

## Clinical Case and Literature Analytical Review of Metaplastic Breast Cancer

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### Abstract

*Basis: metaplastic mammary cancer is a rare type of tumor with high aggressiveness of mammary gland cancer, and skin scarring (wound formation) causes much more complexity in clinical practice, dramatically reducing the patient's quality of life. Today, there are no standard treatment guidelines for the treatment of metaplastic breast cancer, and this skin-related condition associated with breast tumors limits treatment options. Diagnosis: in this article we will provide information on the effectiveness of metaplastic mammary gland cancer and skin scarring in the treatment of a patient with exudation(detachment) and acute odor based on his immunogystochemical and molecular-genetic profile. Intervention: in a lawsuit with docetaxel + carboplatin AUK 5.5, the patient showed severe pain in the patient after taking Course 3, increased bleeding marks in the injured area, no change in the tumor was observed when evaluated. When treated by changing the scheme to CAP (Endoxan, doxorubicin, carboplatin) +bevasizumab(based on the molecular-genetic examination profile), there was a complete end to the skin wound and a decrease in the size of the tumor.In the next stage, the patient was treated with radical mastectomy and radiation therapy. Result: The patient's quality of life improved after complex treatment, the patient's condition improved, and the disease regressed. Conclusion: This study showed that the treatment of metastatic breast cancer should be based on immunohistochemical and molecular-genetic profiling, and that this approach yields good results.*

Keywords: Metastatic breast cancer, Case report, bevacizumab, CAP regimen.

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## 1. Introduction

Today, mammary cancer in women is considered a malignant tumor with the highest frequency of occurrence in the world. And is one of the main causes of the highest cancer-related mortality rate in women. Metastatic breast cancer is a rare, highly aggressive form of breast cancer that accounts for 0.12-0.35% of all breast cancers. One of the most common symptoms of metastatic breast cancer is a painless, large breast lump. Skin scarring occurs when mammary tumor cells proliferate and skin invasion occurs, and this condition can often be accompanied by tumor bleeding, varying degrees of pain, various secretions (exudation), and an unpleasant odor. Skin lesions not only reduce the patient's quality of life, but also reduce the likelihood of radical mastectomy and prevent radical treatment. In this situation, we observed that studying the patient's immunohistochemical and molecular-genetic

profile and conducting treatment based on this gave good results, even achieving disease regression in the patient.

### Clinical case description

Patient Kazakbaeva Musallam was born in 1964. In 2021, she noticed a small lump in her left breast, but did not seek medical attention. In April 2022, the patient was referred to the Republican Specialized Scientific and Practical Medical Center of Oncology and Radiology with a tumor that had broken down, an open wound, and bleeding (Figure 1). The patient underwent a general examination at the hospital, including breast ultrasound, mammography, breast MRI, biopsy, molecular-genetic and immunohistochemical examinations. After the examinations, the patient was diagnosed with C50.4 – Left breast cancer, cT4N1M0, stage III, clinical group II. Was diagnosed with tumor breakdown (necrosis), metaplastic carcinoma.



**Figure 1. Metastatic breast cancer with tumor necrosis**

### Examination results:

**Visual:** A necrotic center with an oval-shaped ulcer with a diameter of 4.0 cm is described in the upper-outer quadrant of the left breast, closer to the areola. The skin around the

wound is hyperemic and infiltrated. The size of the mammary glands is slightly increased. During palpation in the wound zone, a dense formation with uneven contours measuring 5.0 X 5.0 cm is felt.

**Ultrasound examination from 20.04.22 years:** in the left mammary gland, under the sucker (areola), a tumor (tumor) derivative with a volume of 53.1 x 21.7 x 25.6 mm is detected in the central part. The shape is an irregular oval. The contours are uneven. Calcifications up to 2.2 mm in diameter were detected. In the axillary lymph nodes, infiltrated oval-shaped formations with dimensions up to 10x8 mm on the right and up to 32x21 mm on the left, with uneven contours, hypoechoic. Conclusion: signs of a volumetric formation of the left breast, lymphadenopathy in the left axillary region (BI-RADS 5 on the left).

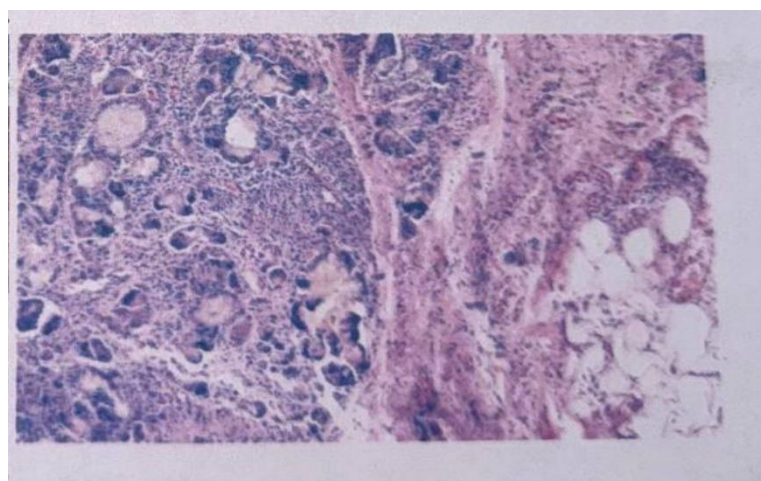
**25.04.22 years Breast MRI:** in the subareolar parts of the left breast. Single-volume images, irregularly ovoid in shape, with a clearly uneven contour, measuring 5.0 x 4.0 cm and 1.4 x 1.0 cm, with high signal on DWIBS. Left axillary region lymph nodes up to 3.0 cm, with high signal on DWIBS. Signs of mastopathy on the right.

**Mammography 25.04.22 years conclusion:** A mass, calcification, and microcalcification are detected in the left breast. BI-RADS-5-changes are characteristic of breast cancer.

BIOMARKER	VAF (%)	APPROVED TREATMENTS FOR PATIENT DISEASE	BIOMARKER SCORE	OTHER TREATMENTS	DRUG APPROVAL	BIOMARKER SCORE	TRIALS
TMB-L Mut/Mb: 2.36	-	No therapies or clinical trials related to this biomarker					
MS-stable Score: 2.63	-	No therapies or clinical trials related to this biomarker					
KMT2C p.W1056* Exon 20 of 59	8.47	No approved therapy identified for the patient disease		<a href="#">E</a> Fulvestrant <a href="#">E</a> Olaparib	Off-label	2	0
KMT2C p.Y816* Exon 14 of 59	13.08			<a href="#">E</a> Bevacizumab <a href="#">E</a> Adavosertib <a href="#">E</a> VEGFR inhibitors	Off-label	2	0
TP53 p.C135Y Exon 5 of 11	4.38	No approved therapy identified for the patient disease				2	0

**Immunohistochemical examination:** Bcatenin-positive, Vimentin-positive. Ki-67 - 80 %. ER-negative, PR-negative, CD34-negative, CD10-positive. Summary:

Metaplastic carcinoma. ICD-O: 8575/3- metaplastic carcinoma, NOS.



**Histological examination (Figure 3)**

**Histological examination: Undifferentiated sarcomatous tumor of the left breast**

nodes - epithelial cell atypia is detected. CT scans of the head, chest, and abdomen did not reveal distant metastases. The large breast tumor was painless, but the patient's quality

Cytological examination: puncture of the axillary lymph

of life was relatively reduced due to the discharge and unpleasant odor in the area of the skin wound. The ECOG functional status level is 0. The patient was discussed at a consultation consisting of a chemotherapy specialist, a radiologist, and an oncomammologist. Taking into account the following: Based on the results of the comprehensive examination, the pathohistological report, and the results of the immunohistochemical (IGX) study, a diagnosis of metaplastic carcinoma was made. According to the council's decision, the patient was prescribed neoadjuvant chemotherapy (nPXT). Treatment regimen: Docetaxel + Carboplatin with AUK 5.5, a total of 4 courses were conducted, and a review was scheduled by the council. However, after the patient received the 3rd course, the patient experienced severe pain and increased bleeding in the affected area, and no changes were observed in the tumor during the assessment (Figure 4). The patient was discussed at the re-Concilium and recommended to undergo a total of up to 6 courses, changing the treatment scheme to CAP (Endoxan, doxorubicin, carboplatin) +bevasizumab (based on molecular-genetic profile). (TP-53 was added to bevasizumab target therapy due to a positive mutation (when patients with a positive TP53 mutation will be vgf-

diagnosed and thus bevasizumab target is sensitive to the drug molecular-genetic examination based on the profile)) 2 course examination after receiving chemotherapy, the patient observed a decrease in the area injured in the control dynamics. There is no hyperemia of the skin around the wound, and palpation of the wound reveals a 1x1.5 cm mass. (Figure 5) The patient feels much better, and his quality of life has been restored. The result after the last course of chemotherapy: it can be seen that the skin wound is completely over and the skin tightens (retraction), no hyperemia is observed around it (Figure 6). Contrast-enhanced MRI of the breast showed complete resolution of the tumor. Patient condition and quality of life have also been greatly improved. For this reason, it was made sure to switch to the next treatment stage. The patient was examined by mammologists and a radical mastectomy was prescribed for surgery. On 29.09.22, a radical mastectomy was performed on Madden. According to the results of histological examination of the surgical material, it was proven that the tumor had completely disappeared. (There are clearly expressed fibrosis, hemosiderosis, and foci of granulomatous inflammation.

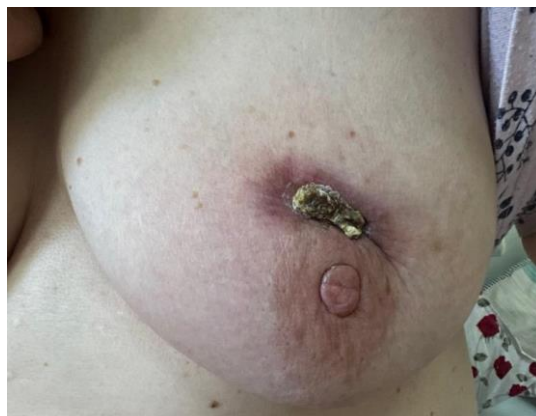


**Figure 4. No change in the tumor was observed with increasing bleeding.**



**Figure 5. Condition after 3-course CAP+bevacizumab regimen**

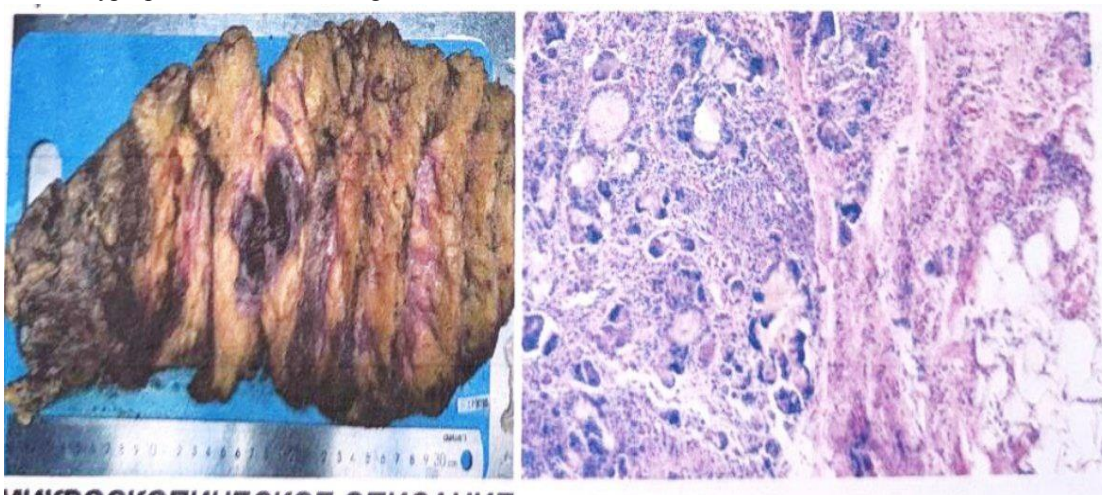
DCIS (intraductal, i.e. in situ component within the mammary tract) — was not detected.



**Figure 6. Condition after 6-course CAP+bevacizumab regimen**

One fibrosis furnace has been recorded. Prevalence: skin — negative. The suction is negative. Resection margins: All resection margins (superior, inferior, posterior, lateral, medial) are intact (without tumor cells). Regional lymph nodes: Reactive hyperplasia and stromal angiomatosis were

detected in 21/21 lymph nodes. Intravascular invasion: Not noted. Pathological stage (pTNM, AJCC 8th edition): ypT0N0Mx. RCB: RCB-0 (pCR — complete pathological response). (Figure7)



**Figure 7. Operative material and histological appearance of the tumor**

The patient was prescribed radiation therapy (50 Gray SOD) and capecitabine 6-week regimen (14 days on, 7 days off) after surgery. The patient has been taking 300mg of Jack Russell terrier and is observed every 3 months. The following examinations were carried out when the patient came last in the observation for 2 years.

**Scintigraphy (06.02.2025):** No metastatic (migratory) tumor foci were detected in the skeletal bones.

**MRI of the lumbar and sacral spine (26.09.2025):** Signs of degenerative changes (i.e., spinal disc degeneration -

osteochondrosis) were detected in the lumbar and sacral spine. The L5 vertebra is partially fused to the sacrum on the left side.

**MRI of the pelvic organs (09.09.2025):** No pathological structures or changes were detected in the pelvic organs.

**MSCT of the chest organs (09.09.2025):** Post-mastectomy (breast removal) from the left side. No focal or inflammatory (infiltrative) changes were detected in the lungs.

**CT scan of the abdominal organs (09.09.2025):** Signs of chronic cholecystitis (inflammation of the gallbladder). A cyst (a cavity filled with liquid) was detected in the right kidney.

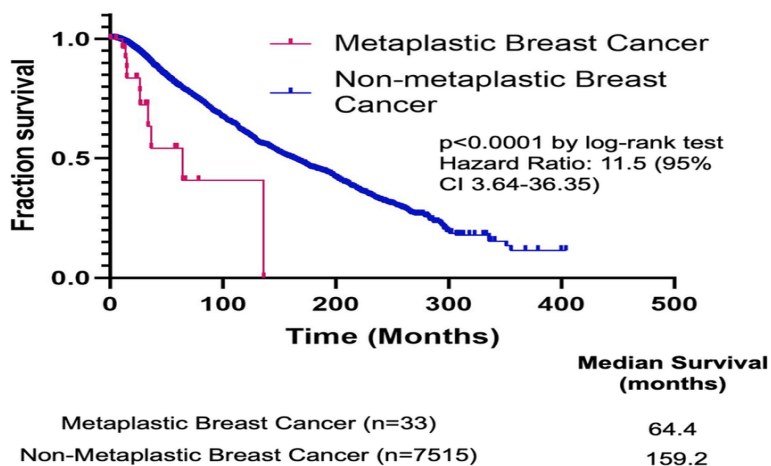
**MRI of the brain (09.09.2025):** No pathological changes were detected in the brain tissue. The patient achieved disease regression.

**2. Discussion**

In 2022, an estimated 2.3 million women worldwide were diagnosed with breast cancer. An estimated 670,000 women died from the disease that year. 1 in 20 women (i.e. ~5%) will develop breast cancer in their lifetime. If current trends continue, new cases are expected to reach 3.2 million annually by 2050, and deaths are expected to reach 1.1 million.[1] The incidence rate of breast cancer in Uzbekistan was ~11.2 / 100,000 women (2019). At the same time, despite the low detection rate of the disease, the mortality rate was noted to be close to that of developed countries. Metastatic breast cancer (MBC) is a rare, highly aggressive pathological type of breast cancer characterized by high levels of heterogeneity.(15) The incidence of MBC

was reported to have increased from 0.12 to 0.35 per 100,000 women. The mortality rate increased from 0.01 to 0.12 [1]. Metaplastic mammary gland cancer (MTR): occurs in 0.2–5% of cases, is extremely aggressive, with an average life expectancy of 10-13 months after the detection of metastasis (mts). Pathomorphology: consists of epithelial and mesenchymal structures. It is mainly low-grade and basal-like (90% ER-/PR-, HER2-). TP53 (>60%) and PIK3CA (>40%) gene mutations are common. Metastases to regional lymph nodes are less common (15–20%), which is lower than for invasive NST (no-special type) carcinoma. The likelihood of hematogenous metastasis is high (metastatic form in 10% of cases from the onset of the disease). It is most common in squamous cell and ductal cell histotypes. The risk of metastasis in MTR is twice as high as in typical breast cancer. There is a low susceptibility to chemotherapy, but there have been reported cases of effective treatment with targeted (target) and immunotherapy methods in the literature. There is currently no specific pathognomic mutation in metaplastic mammary gland cancer.

**Overall Survival**



Metaplastic mammary gland cancer (MBC) is a rare but very aggressive species. It is often large-celled, sarcomatoid, or mixed-structure. This tumor is resistant to conventional chemotherapy regimens and has a poor prognosis, with a 5-year survival rate of around 35–50%. In clinical practice, this type is often confused with triple-negative breast cancer (TNBC), but its molecular profile is different. The goal of the study is to improve the quality of life of patients by improving the diagnostic and treatment approaches to this disease. Typically has a triple-negative (ER-, PR-, HER2-) phenotype. Is low-sensitivity (chemoresistant) to chemotherapy. Survival (survival) rates

are much lower than other species: 5-year total survival: 50-60% at Triple-negative MBC: 35-40% most common in women aged 45-65 years. According to the latest classification of the World Health Organization for female reproductive system and breast tumor diseases, MBC is divided into 6 subtypes:

1. squamous cell carcinoma (SCC),
2. spindle cell carcinoma,
3. low-grade SCC,

4. mesochemically differentiated metaplasia carcinoma,
5. fibromatosis metaplasia carcinoma,
6. mixed metaplasia carcinoma.

Currently, in clinical practice, the Vogts and Norris classification is widely used, according to which MBC is divided into 5 subtypes: spindle cell carcinoma, SCC, carcinosarcoma, stromal carcinoma, osteoclast giant cell carcinoma [3]. The most common subtype in Western countries is spindle cell carcinoma, while in Eastern countries it is SCC. The pathological tumor of this patient was a mixed heterogeneous form of metaplastic carcinoma and adenocarcinoma, which is very rare in clinical practice. The pathology of the metaplastic carcinoma was of the SCC type. The most common clinical presentation of MBC is a painless breast mass, and lymph node metastases are uncommon.[4-6] pathological features of MBC are usually triple negative (triple negative).[7-9] In this patient, the breast tumor was large but painless at the onset of the disease, and the pathological features were consistent with the literature. Regarding the prognosis of breast metaplasia, there is generally the following opinion. Compared to triple negative breast cancer, we can see that the prognosis of MBC is even worse, which has a more invasive nature, making it much more likely to relapse as well as give distant metastases [3]. Because most patients with MBC are triple-negative, they are unlikely to achieve complete regression from hormone therapy or post-operative targeted therapy. In addition, MBC is considered to have low sensitivity to chemotherapy. Although anthracyclines have been recommended for the treatment of MBC in previous studies,[9] there is still no standard systemic treatment regimen for MBC. In this case, there was no change in the tumor in the breast after three-cycle chemotherapy with docetaxel + carboplatin AUK 5.5, which may be related to the patient's tumor heterogeneity. A positive effect was observed when treated by modifying the CAP (Endoxan, doxorubicin, carboplatin) +bevasizumab(based on the molecular-genetic examination profile) scheme, which suggests that this treatment method can be effective if treatment is carried out in heterogeneous breast cancer with metastatic carcinoma mainly to the immunogystochemical and molecular profile. Skin ulcers in breast cancer are a complex clinical problem that occurs due to the relentless growth of the tumor and damage to the skin. Skin ulcers associated with cancer are usually accompanied by bleeding, fluid discharge from the ulcer, persistent pain, and a sharp unpleasant odor; such conditions negatively affect the patient's mental state and quality of life, further

aggravating their condition. Sometimes in severe cases, skin wounds over a long period of time bitmaydi.Va, damage to necrossed tissue by bacteria or other infections can lead to the development of sepsis, as well as the development of a death condition as a result of aggressive and rapid growth of the tumor. Skin ulcers, which are common in some types of breast cancer, not only severely reduce the mental state and quality of life of patients, but also complicate treatment. Currently, antitumor therapies such as chemotherapy, hormone therapy, immunotherapy, targeted therapy, and surgery are the main methods for treating skin wounds. In addition, long-term chemotherapy, radiotherapy, and other treatments can cause or exacerbate skin ulcers (if not based on molecular-genetic profiling and immunohistochemical profiling). For example, paclitaxel has been found to cause skin ulcers.[11] Experimental studies have shown that paclitaxel causes skin ulcers in mice, and the severity of the ulcers is positively correlated with the dose of paclitaxel.[12] There are currently few clinical trials for breast cancer with skin lesions, but several case reports have been published. For example, a 31-year-old patient was diagnosed with advanced breast cancer, a skin lesion of a t4bn3bm0-stage tumor, while the patient was treated with 4 cycles of cyclophosphamide, epirubicin and 5-FU, and 4 cycles of paclitaxel and rapamycin targeted therapy. The patient achieved partial remission and had a significant improvement in quality of life; no recurrence was observed 1 year after radical mastectomy.[13] Another 68-year-old patient was also studied who had received long-term trastuzumab (>400 times) and aromatase inhibitors, resulting in a >9-year disease-free survival.[14] A complex treatment including chemotherapy, radiotherapy, surgery, and skin grafting was performed on an elderly patient with a large breast tumor and severe skin lesions. The tumor was removed and the severe skin ulcer healed. Although the tumor recurred after 1 year, the patient's quality of life was significantly improved.[15]

Because MBC is a rare and highly invasive tumor, prospective studies are scarce. Most of the available data are based on retrospective studies, and there are currently no clinical guidelines for the standard treatment of MBC. Therefore, in clinical practice, it is necessary to choose the optimal treatment method that is appropriate for the individual situation of each patient. It was considered that examining the patient's immunohistochemical and molecular-genetic profile and conducting treatment based on this could help achieve better results. In this case, after the combination of the patient's breast tumor CAP (Endoxan, doxorubicin, carboplatin) +bevasizumab(based on the molecular-genetic examination profile), a complete

end to the skin wound and a decrease in tumor size were observed. This suggests that CAP (Endoxan, doxorubicin, carboplatin) +bevasizumab(based on molecular-genetic examination profile) may have a good therapeutic effect in breast cancer patients with skin ulcers.

In conclusion, the tests carried out by our patient, based on the results of the treatment, should pay attention to the following when treating the patient: treatment of metaplastic mammary gland cancer should be carried out based on clinical recombinations, immunogystochemical and molecular-genetic profile; triple negative and metaplastic mammary cancer differ from each other in molecular profile, cell composition and sensitivity to chemotherapy; The main treatment for metaplastic mammary gland cancer is surgical treatment in the early stages, chemotherapy, immunotherapy and target therapy in late and diffuse cases; the appointment of a systematic claim in non-removable or metastatic metaplastic mammary gland cancer should be determined based on the immunogystochemical, molecular-genetic and immunological profile of the tumors; In our clinical case presented above, the patient's first-line treatment with a triple-negative breast cancer-like regimen (Docetaxel+Carboplatin) did not yield results. When an anthracycline-based circuit is applied (CAP (Endoxan, doxorubicin, carboplatin) +bevasizumab (when TP-53 is positive)), it can be seen that the Resultate is very good, even if the patient has observed complete regression.

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