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#### Contents

Thrice Monthly Volume 11 Number 25 September 6, 2023

#### **REVIEW**

5840 Mechanism and recent updates on insulin-related disorders

Kumar S, Senapati S, Bhattacharya N, Bhattacharya A, Maurya SK, Husain H, Bhatti JS, Pandey AK

#### **MINIREVIEWS**

5857 Progress in the study and treatment of peri-device leak after left atrial appendage closure Oi YB, Chu HM

#### **ORIGINAL ARTICLE**

#### **Case Control Study**

- 5863 Application of lesser trochanteric reduction fixator in the treatment of unstable intertrochanteric fractures Hui YM, Zeng G, Liu PY, Chai B
- 5870 Risk factors for post-traumatic stress disorder among young and middle-aged cancer patients in the intensive care unit: A case-control study

Chen L, Wang GZ, Chi YY, Zhao J

#### **Retrospective Cohort Study**

Effect of different ventilation methods combined with pulmonary surfactant on neonatal acute respiratory 5878 distress syndrome

Qing Q, Zha P, Dai LY, Wang Y

#### **Retrospective Study**

5887 Hepatic MR imaging using IDEAL-IQ sequence: Will Gd-EOB-DTPA interfere with reproductivity of fat fraction quantification?

Tian Y, Liu PF, Li JY, Li YN, Sun P

5897 Conservative management of multi-trauma induced peritonitis: Experience, outcomes, and indications Chen Q, Zhu T, Liu JK, Ding J, Chen L

5903 Analysis of prognostic factors in patients with emergency sepsis

Ning XL, Shao M

#### **CASE REPORT**

5910 Clinicopathological study of malignant peripheral nerve sheath tumors in the head and neck: Case reports and review of literature

Li L, Ma XK, Gao Y, Wang DC, Dong RF, Yan J, Zhang R



<u> </u>	World Journal of Clinical Cases
Conten	ts Thrice Monthly Volume 11 Number 25 September 6, 2023
5919	Synchronous multiple lung cancers with hilar lymph node metastasis of small cell carcinoma: A case report
	Yoshino R, Yoshida N, Yasuda S, Ito A, Nakatsubo M, Yuzawa S, Kitada M
5926	Ultrasound-guided carotid angioplasty and stenting in a patient with iodinated contrast allergy: A case report
	Li L, Wang ZY, Liu B
5934	Parathyroid carcinoma: Three case reports
	Shi C, Lu N, Yong YJ, Chu HD, Xia AJ
5941	Median neuropathy after multiple punctures of the forearm for catheterization: A case report
	Suzuki T, Matsui Y, Momma D, Endo T, Iwasaki N
5947	Novel <i>COL4A3</i> synonymous mutation causes Alport syndrome coexistent with immunoglobulin A nephropathy in a woman: A case report
	Chen YT, Jiang WZ, Lu KD
5954	Non-retroareolar male mucinous breast cancer without gynecomastia development in an elderly man: A case report
	Sun Q, Liu XY, Zhang Q, Jiang H
5962	Autosomal dominant non-syndromic hearing loss caused by a novel mutation in <i>MYO7A</i> : A case report and review of the literature
	Xia CF, Yan R, Su WW, Liu YH
5970	Predicting apical hypertrophic cardiomyopathy using T-wave inversion: Three case reports
	Kang L, Li YH, Li R, Chu QM
5977	Bilateral thigh pyomyositis in an otherwise healthy middle-aged woman: A case report
	Cui M, Zhang G, Zhang N, Han L, Ma ZQ
5982	Creutzfeldt-Jakob disease presenting as Korsakoff syndrome caused by E196A mutation in <i>PRNP</i> gene: A case report
	Zhang YK, Liu JR, Yin KL, Zong Y, Wang YZ, Cao YM
5988	Incomplete distal renal tubular acidosis uncovered during pregnancy: A case report
	Seong EY, Kim DW, Kim HJ, Rhee H, Song SH
5994	Single omental metastasis of renal cell carcinoma after radical nephrectomy: A case report
	Chung JW, Kang JK, Lee EH, Chun SY, Ha YS, Lee JN, Kim TH, Kwon TG, Yoon GS
6000	Myeloid sarcoma as the only manifestation in a rare mixed lineage leukemia-fusion-driven acute myeloid leukemia: A case report
	Tang SJ, Zhang QG
6005	Carotid-cavernous fistula following mechanical thrombectomy of the tortuous internal carotid artery: A case report
	Qu LZ, Dong GH, Zhu EB, Lin MQ, Liu GL, Guan HJ



Conton	World Journal of Clinical Cases
Conten	Thrice Monthly Volume 11 Number 25 September 6, 2023
6012	Successful treatment of a case of COVID-19 pneumonia following kidney transplantation using paxlovid and tocilizumab
	Chen Q, Niu YL
6019	Diagnosis and treatment of Whipple disease after kidney transplantation: A case report
	Chen Q, Niu YL, Zhang T
6025	Monkeypox presenting as a chancre-like rash: A case report
	Zhu WF, Song SJ, Wei LW, Qiao JJ



#### Contents

Thrice Monthly Volume 11 Number 25 September 6, 2023

#### **ABOUT COVER**

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The primary aim of World Journal of Clinical Cases (WJCC, World J Clin Cases) is to provide scholars and readers from various fields of clinical medicine with a platform to publish high-quality clinical research articles and communicate their research findings online.

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CASE REPORT

# Non-retroareolar male mucinous breast cancer without gynecomastia development in an elderly man: A case report

Qiang Sun, Xu-Yan Liu, Qi Zhang, Hai Jiang

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## Abstract

#### BACKGROUND

Male breast cancer (MBC) is an extremely rare condition and accounts for less than 1% of all breast cancers, and malignant tumors occur in less than 1% of the affected men. Mucinous breast cancer is extremely rare and accounts for 2% of all invasive breast cancers. Generally, MBC is accompanied by a retroareolar mass.

#### CASE SUMMARY

Herein, we report a case of male mucinous breast carcinoma (MMBC) without gynecomastia development and with mass localization outside the common retroareolar region, wherein the mass was a painless nodule in the right breast of a 64-year-old man. We also discuss the clinical and pathological characteristics of this unusual tumor. The excised breast specimen showed pure mucinous carcinoma. The patient had strong expression of estrogen and progesterone receptors, a low Ki-67 proliferation index of the tumor cells, and negative pathological axillary lymph nodes. The patient underwent modified radical mastectomy and axillary lymph node dissection, followed by tamoxifen hormone therapy.

#### CONCLUSION

To the best of our knowledge, this is the first case report of MMBC in the nonretroareolar region of the nipple without gynecomastia development. Mucinous tumors are easily missed during diagnosis, and the incidence of axillary lymph node metastases of chest mucinous tumors has increased.

Key Words: Breast cancer; Male; Mucinous adenocarcinoma; Nipple; Case report

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**Core Tip:** We not only report a rare case, but also discuss the clinical and pathological characteristics of this unusual tumor. Though a summary of a limited number of cases and a comparison with female breast cancer, we reveal some interesting features of male mucinous breast cancer. It is helpful to distinguish the rare male disease.

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#### INTRODUCTION

Male breast cancer (MBC) is particularly uncommon, accounting for approximately 1% of all breast cancer cases[1-3]. Known risk factors for MBC include old age, high estradiol levels, Klinefelter's syndrome, radiation exposure, gynecomastia, family history of breast cancer, and Breast Cancer 1 protein (BRCA1) and BRCA2 mutations[4]. The most common malignancy in MBC patients is invasive ductal carcinoma, and mucinous carcinoma is extremely rare [5,6]. Anatomically, the male breast comprises the external nipple, areola, internal lymph nodes, adipose tissue, and ducts. The glandular portion of the male breast is located mainly posterior to the nipple-areola complex[7]. MBC occurrence most often involves remarkable gynecomastia development and a retroareolar mass [8-10]. We herein report a case of non-retroareolar male mucinous breast carcinoma (MMBC) without gynecomastia development and review similar cases documented in the literature.

#### **CASE PRESENTATION**

#### Chief complaints

A 64-year-old male presented at the hospital with a painless mass in the right chest for 4 mo.

#### History of present illness

The patient had a mass over the right lateral nipple for 4 mo, which grew from the size of a pea to the size of an egg yolk, without pain.

#### History of past illness

The patient with no history of smoking or drinking, no history of hepatitis, no history of cardiovascular disease, and no history of long-term drug use.

#### Personal and family history

There was no significant personal or family history.

#### Physical examination

The patient was 178 cm in height and 58 kg in weight, with body mass index (BMI): 18.3 kg/m<sup>2</sup>. Physical examination indicated an approximately 2.0 cm × 1.5 cm-sized nodule present 2.0 cm above the right lateral nipple.

#### Laboratory examinations

Serum six-sex hormone test revealed the following findings: (1) Follicle-stimulating hormone: 12.60 IU/L (normal: 1.27-19.26 IU/L); (2) Luteinizing hormone: 7.66 IU/L (normal: 1.24-8.62 IU/L); (3) Estradiol: 0.00 pg/mL (normal: < 25-38.95 pg/mL); (4) Testosterone: 3.37 ng/mL (normal: 1.75-7.81 ng/mL); (5) Prolactin: 16.83 ng/mL (normal: 2.64-13.13 ng/mL); and (6) Progesterone: 0.00 ng/mL (normal: 0.14-2.06 ng/mL).

#### Imaging examinations

Ultrasound examination revealed the following information: A subcutaneous hypoechoic lesion was located 2.0 cm from the nipple edge on the lateral side of the right nipple and had a size of approximately 1.88 cm × 1.13 cm, with clear borders and no blood flow signal within it. Computerized tomography (CT) reveals posterior nipple glands and postoperative defects from outpatient surgery (Figure 1).

### MULTIDISCIPLINARY EXPERT CONSULTATION

According to histopathological examination and immunohistochemistry analysis of the excised tissue, multidisciplinary consultation by the Department of Breast Surgery, Oncology, Ultrasound, and Pathology made the diagnosis - non-





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**Figure 1 Preoperative and postoperative imaging corresponding surgical specimen and pathology analysis.** A: Ultrasound image of the left breast region at the upper outer area of the nipple demonstrating a 1.88-cm oval, parallel isoechoic mass; B: Surgical specimens showing the position of the surgical scar; C: Computerized tomography reveals posterior nipple glands (the arrow points to the position where the back of the nipple is located); D: Postoperative defects from outpatient surgery (the arrow points to the location of the residual cavity after removal of the mass); E: Histopathological examination of the excised breast tissue showing a nodular lesion with relatively clear borders in the breast. Homogeneous clusters of tumor cells containing small nuclei together with slightly larger round nuclei were suspended in abundant mucus material (mucus lake). The tumor invaded the surrounding adipose tissue and muscle tissue and did not invade the skin or subcutaneous tissue. The ductal tissue of the breast was visible in the periphery, and no intraductal cancer changes were seen (hematoxylin-eosin, 200 ×); F: Pathology of the nipple and posterior nipple, and no cancerous tissue invasion was seen in the nipple and subpapillary ducts, and Paget's changes were not seen in the skin (hematoxylin-eosin, 20 ×).

retroareolar MMBC without gynecomastia (Figure 2).

#### **FINAL DIAGNOSIS**

The patient was given the diagnosis of male mucinous breast carcinoma.

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Figure 2 Pathology and immunohistochemistry analysis. A: Image showing clusters of tumor cells suspended in abundant extracellular mucin and separated by ciliated fibrous intervals containing capillaries; B: Estrogen receptor (2+); C: Progesterone receptor (2+); D: AR (-); E: Ki-67 (5%); F: CerbB-2 (-) (scale: 100 µm; 200 ×).

#### TREATMENT

Examination and ultrasound revealed a mass located anterior to the pectoralis major fascia that can be differentiated from a muscle-derived mass. Subcutaneous fibroadenomas are slow growing and occasionally painful. In gynecomastia, the masses are mostly located behind the nipple and are not very well defined with a soft texture. Lymphomas, which are located in the chest 2.0 cm from the nipple in a non-normal lymphatic anatomical location, are more difficult to distinguish and require pathological analysis for identification. The outpatient surgeon diagnosed a possible benign fibroadenoma, which was surgically removed on December 12, and found the tumor lacked a capsule and the specimen was brittle. According to histopathological examination and immunohistochemistry analysis of the excised tissue, multidisciplinary consultation by the Department of Breast Surgery, Oncology, Ultrasound, and Pathology made the diagnosis - non-retroareolar MMBC without gynecomastia. The patient was hospitalized and underwent modified radical mastectomy (MRM) for breast cancer on December 30, 2022, Intraoperatively, the gynecomastia was seen to be very thin, but the area was equivalent to that of a female. Pathological return: No cancerous tissue invasion of the nipple and pectoralis major fascia, peri-cancerous breast: Granulomatous inflammation, postoperative lymph nodes: 0/20 (extrapectoralis minor 0/19; post-pectoralis minor 0/1), pT2N0M0.

#### OUTCOME AND FOLLOW-UP

Postoperative axillary and supracostal arch drains were less than 20 mL for three consecutive days starting on postoperative day 6 and were removed on day 9. The patient had no adverse complaints. The flap hemorrhage in the operative area was normal. Perioperative care was equivalent to that of female breast cancer (FBC) and no significant discomfort for the patient during treatment. Tamoxifen (20 mg/d) was administered as adjuvant therapy (Figure 3). The patient was followed up every three months in the outpatient clinic. The follow-up tumor marker carbohydrate antigen 153 fluctuated in the fifth month, and CT and ultrasound showed no abnormality.

#### DISCUSSION

MBC occurrence in men accounts for less than 1% of all breast cancer cases, and malignant tumors develop in less than 1% of affected men[11]. Different risk factors concurrently impact MBC development, including clinical disorders related to hormonal imbalance, such as obesity, testicular disease, and radiation exposure; suspected epidemiological risk factors are prostate cancer, prostate cancer treatment, occupational exposure, dietary factors, and alcohol intake[12]. By contrast, carrying a BRCA2 mutation confers a lifetime risk for MBC to the male carrier, which is approximately 80-100 times





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#### Figure 3 Timeline of disease course.

higher than that in the general population[13]. The rate of mucinous adenocarcinoma of all invasive breast drops from 4% to 2%[2,14]. Mucinous breast cancer rarely occurs in men. A single-center trial retrospectively assessed 16868 breast cancer patients over 10 years, with 72 cases of MBC accounting for 0.42% of the total patient population and six cases of mucinous adenocarcinoma accounting for 8.33% of the total MBC patient population[15].

The presence of extracellular mucin on microscopic observation is the basis for the microscopic diagnosis of mucinous breast cancer, defined as pure mucinous cancer and mixed mucinous cancer (MMC) at a cutoff of 90%. MMC can be further differentiated into partially mixed mucinous adenocarcinoma and mixed mucinous adenocarcinoma at a cutoff of 50%. Immunohistochemistry analysis revealed that the expression of estrogen and progesterone receptors was positive, and that of the androgen receptor was negative.

A 71-year-old MBC patient was treated by a physician in Virginia in the 1970s[16]. Although he had bilateral breast cancer, the pathology was not fully documented. However, searches for PubMed, several cases of male mucinous breast cancer cases have been successfully treated in recent decades. We have summarized and analyzed mucinous adenocarcinoma cases among men (Table 1). As assessed using hematoxylin-eosin staining, all patients had mucinous adenocarcinoma[8-10,17-22]. In one case, the lesion type was mixed invasive ductal carcinoma (IDC) component[17], and in another case, the lesion type was concurrent breast mucinous carcinoma and extramammary lymphoma[8]. The patient's age ranged from 35 to 83 years, with a mean age of 69.3 years. The history of onset ranged from 2-96 mo, with a median time of nearly 12 mo, and swelling of the retroareolar region is the main factor for tumor development. No significant difference was noted in the location of the masses to the left and right (four left and five right). All of them were located posterior to the nipple-areolar region, except for one case wherein the mass was present in the axillary position. The mass diameter was used as a statistical criterion, with a minimum value of 13 mm, a maximum value of 95 mm, and a mean diameter length of 44.5 mm. Four of the eight patients who reported lymph node metastasis had combined lymph node metastasis (50%). HER-2/CerbB-2 was tested in four patients with non-amplified or negative expressions. BRCA testing was negative in two patients with combined diffuse large B-cell tumors and those with an IDC component. All patients had MRM at the correct location. A Japanese patient underwent MRM after two resections of enlarged masses within a period of 3 years until the fifth year, which was when the mass recurred and showed ipsilateral axillary lymph node enlargement[22]. Postoperative adjuvant therapy revealed the following findings: All patients were treated with tamoxifen hormone therapy, and two patients with positive axillary lymph nodes received radiotherapy; chemotherapy combined with hormone therapy was observed in four patients before 2010 but not in four patients after 2010. Patients underwent follow-up for a maximum of 60 mo and a minimum of 8 mo after surgery, and no recurrence or metastasis was reported during the postoperative period of MRM, regardless of whether they had combined axillary lymph node metastases.

Having presented the case, we now move on to discuss the broader implications and findings. In summary, the median age of onset of mucinous adenocarcinoma in men is above 70 years. The history of onset of MMBC patients is longer than a year, and the average mass size is greater than 40 mm; however, MMBC is frequently overlooked. The chief complaint and the primary clinical manifestation of patients are swelling behind the nipple region or skin changes in the nipple region. Patients with axillary metastatic lymph nodes had a predominantly 1-year history and a smaller average mass size than the other patients; hence, it cannot be speculated that the length of history and mass size are the key factors attributed to the occurrence of lymph node metastasis. Generally, the trend in postoperative adjuvant therapy has switched from chemotherapy combined with endocrine therapy before 2010 to predominantly hormone therapy alone after 2010, considering that it was influenced by the treatment of luminal-type FBC, while the treatment strategy changed the same. All patients had better prognoses than men with nonspecific breast cancer. Previous case reports have shown that the retroareolar mass usually occurs with gynecomastia and is in the inner margin of the nipple[22]. Another case of

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Ref.	Country	Age (yr)	Case history (yr)	Laterality	Past history	Tumor max- diameter	Tumor location	Pathology characteristic	Lymphatic metastasis	ER	PR	HER2/CerbB- 2	KI67 %	BRCA	Surgery	Adjuvant therapy	DFS (mo)
Fujikawa <i>et al</i> [ <mark>20]</mark> , 1998	Japan	35	2	Right	Negative	80	Areola	М	Negative	Positive	Positive	None	None	None	MRM	C + TAM	30
Peschos <i>et al</i> [ <b>19</b> ], 2008	Greece	83	None	Left	None	70	Areola	М	None	Positive	Positive	None	None	None	MRM	C + TAM	None
Hammedi <i>et al</i> [ <mark>10]</mark> , 2010	Tunisia	75	2 mo	Right	Negative	40	Areola	М	Positive + 2	Negative	Positive	Negative	None	None	MRM	C + R + TAM	36
Dragoumis <i>et al</i> [ <mark>21</mark> ], 2012	Greece	59	1	Right	Negative	30	Areola	М	Positive	Positive	Positive	Negative	None	None	MRM	C + R + TAM	74
Imakado and Masuda <mark>[22]</mark> , 2012	Japan	72	3	Left	Negative	20	Areola- aside	М	Positive	Positive	Positive	None	None	None	MRM	ТАМ	60
Gupta <i>et al</i> [ <mark>18</mark> ], 2015	India	73	8	Right	Negative	95	Areola	М	Negative	Positive	Positive	Middle 2	11	None	MRM	TAM	8
Kim and Lee[8], 2021	Korean	78	1	Left	Negative	35	Areola	M + B-cell	Positive + 2	None	None	None	None	Negative	MRM	C + TAM	11
Takahashi <i>et al</i> [17], 2021	Japan	75	None	Right	Sister breast cancer	13	Axilla	M + IDC	Negative	Positive	Positive	Negative	33	Negative	MRM	TAM	24
Ahmed <i>et al</i> [9], 2022	United States	74	1	Left	Thyroid cancer	18	Areola	М	Negative	None	None	None	None	None	MRM	TAM	48

ER: Estrogen receptor; PR: Progesterone receptor; BRCA: Breast cancer susceptibility gene; DFS: Disease free survival; TAM: Tamoxifen; MRM: Modified radical mastectomy; M: Mastectomy; C: Chemotherapy; R: Radiotherapy.

mucinous breast cancer combined with Paget's disease also had a nipple-centered clinical presentation[17]. We present the first case of MMBC in the non-retroareolar region of the nipple. The patient had no evident signs of gynecomastia, and the mass was located on the upper outer nipple at an easily misdiagnosed distance. The absence of cancerous tissue in the nipple and posterior glands confirmed this finding. Similar to this finding, Mizutani *et al*[23] reported a rare case of cutaneous mucinous adenocarcinoma in a 78-year-old man. In the fourth year of follow-up review after prostate cancer treatment, an abnormally enlarged axillary lymph node (10 mm) was found, and a whole-body examination revealed the presence of a 30-mm-sized mass in the patient's inner upper right chest. For several years, the patient complained of a mass in the right chest but did not pay close attention to it; eventually, the mass was surgically excised as a benign 1-cm margin plus axillary lymph node dissection, and no breast tissue was found in the pathological specimen, but the enlarged axillary lymph node, which was the patient's chief complaint, demonstrated mucinous adenocarcinoma metastasis [23]. This led to the following conclusions: (1) Mucinous tumors are easily missed; and (2) The incidence of axillary lymph node metastases of chest mucinous tumors is higher than that anticipated. Considering the previously mentioned three surgical recurrence cases in Japan<sup>[22]</sup> and the 50% rate of axillary lymph node metastasis in cases of male mucinous adenocarcinoma, as summarized here, MRM, including treatment for axillary lymph nodes, is an essential treatment approach for MMBC patients. Because of the rarity of MBC, most of the affected patients have not been assessed in treatment studies in past studies; therefore, treatment strategies for MBC have been largely extrapolated from evidence for FBC[24,25]. Based on immunohistochemical characteristics, mucinous adenocarcinoma of the male breast is equivalent to the luminal-type treatment strategy for postmenopausal FBC<sup>[26]</sup>.

In our case, the patient's gynecomastia symptoms are not visible because of the patient's low BMI and the absence of fat encapsulation in the gland beneath the skin. The patient was considered to have an atypical clinical presentation of MMBC, and MRM is essential. Because of the strong expression of the hormone receptors (estrogen and progesterone receptors), low tumor cell proliferation index indicated by Ki67, and negative pathological axillary lymph nodes, the patient would have a well-predicted prognosis. A 5-year outpatient follow-up with endocrine treatment is required.

#### CONCLUSION

We encountered a rare case of MMBC. It was difficult to differentiate from MBC because the patient had no representative clinical indications of gynecomastia, and the mass was located distant from the nipple region. A diagnosis of male mucinous breast cancer should be considered, even when the body surface mass on the male chest is not located in the retroareolar region, and MRM and endocrine treatment is necessary.

#### FOOTNOTES

Author contributions: Sun Q designed the proposal and drafted the manuscript; Liu XY participated in immunohistochemical stain and analysis; Jiang H and Sun Q carried out the ultrasound analysis; Sun Q participated in data collection; Sun Q, Zhang Q, Liu XY, and Jiang H participated in total data analysis; and all authors read and approved the final manuscript.

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