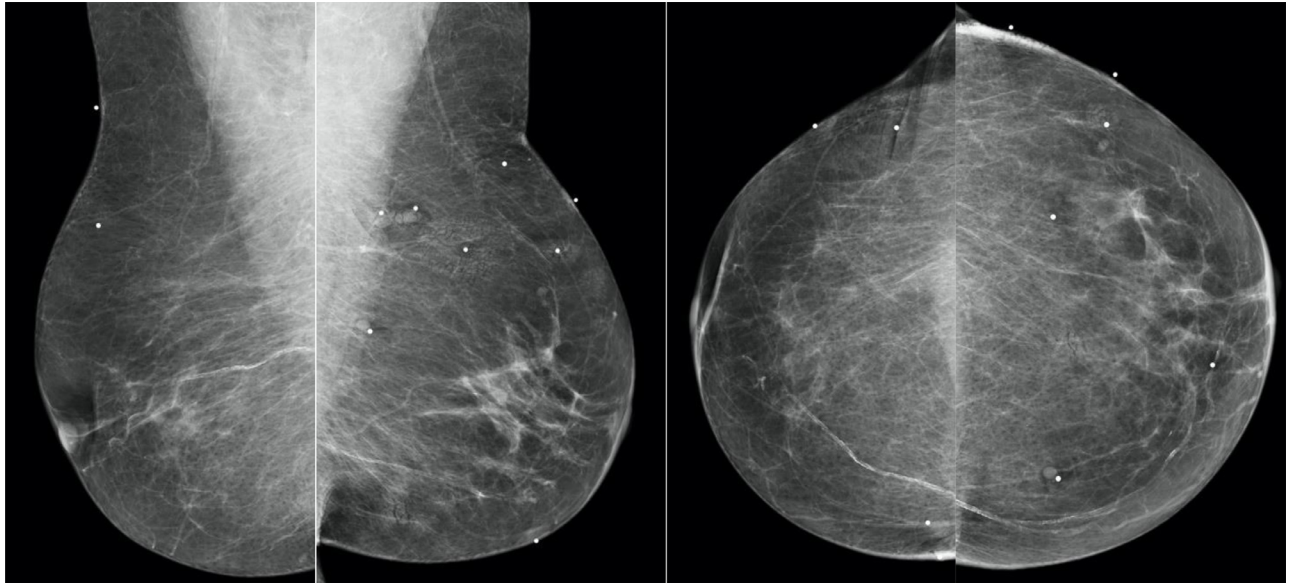


Fig. 5 – 2021 bilateral MLO and CC screening mammograms are normal, with mild post lumpectomy changes in the right breast with asymmetrically slightly smaller right breast and periareolar skin scar visualization.

Recent studies of particular impact in this patient cohort include the TAILORx study, Hughes trials, and CARG-BC score development. Treatment for breast cancer in elderly females differs from treatment in younger populations, largely due to biological changes in elderly females. Over 80% of primary breast cancer in the elderly are ER positive [20]; for hormone-sensitive breast cancers, the use of endocrine therapy, usually aromatase inhibitors or Tamoxifen, is recommended [21,22]. However, third-generation aromatase inhibitors (such as Anastrozole) have been demonstrated to be more effective, better tolerated, and now considered the treatment of choice in elderly patients with hormone positive breast cancer [23,24]. Adjuvant chemotherapy, a commonly used treatment for breast cancer in the general population, does not significantly improve 5-year survival or recurrence in the elderly, and is associated with a higher rate of toxicity in this population [25,26].

The TAILORx study published in 2018, studied 10,273 patients and found similar efficacy in adjuvant endocrine therapy and chemoendocrine therapy for hormone-receptor-positive, HER2-negative, axillary node-negative breast cancer, suggesting chemotherapy is not beneficial in this patient population [27]. The benefits of chemotherapy have mainly been observed in ER negative cases [28]. Though the benefits and tolerability of endocrine therapy does not depend on age, research has shown chemotherapy tolerability decreases with age [28,29]. The recent 2021 Cancer and Aging Research Group-Breast Cancer (CARG-BC) score has been developed as a risk calculation tool to predict chemotherapy toxicity in treatment of early stage breast cancer in the elderly; the goal is to make chemotherapy a safer and more accessible treatment option in this group [30].

Surgery remains the main treatment for breast cancer in all age groups, and guidelines indicate that elderly patients should be offered the same surgery as younger pa-

tients [28]. Elderly women with breast cancer have significantly better overall and cancer-specific survival when they received surgery, and surgery is the most important factor associated with better survival, more so than age, stage, and ER/PR/HER2 status [29]. Despite this, research has shown that the elderly are less likely to undergo surgery for breast cancer [30,31].

Management of the axilla is an important component of the care paradigm, with sentinel node biopsy typically not indicated in node negative women ≥ 70 years of age with early-stage hormone receptor positive, HER2 negative invasive breast cancer [31]. Similar survival statistics have been shown for women ≥ 70 years treated for ER+ HER2- breast cancer with negative and positive sentinel lymph node biopsy if patients received hormone therapy [32–34]. However, some studies argue that sentinel lymph node biopsy should not be eliminated altogether. A retrospective analysis of data from the National Cancer Database and Mayo Clinic Rochester found that approximately 15% of women with hormone receptor positive breast cancer aged 70+ were found to be node positive, with the proportion increasing as stage and grade increased [35]. This indicates that some elderly breast cancer patients may be undertreated when clinicians follow current treatment guidelines [36]. Furthermore, a recent study evaluating the effect of nodal surgery on survival found that patients 70+ with low grade ER+ cancer who received nodal surgery had significantly higher overall survival than those who didn't receive nodal surgery, even when stratifying by receipt of endocrine therapy [37]. Overall, tumor stage, patient comorbidities, receptor positivity, endocrine therapy, and potential complications of nodal surgery should be taken into consideration when deciding on individual treatment for locoregional spread.

Similarly, the care algorithm regarding radiation therapy is evolving. The Hughes study found a small improvement in

locoregional recurrence with the addition of radiation therapy to lumpectomy with Tamoxifen, so significant difference in terms of survival and thereby raised the question of the benefits versus morbidities associated with radiation therapy [14]. Two studies of elderly patients with early stage breast cancer and no nodal involvement found that radiotherapy has a significant, but modest, reduction in local recurrence, but did not impact overall survival [38,39]. Furthermore, no difference was found in ipsilateral breast tumor recurrence, BCSS, or overall survival between elderly patients with hormone receptor positive, node negative breast cancer who received breast conserving surgery with radiation or who received breast conserving surgery without radiation [37]. It has been reported that patients aged 70 years and older with low-risk early breast cancer breast conserving therapy can avoid breast irradiation with <3% chance of relapse [40]. Overall, these compiled studies point toward two potential views towards adjuvant radiation therapy: 1. adjuvant radiation therapy offers a potentially small benefit to prevent recurrence, but probably does not improve survival or 2. adjuvant radiation therapy offers no additional benefit when compared to other guideline adherent options. Either way, the overall benefit of radiation therapy is small or negligible, and risks and benefits should be considered with the patient to determine what is best on a case-by-case basis. Ultimately, these guidelines aim to provide elderly patients who have high survivability breast cancers subtypes with the most effective, least morbid treatment options while also ensuring patients are not over- or undertreated - a line that to some extent remains undetermined. Recommendations from the European Society of Breast Cancer Specialists and the International Society of Geriatric Oncology include the utilization of geriatric assessment tools as well as chemotherapy toxicity prediction tools to guide the use of more taxing treatments [41].

Conclusion

Mucinous carcinoma of the breast is often ER+/PR+ and carries a good prognosis and overall survival rate. The elderly has often been considered an undertreated population in the treatment of breast cancer. For early state, hormone receptor positive breast cancers in the elderly, breast conserving surgery with adjuvant administration of third-generation aromatase inhibitors is recommended. Axillary surgery, chemotherapy and radiation therapy may all be avoided given the appropriate clinical context.

Patient Consent Statement

Written informed consent for publication of this case was obtained from the patient and is available upon request. Additionally, the patient has received and approved the final version of this manuscript.

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