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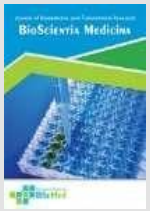

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Achieving Resectability in Giant Primary Breast Leiomyosarcoma Via Transarterial Chemoembolization: A Novel Neoadjuvant Strategy

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A B S T R A C T

Background: Primary leiomyosarcoma (LMS) of the breast is an exceptionally rare and aggressive non-epithelial malignancy, constituting less than 0.1% of all breast neoplasms. Due to the scarcity of cases, no standardized consensus exists regarding neoadjuvant protocols. Large, locally advanced tumors often present with chest wall fixation, rendering upfront resection difficult or impossible without extensive morbidity. This study explores the novel application of Transarterial Chemoembolization (TACE)—traditionally reserved for hepatic malignancies—as a neoadjuvant strategy to downstage a giant breast LMS. **Case presentation:** We present the case of a 40-year-old female presenting with a rapidly enlarging, painless, giant mass in the right breast measuring 19 x 18 x 15 cm. Clinical and radiological evaluation (CT Thorax) revealed a heterogeneous, hypervascular mass fixed to the pectoralis major muscle, classified as BIRADS 5. Core needle biopsy confirmed high-grade Leiomyosarcoma. Due to the tumor's size and fixation to the chest wall, the patient underwent preoperative TACE using 35 mg Doxorubicin followed by embolization of the supplying branches of the right internal mammary and thoracoacromial arteries. Post-procedure, the tumor volume significantly decreased (downsized to approx. 15 cm), and critically, the mass detached from the chest wall, becoming mobile. The patient subsequently underwent a successful total mastectomy with clear margins (R0 resection). **Conclusion:** TACE offers a promising, minimally invasive neoadjuvant alternative for hypervascular, giant breast sarcomas. By inducing tumor necrosis and reducing vascularity, TACE can facilitate resectability in initially fixed tumors, potentially converting inoperable cases into candidates for R0 resection while minimizing intraoperative blood loss.

1. Introduction

Breast cancer remains the most prevalent malignancy among women globally, with the vast majority of cases being epithelial in origin, specifically invasive ductal or lobular carcinomas.[1] However, lurking in the shadows of these common carcinomas is a heterogeneous group of non-epithelial malignancies arising from the mesenchymal connective tissue of the breast: the primary breast sarcomas (PBS). These tumors are distinct clinical and pathological entities, accounting for less than 1% of all breast malignancies and fewer than 5% of all soft tissue sarcomas worldwide.[2] Unlike carcinomas, which spread via the lymphatic system to regional nodes, breast sarcomas exhibit a predilection for hematogenous dissemination, bypassing the axilla to seed the lungs, liver, and bones directly.

Within this rare subset of mesenchymal neoplasms, primary leiomyosarcoma (LMS) of the breast stands out as an exceptionally uncommon

diagnosis.[3] While leiomyosarcomas are frequently encountered in the uterus, gastrointestinal tract, or retroperitoneum, their occurrence as a primary tumor in the breast is a pathological curiosity, documented largely through sporadic case reports rather than large-scale registry data. The precise cell of origin for primary breast LMS remains a subject of academic debate; it is hypothesized to arise either from the smooth muscle cells lining the vascular, lymphatic, or nipple-areolar complex structures or potentially from the myoepithelial cells via a process of dedifferentiation. Regardless of its origin, the clinical behavior of breast LMS is characterized by aggressive local growth and a high propensity for recurrence, presenting a formidable challenge to the surgical oncologist.[4]

The rarity of this pathology presents a significant challenge to the oncological community, as there are no randomized controlled trials to guide management.[5] Consequently, current treatment protocols are largely extrapolated from data on soft tissue sarcomas of the extremities or retroperitoneum, rather than breast-specific guidelines. The cornerstone of curative treatment for primary breast LMS remains surgical resection with wide negative margins (R0 resection). Unlike breast carcinomas, where margin width is debated in the context of millimeters, sarcomas require a distinct cuff of healthy tissue to prevent the high rates of local recurrence associated with positive or "close" margins.[6]

However, the anatomical constraints of the breast and chest wall often complicate this surgical objective. Patients with high-grade leiomyosarcomas frequently present with "giant" tumors—defined as exceeding 10 cm in diameter—due to the rapid doubling time characteristic of these aggressive mesenchymal malignancies. By the time of presentation, these massive tumors have often distorted the normal breast architecture entirely and, more critically, have invaded the deep fascial planes. In cases of giant tumors (>10 cm) or those presenting with fixation to the thoracic wall (involving the pectoralis major, pectoralis minor, intercostal muscles, or even ribs), achieving an R0 resection is surgically treacherous.

The surgeon is faced with a difficult binary choice: proceed with a standard mastectomy that risks leaving microscopic disease behind (R1/R2 resection) due to the tumor's adherence to the chest wall, or perform an upfront radical en bloc chest wall resection.[7] The latter, while oncologically sound, is a morbid procedure involving the removal of ribs and soft tissue, necessitating complex reconstruction with myocutaneous flaps and prosthetic mesh. Furthermore, these hypervascular giant tumors are associated with significant intraoperative hemorrhage, increasing the perioperative risk for the patient. Therefore, the concept of "downstaging"—reducing the tumor's size and vascularity before definitive surgery—becomes paramount in the management of these complex cases.

In the realm of carcinomas, neoadjuvant chemotherapy (NACT) is a well-established standard to downstage locally advanced tumors. However, the efficacy of systemic NACT in soft tissue sarcomas is far less predictable.[8] The standard regimens, typically Anthracycline (Doxorubicin) and Ifosfamide-based, yield variable response rates in leiomyosarcomas. A significant physiological barrier limits the effectiveness of systemic therapy in giant sarcomas: the tumor microenvironment itself.

Large sarcomas often develop a chaotic, inefficient vasculature with high interstitial fluid pressure and extensive areas of central necrosis. This "necrotic core" is poorly perfused, preventing systemic chemotherapy agents from reaching the tumor cells in cytotoxic concentrations. To achieve adequate intratumoral drug levels, one would have to escalate the systemic dose to levels that induce severe toxicity, such as myelosuppression, cardiomyopathy (a known risk of Doxorubicin), and renal failure. Consequently, many patients with giant leiomyosarcomas progress through systemic chemotherapy or suffer toxicity without achieving the structural regression needed to facilitate surgery. This therapeutic deadlock highlights an urgent unmet need for localized, high-intensity treatments that can bypass systemic limitations.[9]

Enter transarterial chemoembolization (TACE), a technique borrowed from the interventional radiology playbook for hepatocellular carcinoma (HCC). TACE is a minimally invasive locoregional therapy that capitalizes on the specific vascular anatomy of tumors. The procedure involves catheterizing the arterial branches feeding the tumor and injecting a high concentration of chemotherapy directly into the tumor bed, followed immediately by the injection of embolic agents (such as particles, beads, or foam) to occlude the vessels. This approach creates a powerful "double hit" therapeutic effect: (1) High Local Drug Concentration: By infusing chemotherapy directly into the afferent artery, the concentration of the drug within the tumor tissue can be 10 to 100 times higher than what is achievable via intravenous administration, maximizing the cytotoxic effect on the tumor cells while minimizing systemic exposure and side effects; (2) Ischemic Necrosis: The subsequent embolization cuts off the blood supply, inducing acute hypoxia and starvation of the tumor cells. This is particularly devastating to high-grade sarcomas, which have high metabolic demands. Furthermore, the cessation of blood flow prevents the "washout" of the chemotherapy drug, trapping it within the tumor tissue for a prolonged duration (the "dwell effect").

Despite its established success in visceral oncology (liver and kidney tumors), the application of TACE for extra-hepatic soft tissue sarcomas—specifically in the breast—is novel and significantly under-reported in medical literature. The breast receives its blood supply primarily from the internal mammary artery and the lateral thoracic artery, vessels that are amenable to super-selective catheterization. This anatomical accessibility suggests that the breast is, in theory, an ideal site for locoregional endovascular therapy, particularly for hypervascular tumors like leiomyosarcoma.[10]

Current literature on the use of TACE for breast malignancies is sparse, generally limited to salvage therapy for recurrent metastatic disease or palliative bleeding control. There is a paucity of data regarding its utility as a neoadjuvant strategy to convert inoperable or borderline-resectable primary breast sarcomas into resectable candidates. This manuscript aims to bridge this gap by documenting a rare and complex case of a giant (19 cm) primary breast leiomyosarcoma that was initially fixed to the chest wall. We describe the successful implementation of preoperative TACE as a strategic maneuver to induce tumor necrosis, reduce tumor volume, and critically, detach the tumor from the underlying pectoralis muscle. We provide a comprehensive analysis of the pathophysiological rationale, the detailed interventional technique, and the surgical outcome. By presenting this case, we aim to propose TACE not merely as a palliative option, but as a viable, active neoadjuvant strategy in the multidisciplinary algorithm for giant, hypervascular breast sarcomas, potentially redefining resectability in cases previously deemed surgically prohibitive.

2. Case Presentation

A 40-year-old premenopausal female presented to the Surgical Oncology outpatient clinic of a tertiary referral center with a chief complaint of a grotesque, massive lump occupying her entire right breast. The clinical timeline was notable for the explosive velocity of the tumor's growth (Table 1). The patient reported first identifying a small, palpable nodule, described as "marble-sized" (approximately 2 cm), located in the upper outer quadrant of the right breast only three months prior to consultation. Over this short interval, the mass underwent an aggressive acceleration phase, expanding relentlessly to the size of a soccer ball.

The subjective experience of the patient provided crucial diagnostic clues distinguishing this pathology from inflammatory breast carcinoma or abscesses. Despite the massive distortion of the breast architecture, the patient reported a remarkable absence of deep, visceral, or nociceptive pain. She described the sensation primarily as a "heavy, dragging discomfort" caused by the physical weight of the tumor pulling on the chest wall. This clinical feature is consistent with the pathophysiology of sarcomatous growth, which typically displaces

peripheral nerves rather than infiltrating the perineural sheaths—a behavior often seen in invasive ductal carcinomas. A comprehensive review of systems yielded negative results for constitutional "B-symptoms." There was no history of fevers, chills, or night sweats, ruling out systemic infectious etiologies or lymphoproliferative disorders like lymphoma. Furthermore, the patient had maintained a stable weight, suggesting the absence of the cancer cachexia often associated with metastatic burdens. A detailed pedigree analysis revealed no family history of breast, ovarian, or soft tissue malignancies across two generations, making a hereditary cancer syndrome (such as BRCA1/2 mutation or Li-Fraumeni Syndrome) less likely. The patient was nulliparous and had no history of hormonal contraception use or hormone replacement therapy. Crucially, she had no history of prior thoracic radiation therapy (such as for Hodgkin's lymphoma), which is a known risk factor for radiation-induced angiosarcoma of the breast.

Upon admission, the patient's general condition was preserved, with hemodynamic parameters within normal limits (Blood Pressure 120/80 mmHg, Heart Rate 88 bpm), indicating that the tumor, despite its size, had not yet induced high-output cardiac failure or systemic shock. On inspection, the physical deformity was profound. A giant, multilobulated mass occupied the entirety of the right breast, obliterating the normal anatomical landmarks. The overlying skin displayed classic signs of extreme vascular demand and lymphatic congestion. There was marked peau d'orange (edema of the dermis), not due to lymphatic tumor emboli as seen in inflammatory carcinoma, but rather due to mechanical obstruction of lymphatic return by the sheer bulk of the tumor. Prominent, dilated, tortuous subcutaneous veins (caput medusae appearance) were visible, mapping across the superior hemisphere of the breast, indicating significant collateral blood flow recruitment to feed the hypermetabolic neoplasm. On the inferomedial aspect, an area of pressure necrosis had evolved into an active ulcerative lesion with friable granulation tissue and contact bleeding, a consequence of the tumor outgrowing its cutaneous blood supply. The nipple-areola complex was completely effaced and distorted laterally. On palpation, the dimensions were clinically estimated at 19 x 18 x 15 cm. The consistency was heterogeneously firm—stony hard areas corresponded to viable solid tumor, while softer, fluctuant areas likely represented intratumoral hemorrhage or cystic degeneration. The most critical finding for surgical planning was the mobility assessment. On bimanual examination, the mass was fixed to the deep structures. Maneuvers to contract the pectoralis major (hands-on-hips press) confirmed that the tumor did not move independently of the muscle, indicating deep fascial invasion and fixation to the chest wall. Palpation of the regional nodal basins (axillary, supraclavicular, and infraclavicular) revealed no lymphadenopathy. This clinical finding is a hallmark distinction of breast sarcomas compared to carcinomas; sarcomas spread primarily via the hematogenous route and rarely metastasize to regional lymph nodes (<5% of cases), sparing the patient the need for axillary lymph node dissection.

A comprehensive biochemical profile was obtained to assess the patient's fitness for intervention (Table 2). Hemoglobin was 10.2 g/dL. This mild microcytic anemia was attributed to chronic disease status and intermittent bleeding from the ulcerative lesion. Leukocytes were 8,500/µL, and platelets were 350,000/µL, ruling out paraneoplastic leukemoid reactions or marrow suppression. Liver enzymes (AST 22 U/L, ALT 25 U/L) and renal function (Creatinine 0.7 mg/dL, eGFR >90 mL/min) were within normal limits. These values were pivotal, as normal renal function is a prerequisite for the administration of iodinated contrast media during both CT imaging and the TACE procedure. PT and APTT were normal, ensuring the safety of femoral arterial puncture. Contrast-enhanced Computed Tomography (CT) of the thorax provided a roadmap for therapy. The scan visualized a massive, heterogeneously enhancing soft tissue mass replacing the right breast parenchyma, measuring 18.93 x 15.74 x 19.10 cm.

Table 1. Summary of clinical findings on admission.

CATEGORY	CLINICAL FINDING	CLINICAL SIGNIFICANCE
Patient Profile	40-year-old female, Premenopausal	*Young age for malignancy; premenopausal status relevant for hormonal assessment.*
Chief Complaint	Massive right breast lump with explosive growth (marble to soccer-ball size in 3 months)	*Rapid doubling time suggestive of high-grade sarcoma rather than typical carcinoma.*
Symptomatology	"Heaviness" and dragging sensation. **Absence** of deep nociceptive/visceral pain.	*Suggests displacement of peripheral nerves (pushing border) rather than perineural infiltration.*
Constitutional Symptoms	No fever, no night sweats, no weight loss.	*Rules out systemic lymphoma (B-symptoms) or advanced cancer cachexia.*
Oncological Risk Factors	Nulliparous, no hormonal contraception, BRCA negative (pedigree), no prior radiation.	*Absence of typical carcinoma risk factors; absence of radiation excludes radiation-associated angiosarcoma.*
Vital Signs	BP 120/80 mmHg, HR 88 bpm.	*Hemodynamically stable despite massive tumor burden.*
Local Inspection	Giant multilobulated mass, *peau d'orange*, dilated subcutaneous veins (caput medusae), active ulceration with bleeding.	*Indicative of extreme vascular demand (collateral recruitment) and mechanical lymphatic obstruction.*
Local Palpation	19 x 18 x 15 cm. Heterogeneously firm consistency. **FIXED** to pectoralis major and chest wall.	***Critical Finding:** Fixation indicates deep fascial invasion, classifying the tumor as unresectable/T4 upfront.*
Lymphatic Status	No palpable axillary, supraclavicular, or infraclavicular lymphadenopathy.	*Consistent with sarcomatous spread (hematogenous) rather than carcinoma (lymphatic).*

The tumor exhibited a "sunburst" pattern of enhancement, with a vividly enhancing periphery representing viable, hypervascular tissue, and a large central hypodense area representing spontaneous necrosis due to rapid growth outstripping angiogenesis. In the axial and sagittal planes, the retromammary fat space was completely obliterated. The posterior margin of the tumor showed an indistinct, irregular interface with the pectoralis major muscle, strongly suggesting macroscopic invasion. While there was no frank destruction of the cortical bone of the ribs, the proximity of the tumor to the

intercostal spaces raised concerns for chest wall integrity during resection. High-resolution lung windows revealed no pulmonary nodules, confirming the disease was locally advanced but non-metastatic (M0). The radiological features were classified as BIRADS 5 (Highly Suggestive of Malignancy). To guide the neoadjuvant strategy, a core needle biopsy was performed under ultrasound guidance. Hematoxylin and Eosin (H&E) staining revealed a high-grade malignant neoplasm composed of spindle-shaped cells arranged in intersecting fascicles (herringbone pattern). The cells displayed significant nuclear pleomorphism, coarse chromatin, and a high mitotic rate. Final diagnosis in this case was primary high-grade leiomyosarcoma of the right breast (cT4N0M0).

Table 2. Pre-procedural diagnostic evaluation and diagnosis.

PARAMETER / MODALITY	RESULT / FINDING	CLINICAL INTERPRETATION & SIGNIFICANCE
I. BIOCHEMICAL & HEMATOLOGICAL PROFILE		
Hemoglobin	10.2 g/dL	*Mild anemia attributed to chronic disease status and intermittent bleeding from tumor ulceration.*
Organ Function	Creatinine: 0.7 mg/dL (eGFR >90) LFTs: Normal	*Patient fit for iodinated contrast administration and chemotherapy clearance.*
Coagulation Profile	PT / APTT: Normal	*Ensures safety for femoral arterial puncture during TACE.*
II. RADIOLOGICAL IMAGING (CT THORAX WITH CONTRAST)		
Tumor Dimensions	18.93 x 15.74 x 19.10 cm	*Giant tumor volume replacing entire breast parenchyma.*
Morphology	Heterogeneous "sunburst" enhancement with large central hypodensity.	*Suggests viable hypervascular periphery with extensive central necrosis due to rapid growth.*
Invasion Status	Indistinct posterior margin with pectoralis major.	***Strongly suggestive of macroscopic muscle invasion (Chest Wall Fixation).***
Staging (M-Status)	No pulmonary nodules.	*Locally advanced disease without distant metastasis (M0).*
III. HISTOPATHOLOGY (CORE NEEDLE BIOPSY)		
Microscopy	High-grade malignant spindle cells in fascicular (herringbone) pattern.	*Characteristic morphology of sarcoma; high mitotic rate noted.*
FINAL DIAGNOSIS: Primary High-Grade Leiomyosarcoma of the Right Breast (cT4N0M0)		

The case was discussed at the multidisciplinary tumor board (MDT). The consensus was that upfront surgery would likely result in an R1 (microscopically positive) or R2 (macroscopically positive) resection due to the chest wall fixation (Table 3). Furthermore, the hypervascular nature of the tumor posed a risk of massive intraoperative hemorrhage. Systemic chemotherapy was considered, but given the large necrotic core and the typically poor perfusion of giant sarcomas, TACE was selected as a novel neoadjuvant "bridge to resectability". The procedure was performed in the angiography suite by an interventional

radiologist. Under local anesthesia (2% Lidocaine), a 5-French vascular sheath was introduced via the right common femoral artery using the Seldinger technique. A 5-French catheter was advanced into the aortic arch and utilized to selectively catheterize the right subclavian artery. Digital subtraction angiography (DSA) was performed, revealing a dramatic "tumor blush"—a dense cloud of contrast enhancement signifying the tumor's rich vascular bed. The angiogram mapped the arterial supply, identifying hypertrophied feeder branches arising primarily from the right internal mammary artery (RIMA) and the thoracoacromial artery. The lateral thoracic artery also contributed minor feeders. To minimize collateral damage to the skin and healthy chest wall tissues, a microcatheter (2.7-French) was coaxially advanced super-selectively into the specific tumoral feeder branches. Once a stable position was achieved, Doxorubicin (35 mg) diluted in 20 mL of saline was infused manually over 30 minutes. The intra-arterial route ensured the tumor was bathed in a high concentration of the anthracycline, maximizing the cytotoxic effect on the spindle cells. Immediately following the chemotherapy infusion, embolization was performed to trap the drug and induce ischemia. Polyvinyl alcohol (PVA) particles, sized 300-500 microns, were mixed with contrast and injected under fluoroscopic guidance. This specific particle size was chosen to occlude the distal arteriolar bed of the tumor without passing through to the pulmonary circulation. The procedure was terminated when the "pruning" effect was visualized—complete stasis of contrast flow in the feeding vessels and the total disappearance of the tumor blush on control angiography. The patient was monitored for 24 hours. She developed a mild "Post-Embolization Syndrome," characterized by a low-grade fever (37.8°C) and transient, aching pain in the right breast, caused by the acute ischemic necrosis of the tumor tissue. This was managed conservatively with oral paracetamol and tramadol. Importantly, there was no evidence of systemic toxicity; complete blood counts remained stable with no leukopenia or thrombocytopenia, confirming the systemic safety of the locoregional approach.

One month post-TACE, the patient returned for re-evaluation four weeks after the procedure, allowing time for the inflammatory response to subside and the necrotic process to mature. The physical changes were striking. The previously tense, rock-hard tumor had become noticeably softer. The skin ulceration, previously active and bleeding, had formed a dry eschar with granulation tissue at the edges. The most clinically significant finding, however, was the change in mobility. On palpation, the mass was no longer fixed to the chest wall; it could be manually displaced independently of the pectoralis muscle contraction. This "de-tethering" effect suggested that the invasive interface between the tumor and the muscle had undergone necrosis and fibrotic retraction. Repeat CT Thorax demonstrated a measurable reduction in tumor volume. The dimensions had decreased to 15.45 x 11.3 x 13.45 cm, representing a volumetric reduction of approximately 40%. Morphologically, the scan showed a more defined demarcation between the posterior aspect of the tumor and the pectoralis major muscle. A distinct fat plane, previously obliterated, was now visible in several areas, confirming the downstaging from "fixed/unresectable" to "mobile/resectable."

Based on the favorable response—specifically the conversion from fixed to mobile status—the patient was cleared for curative-intent surgery. The patient underwent a right total simple mastectomy. A wide transverse Stewart incision was designed to encompass the nipple-areola complex, the previous biopsy tract, and the inferomedial ulceration site, ensuring all potentially contaminated skin was removed. Skin flaps were raised to the clavicle superiorly, sternum medially, latissimus dorsi border laterally, and rectus sheath inferiorly. Upon reaching the deep plane, the utility of the TACE became evident. The tumor was found to be encapsulated within a fibrous pseudocapsule. Although there were dense adhesions to the pectoralis fascia, these were fibrotic rather than infiltrative. Unlike the pre-TACE state,

where the tumor was "stuck" to the muscle, the surgeon was able to dissect the tumor off the pectoralis major muscle using electrocautery without needing to resect the muscle itself or the underlying ribs. A remarkable feature of the surgery was the minimal blood loss (<300 mL). The pre-operative embolization of the RIMA and thoracoacromial feeders had effectively devascularized the tumor, turning what is typically a bloody operation into a dry field. The wound was irrigated, and two suction drains were placed in the axilla and sternal gutter. The skin was closed primarily without tension.

Macroscopic examination revealed the explanted specimen revealed a large, circumscribed mass. On the cut section, extensive areas of yellow-grey necrosis were observed, estimated to involve 60-70% of the tumor volume. This extensive necrosis was consistent with the ischemic and cytotoxic effects of the TACE. On microscopic examination, sections from the viable areas confirmed the diagnosis of high-grade Leiomyosarcoma. The necrotic areas showed ghost cells and fibrosis. The most critical oncological metric was achieved: all surgical margins—superior, inferior, medial, lateral, and deep (posterior)—were free of tumor cells (R0 Resection). The deep margin, which was the area of greatest concern, was clear, validating the decision to spare the chest wall. The patient's recovery was uncomplicated. Drains were removed on postoperative day 3, and she was discharged home. She was subsequently referred to radiation oncology for adjuvant chest wall radiotherapy to further reduce the risk of local recurrence.

Table 3. Follow-up, treatment strategy, and clinical outcome.

TIMELINE / PHASE	INTERVENTION & FINDINGS	CLINICAL OUTCOME & SIGNIFICANCE
PHASE I: NEOADJUVANT INTERVENTION (SEPT 30, 2024)		
Procedure	**Transarterial Chemoembolization (TACE)** *Agents:* Doxorubicin 35mg + PVA Particles (300-500μm)	*Targeted delivery to RIMA and Thoracoacromial arteries.*
Immediate Response	Disappearance of tumor blush on angiography.	*Successful devascularization; minimal post-embolization syndrome observed.*
PHASE II: 1-MONTH POST-TACE ASSESSMENT		
Clinical Status	Tumor softened; skin ulcer granulated. **Became MOBILE** (detached from chest wall).	***Critical Milestone:*** *Conversion from "Fixed/Unresectable" to "Mobile/Resectable".*
Radiological Status	Size reduced to 15.45 x 11.3 cm. Distinct fat plane visible with pectoralis major.	*Achieved **~40% Volumetric Reduction** (Downstaging).*
PHASE III: DEFINITIVE SURGICAL MANAGEMENT		
Surgery	**Right Total Simple Mastectomy** with *en bloc* pectoralis fascia resection.	*Fibrotic adhesions allowed dissection without chest wall resection.*
Intraoperative	Encapsulated tumor; minimal blood loss (<300 mL).	*TACE effectively reduced vascularity, minimizing surgical morbidity.*
PHASE IV: FINAL PATHOLOGY & OUTCOME		
Macroscopic Pathology	Extensive central necrosis (est. 60-70%).	*Confirms cytotoxic and ischemic efficacy of the TACE procedure.*
Margin Status	Deep, Superior, Inferior, Medial, Lateral margins negative.	***R0 RESECTION ACHIEVED*** *(Curative intent successful).*
Discharge Plan	Discharged Day 3; Referred for Adjuvant Radiotherapy.	*Rapid recovery due to avoidance of radical chest wall resection.*

3. Discussion

Primary leiomyosarcoma (LMS) of the breast is an extremely rare and distinct clinicopathological entity, representing a diagnostic and therapeutic outlier within the spectrum of breast malignancies.[11] Unlike the prevalent carcinomas that arise from the epithelial lining of the ducts or lobules, LMS originates from the mesenchymal stromal elements. The exact cellular progenitor remains a subject of debate in pathology literature; however, the prevailing consensus points to the smooth muscle cells lining the vascular or lymphatic channels (vascular leiomyosarcoma) or the smooth muscle bundles inherent to the nipple-areola complex (stromal leiomyosarcoma). A subset of cases may also arise from the myoepithelial cells via a mechanism of divergent differentiation, although this is less common.[12]

Crucially, primary breast LMS lacks an epithelial component entirely. This absence is the linchpin of its diagnosis and differentiates it from its two primary mimics: Malignant phyllodes tumor and metaplastic carcinoma (also known as sarcomatoid carcinoma). This differentiation is not merely academic; it dictates the entire therapeutic algorithm. Malignant Phyllodes tumors, while fibroepithelial, typically behave differently regarding chemosensitivity. Metaplastic Carcinomas, despite their sarcomatoid appearance, are fundamentally carcinomas and may require taxane-based regimens and axillary staging, which are unnecessary for pure sarcomas (Figure 1).[13]

Therefore, the accurate diagnosis requires a rigorous histopathological examination supplemented by a targeted panel of immunohistochemical markers. A misdiagnosis can lead to catastrophic under-treatment (such as omitting wide margins) or over-treatment (such as unnecessary axillary lymph node dissection).[14] In our case, the histopathological evaluation played a decisive role. The confirmation of LMS via biopsy provided the biological justification for utilizing Doxorubicin, an anthracycline with established efficacy against smooth muscle sarcomas, rather than standard breast cancer regimens like Paclitaxel or Trastuzumab, which would have been ineffective against this mesenchymal target.

The surgical management of breast sarcomas is governed by a set of biological rules distinct from carcinomas.[15] Carcinomas typically grow via infiltration, sending microscopic tentacles into the surrounding breast tissue, which necessitates margins of millimeters. In contrast, high-grade sarcomas, such as LMS, tend to grow with a "pushing" border. As the tumor expands rapidly, it compresses the surrounding normal tissue, creating a pseudocapsule of reactive fibrosis and compressed parenchyma. While this pseudocapsule may appear to delineate the tumor, it is a treacherous boundary for the surgeon. The pseudocapsule is often infiltrated by microscopic tumor satellites; thus, "shelling out" the tumor along this plane almost invariably results in positive margins and rapid local recurrence. When these tumors exhibit explosive growth—becoming "giant" tumors exceeding 10 cm—they breach the anatomical compartmentalization of the breast.

In the case presented, the tumor's dimensions (19 x 18 x 15 cm) meant it had physically occupied the entire breast envelope and, more critically, had compressed and invaded the deep fascial planes of the pectoralis major muscle. The primary prognostic factor for survival in breast sarcoma is the status of the surgical margin. Studies have repeatedly shown that positive margins are associated with a local recurrence rate as high as 60%, and local recurrence is a harbinger of distant metastasis and death.[16]

Consequently, when a patient presents with a giant tumor fixed to the chest wall, the surgeon faces a debilitating dilemma: (1) Perform a standard mastectomy: This risks cutting through the tumor at the point of fixation (R1/R2 resection), virtually guaranteeing recurrence; (2) Perform a radical en bloc chest wall resection: This involves removing the breast, the pectoralis muscles, and the underlying ribs/intercostal spaces. While oncologically sound, this is a highly morbid procedure associated with significant pain, "flail chest" physiology, and the need for complex plastic reconstruction using mesh or flaps. This binary choice—recurrence versus

mutilation—highlighted the urgent need for a strategy to "downstage" the tumor, retracting it from the danger zone of the chest wall.

Transarterial chemoembolization (TACE) is a cornerstone therapy for Hepatocellular Carcinoma (HCC), but its application in extra-hepatic sarcomas represents an innovative translation of interventional radiology techniques to surgical oncology.[17] The mechanism of action in our patient can be understood as a synergistic "double-hit" phenomenon, combining high-dose cytotoxicity with acute ischemic necrosis. Systemic chemotherapy for giant sarcomas is limited by the "first-pass" metabolism in the liver and the dilution of the drug in the total blood volume. To achieve a lethal concentration within a massive, poorly perfused tumor, one would have to administer systemic doses that are toxic to the bone marrow and heart. By catheterizing the feeding arteries (RIMA and Thoracoacromial), TACE delivers the chemotherapy (Doxorubicin) directly into the tumor bed. This results in an intratumoral drug concentration estimated to be 10 to 100 times higher than what is achievable via systemic intravenous administration. This hyper-concentration overwhelms the cellular efflux pumps that typically confer multidrug resistance to sarcoma cells, maximizing tumor kill while sparing the systemic organs (specifically reducing Doxorubicin-induced cardiomyopathy).

The second, and perhaps more critical, mechanism is the embolization. Sarcomas are angiogenesis-dependent tumors; their rapid growth requires a constant, high-volume blood supply.[18] The injection of polyvinyl alcohol (PVA) particles physically occludes the arterioles feeding the tumor. This induces acute hypoxia, which is lethal to the highly metabolic sarcoma cells. Furthermore, by stopping the blood flow, the embolization prevents the "washout" of the chemotherapy drug. The Doxorubicin is effectively trapped within the tumor tissue for a prolonged period (the "dwell effect"), extending the duration of cytotoxicity from minutes to days.

In our patient, this mechanism was clinically validated. The radiological finding of a massive central necrotic core post-procedure confirms the ischemic efficacy. More importantly, the clinical finding of the tumor becoming "mobile" is directly attributable to the necrosis of the invasive leading edge. The tumor cells infiltrating the pectoralis fascia are dependent on the neovasculature derived from the chest wall perforators. Embolizing these vessels caused the invasive front to necrose and retract, creating a plane of separation that allowed for the preservation of the chest wall.

While TACE is the gold standard for intermediate-stage hepatocellular carcinoma, its use in extra-hepatic sarcomas is limited to sporadic case series. A previous study reported on TACE for advanced soft tissue sarcomas, noting a response rate, but few studies focus specifically on the breast. The current standard of care for neoadjuvant therapy in soft tissue sarcomas is the AIM protocol (Doxorubicin + Ifosfamide + Mesna). However, the literature indicates that the response of leiomyosarcomas to systemic chemotherapy is variable and often modest. A major physiological limitation of systemic therapy in giant tumors is interstitial hypertension. Large tumors develop high internal pressure that prevents systemic drugs from diffusing from the capillaries into the tumor center. Consequently, the drug circulates systemically—causing neutropenia, hair loss, and nausea—without shrinking the tumor effectively.[19]

Our case demonstrates a paradigm shift. TACE provided a rapid volumetric reduction (40% in one month) with virtually no systemic toxicity. There was no leukopenia, no thrombocytopenia, and no cardiac dysfunction. This suggests that TACE could be a superior alternative for specific subsets of patients: (1) Those with giant (>10cm) hypervascular tumors where systemic drug delivery is poor; (2) Patients who are poor candidates for aggressive systemic chemotherapy due to age or comorbidities; (3) Cases requiring urgent local control to prevent fungation, sepsis, or catastrophic hemorrhage from ulcerated lesions.[20]

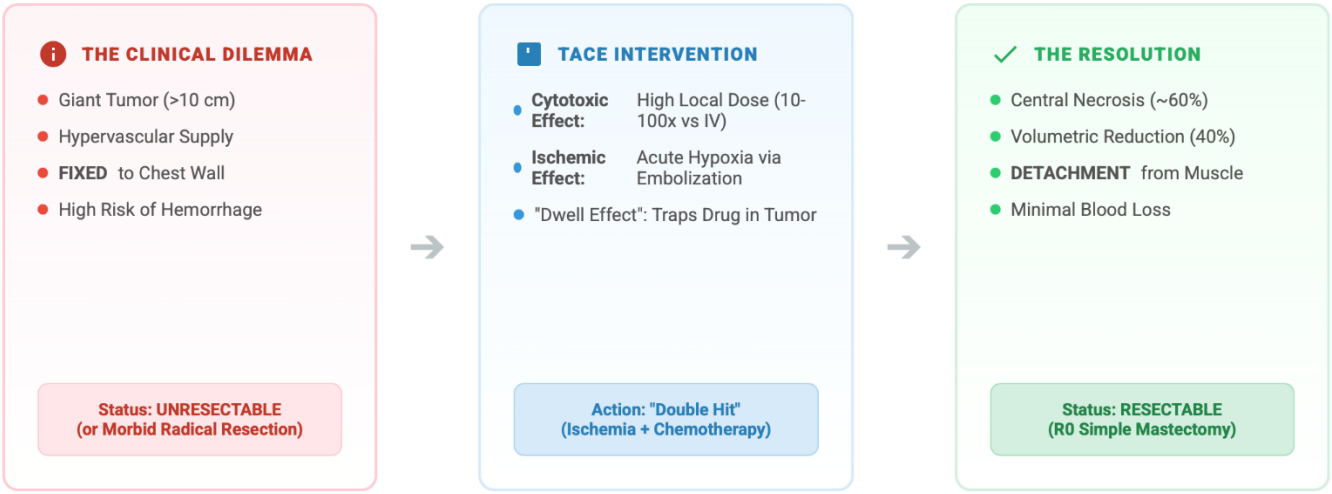

Figure 1. TACE as a "Bridge to Resectability" in giant breast sarcoma.

We acknowledge that this is a single-case report, and while the biological rationale is robust, the efficacy of TACE in breast LMS cannot be generalized without a larger series. The rarity of the disease makes randomized controlled trials unlikely; thus, evidence will likely continue to accumulate via case registries. Furthermore, while we demonstrated excellent local control (R0 resection), the long-term oncological benefit regarding overall survival (OS) and distant metastasis-free survival remains unknown compared to systemic therapy. Future research should focus on the standardization of the embolic agent size and the optimal timing of surgery post-TACE to maximize the "release" effect.

4. Conclusion

Primary leiomyosarcoma of the breast is a rare, aggressive malignancy where surgical resection with negative margins is the only potential cure. In cases of giant, locally advanced tumors presenting with chest wall fixation, upfront surgery carries high morbidity and oncological risk. This case highlights the successful implementation of transarterial chemoembolization (TACE) as a neoadjuvant strategy. By delivering high-dose Doxorubicin directly to the tumor and inducing ischemic necrosis, TACE successfully downstaged the tumor and, crucially, detached it from the pectoralis major muscle. This conversion from "fixed" to "mobile" facilitated an R0 total mastectomy with minimal blood loss. We propose that TACE be considered part of the multidisciplinary algorithm for giant hypervascular breast sarcomas, serving as a "bridge to resectability".

5. References

1. Shaffer K, Harris L, Gentile L, Merrill A, Kellam L, Fillion M, et al. The role of axillary lymph node dissection in breast cancer patients with residual nodal disease after receiving neoadjuvant chemotherapy. Breast Cancer (Auckl). 2025; 19: 11782234251352996.
2. Oner M, Mokbel K. Axillary management in patients with sentinel lymph node micrometastases following neoadjuvant systemic therapy: a call for de-escalation. Transl Breast Cancer Res. 2025; 6: 41.
3. Fan Y, Jin Y, Tian C, Zhang Y, Zhang C, Yu H, et al. Development and validation of machine learning models in predicting prognosis of breast cancer patients with lymph nodes metastasis following neoadjuvant chemotherapy. Breast Cancer (Dove Med Press). 2025; 17: 883–96.

4. Salemis NS, Koliarakis N, Spiliopoulos K, Kimpouri K, Marinos L. Primary cutaneous follicle center lymphoma of the breast: Management of an exceedingly rare malignancy. Intractable Rare Dis Res. 2020; 9(4): 263–5.
5. Mackenzie J, Douglas C. Gynecomastia or rare malignancy? A young man with an unremarkable history proves to have adenoid cystic carcinoma of the breast. Breast J. 2020; 26(3): 502–4.
6. Strait AM, LeBlanc RE, Muller KE. Proliferating pilar tumor: a rare cutaneous entity mimicking breast malignancy on imaging. Breast J. 2020; 26(6): 1251–2.
7. Fehr CA, Went P, Maranta M, Cathomas R. A rare case of breast malignancy in an adolescent woman: Lessons learned from diagnosis and management. Breast Care (Basel). 2021; 16(5): 539–43.
8. Hattingh G, Hanssen D, Medina J, Sanghvi M, Shah A. Osteosarcoma of the breast: a case report of a rare breast malignancy in a patient with prior partial mastectomy. Ann Breast Surg. 2022; 6: 19–19.
9. Vijapura C, Wahab RA. MRI of primary breast leiomyosarcoma. J Breast Imaging. 2024.
10. Bürger M, Marchiori E, Djahjah MC, Correia AH. Primary leiomyosarcoma of the breast papilla: a case report. Arch Breast Canc. 2020; 202–6.
11. Pyra K, Mikos E, Szmygin M, Światłowski Ł, Bibok A, Giurazza F, et al. Transarterial chemoembolization with bleomycin and lipiodol: a novel treatment for giant hepatic haemangiomas. Pol J Radiol. 2025; 90: e465–70.
12. Mu M-Y, Chen Z-X, Cao Y-Z, Fu X-B, Qiu L-J, Qi H, et al. Transarterial chemoembolization combined with intra-arterial infusion of sintilimab and bevacizumab for advanced hepatocellular carcinoma: a phase 2 study. Cancer Lett. 2025; 628(217851): 217851.
13. Chuang W-Y, Shen P-C, Chiu S-H, Huang W-Y, Chang W-C, Lin C-S, et al. Lenvatinib in combination with radiotherapy versus lenvatinib with transarterial chemoembolization for advanced hepatocellular carcinoma. BMC Cancer. 2025; 25(1): 1449.
14. Bruixola G, García R, Gomez F, Escoín C, Palomar L, de la Cueva H, et al. Transarterial chemoembolization with doxorubicin-loaded drug-eluting beads (DEBDOX) in the treatment of breast cancer liver metastases: a pilot study. Ann Oncol. 2015; 26(Suppl 3): iii6.
15. Storozhakova AE, Vladimirova LY, Kit OI, Kolesnikov EN, Snezhko AV, Chernyak MN, et al. Outcomes of transarterial chemoembolization (TACE) of the liver in patients with metastatic triple-negative breast cancer (TNBC). J Clin Oncol. 2020; 38(Suppl_15): e13107–e13107.
16. Lin J-N, Su J-H, Fu T-Y, Shih S-L. Transarterial chemoembolization as a part of multi-modality treatment with drug-eluting beads for locally advanced breast cancer: a case report. Radiol Case Rep. 2021; 16(11): 3383–8.
17. Hori A, Kennoki N, Hori S, Oka S, Nakamura T, Dejima I, et al. Feasibility study of transarterial chemotherapy followed by chemoembolization for recurrent breast cancer. J Vasc Interv Radiol. 2024; 35(4): 516–22.
18. Martin RCG, Robbins K, Fagés JF, Romero FD, Rustein L, Tomalty D, et al. Optimal outcomes for liver-dominant metastatic breast cancer with transarterial chemoembolization with drug-eluting beads loaded with doxorubicin. Breast Cancer Res Treat. 2012; 132(2): 753–63.
19. Ji S, Yin L, Feng L, Wang X. Oral Chinese patent medicine combined with transarterial chemoembolization for the treatment of

unresectable hepatocellular carcinoma: a Bayesian network meta-analysis. Medicine (Baltimore). 2025; 104(36): e44332.

20. Sutanto H, Adytia GJ, Elisa E, Maimunah U. Advances in transarterial chemoembolization for hepatocellular carcinoma: Integration with systemic therapies and emerging treatment strategies. Cancer Pathog Ther. 2026; 4(1): 1–13.