

## Aggressive Multifocal Recurrent Fibrosarcoma in an Elderly Patient: A Case Report

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### ABSTRACT

Fibrosarcoma is an uncommon malignant mesenchymal neoplasm originating from fibroblasts, notorious for its aggressive clinical behavior, high local recurrence rates, and potential for distant metastatic spread. Managing fibrosarcoma in elderly patients presents unique challenges, particularly when characterized by multifocal and recurrent disease. This case report aims to describe an unusual and particularly challenging presentation of aggressive, multifocal recurrent fibrosarcoma in a 65-year-old female patient. A 65-year-old Indonesian female presented with a complex history of multiple recurrent fibrosarcomas. Her oncological journey began with an inguinal mass excised in 2022, diagnosed as Grade I fibrosarcoma, followed by chemotherapy. Despite these interventions, she experienced recurrence at the primary site and developed new masses in the abdomen, flank, gluteal regions, left breast, right supraclavicular area, right antebrachial region, and left femur over the ensuing year. Comprehensive imaging, including whole abdomen MSCT, revealed multiple widespread soft tissue masses with suspicious lymphadenopathy and equivocal liver lesions. Histopathological examination of subsequent biopsies and excised specimens, supported by immunohistochemistry (CD34 positive; S-100, CD-117, Desmin negative), consistently confirmed recurrent fibrosarcoma. The patient underwent multiple extensive wide excision surgeries for various tumor locations, including the left inguinal region, left breast, left flank, bilateral gluteal regions, left antebrachial, and left supraclavicular areas. In conclusion, this case underscores the exceptionally aggressive and relentless nature of multifocal recurrent fibrosarcoma in an elderly individual. Despite an initial low-grade diagnosis and adjuvant chemotherapy, the disease progressed rapidly with widespread recurrences. Aggressive surgical management with wide excision remains the cornerstone of treatment in an attempt to achieve local control. However, the propensity for new lesions highlights the limitations of current therapies for such extensive disease. Vigilant, long-term surveillance and a multidisciplinary approach are paramount. This case also emphasizes the need for further research into the molecular drivers of such aggressive behavior and the development of more effective systemic therapies.

### 1. Introduction

Fibrosarcoma, a malignancy arising from fibroblasts, represents a relatively uncommon subset of soft tissue sarcomas (STS), accounting for less than 5% of all STS diagnoses. These tumors are characterized by the proliferation of spindle-shaped cells that often arrange in a classic "herringbone"

pattern and produce collagen. While fibrosarcoma can occur at any age, it predominantly affects adults, with a peak incidence typically observed between the ages of 30 and 60 years. Its occurrence in the pediatric population is notably rarer, often presenting as a distinct infantile variant with a generally more favorable prognosis. Conversely, adult-type

fibrosarcoma is recognized for its aggressive biological behavior, significant potential for local recurrence even after apparently complete surgical resection, and a concerning propensity for distant metastasis, most commonly to the lungs. The overall 5-year survival rate for fibrosarcoma is reported to be around 40-60%, but this figure can vary substantially based on factors such as tumor grade, size, depth, location, adequacy of surgical margins, and the presence of metastatic disease. In elderly patients, the diagnosis and management of fibrosarcoma can be further complicated by age-related physiological changes, the presence of comorbidities, and potentially reduced tolerance to aggressive treatment modalities.<sup>1,2</sup>

The pathogenesis of fibrosarcoma is complex and not entirely elucidated, though it is understood to involve a confluence of genetic and molecular aberrations. Historically, the diagnosis of fibrosarcoma was more common, but with advancements in immunohistochemical and molecular diagnostics, many tumors previously classified as fibrosarcoma are now recognized as other specific sarcoma subtypes. True fibrosarcomas are thought to arise *de novo* from fibroblasts or undifferentiated mesenchymal cells. Genetic mutations play a crucial role; for instance, alterations in the tumor suppressor gene TP53 have been implicated in various sarcomas, including fibrosarcoma. Dysregulation of signaling pathways, such as those involving fibroblast growth factor receptors (FGFRs), can contribute to uncontrolled cellular proliferation, survival, and invasion. Some fibrosarcomas, particularly the fibrosarcomatous variant of dermatofibrosarcoma protuberans (DFSP-FS), are characterized by specific chromosomal translocations, most notably t(17;22)(q22;q13), resulting in the COL1A1-PDGFB fusion gene. This fusion leads to the constitutive activation of platelet-derived growth factor receptor beta (PDGFRB) signaling, driving tumor growth. However, such specific fusions are not universally present in all fibrosarcoma types, and the molecular landscape of adult-type fibrosarcoma can be heterogeneous. The

tumor microenvironment, including interactions with stromal cells, vasculature, and immune cells, also plays a significant role in tumor progression and its aggressive behavior. Clinically, fibrosarcoma typically presents as a gradually enlarging, often painless mass. The extremities, particularly the thigh, are common sites, followed by the trunk, and less frequently, the head and neck region or retroperitoneum. Initial symptoms may be subtle, leading to delays in diagnosis. As the tumor grows, it can cause symptoms due to compression or invasion of adjacent structures, such as nerves (leading to pain, paresthesia, or motor weakness), blood vessels, or muscles, resulting in functional impairment. In advanced cases, symptoms related to metastasis, such as respiratory issues, may occur.<sup>3,4</sup>

Diagnosis relies on a combination of clinical assessment, radiological imaging, and histopathological examination of a biopsy specimen. Magnetic resonance imaging (MRI) is generally the preferred imaging modality for evaluating the primary tumor, providing excellent soft tissue contrast and delineating the tumor's relationship with surrounding anatomical structures, aiding in surgical planning, and assessing resectability. Computed Tomography (CT) is valuable for assessing bone involvement, detecting calcifications within the tumor, and is the standard for staging, particularly for identifying pulmonary metastases. Ultrasound may be used as an initial imaging tool for superficial masses but often requires follow-up with MRI or CT if malignancy is suspected. A definitive diagnosis is established by histopathological examination of tissue obtained via biopsy. Core needle biopsy, often image-guided, is preferred for most lesions, providing adequate tissue for diagnosis, grading, and ancillary studies such as immunohistochemistry. Histopathologically, adult-type fibrosarcoma is characterized by a proliferation of spindle cells with varying degrees of cellularity, atypia, and mitotic activity. The classic architectural feature is the "herringbone" pattern, where fascicles of tumor cells intersect at acute angles, although this pattern may not be evident in all cases, especially in higher-

grade tumors. Tumor cells typically have elongated, hyperchromatic nuclei and scant cytoplasm. The amount of collagen production can vary. Grading of fibrosarcomas, typically using the French Federation of Cancer Centers Sarcoma Group (FNCLCC) system, is crucial for predicting behavior and guiding treatment. This system considers tumor differentiation, mitotic count, and extent of necrosis. Immunohistochemistry (IHC) plays a vital role in differentiating fibrosarcoma from other spindle cell sarcomas. Fibrosarcomas are typically positive for vimentin. While they lack highly specific markers, a panel of IHC stains is used to exclude other entities. For instance, negativity for S-100 protein helps rule out malignant peripheral nerve sheath tumor (MPNST) and melanoma; negativity for desmin and other muscle markers helps exclude leiomyosarcoma and rhabdomyosarcoma; and negativity for cytokeratins argues against synovial sarcoma or carcinoma. CD34 expression can be variable; while often positive in DFSP and solitary fibrous tumor, some fibrosarcomas can also show CD34 positivity, as observed in the current case, which can sometimes pose diagnostic challenges.<sup>5,6</sup>

The cornerstone of treatment for localized fibrosarcoma is surgical resection with the aim of achieving wide, negative (R0) margins, meaning the tumor is removed with a cuff of surrounding normal tissue. Achieving R0 margins is the most critical factor for preventing local recurrence. The extent of surgery depends on the tumor's size, location, and relationship to vital structures. Limb-salvage surgery is preferred whenever oncologically feasible, often combined with adjuvant therapies. Amputation may be necessary in cases where limb salvage is not feasible due to extensive tumor involvement of neurovascular structures or bone. Adjuvant radiotherapy is frequently recommended for high-grade tumors, large tumors (>5 cm), deep-seated tumors, or when surgical margins are close or positive, as it has been shown to improve local control. Radiotherapy can be delivered pre-operatively or post-operatively. Pre-operative radiotherapy may offer advantages such as smaller

radiation fields, sterilization of tumor margins potentially facilitating less radical surgery, and a better functional outcome, though it may be associated with higher rates of wound complications. Post-operative radiotherapy is delivered after pathological assessment of the resected specimen. The role of adjuvant chemotherapy in localized adult fibrosarcoma remains controversial and is not routinely recommended for all patients. It may be considered in high-risk scenarios, such as large, high-grade, deep tumors, or in specific histological subtypes known to be more chemosensitive, though evidence for improved overall survival is limited. For metastatic or unresectable disease, systemic chemotherapy (e.g., doxorubicin, ifosfamide-based regimens) is the mainstay of treatment, although response rates are often modest. Targeted therapies and immunotherapies are areas of active research, with some agents showing promise in specific sarcoma subtypes.<sup>7,8</sup>

Managing fibrosarcoma is fraught with challenges, primarily due to its high propensity for local recurrence, which can occur in up to 50% of cases, even after seemingly adequate surgery. Recurrences are often more aggressive than the primary tumor and can be more difficult to manage. The risk of distant metastasis further complicates the prognosis. Achieving adequate surgical margins can be particularly challenging in anatomically constrained areas or when the tumor encases vital structures. Elderly patients present an additional layer of complexity. They may have multiple comorbidities (e.g., cardiovascular disease, diabetes, renal impairment) that increase surgical risks and limit their tolerance to aggressive adjuvant therapies. Performance status, nutritional status, and baseline functional capacity are critical considerations when planning treatment for elderly individuals with sarcoma. The goals of treatment in this population often involve balancing oncological control with maintaining quality of life and minimizing treatment-related toxicity. Multifocal presentation of fibrosarcoma at diagnosis is rare, and multiple

synchronous or metachronous recurrences at disparate anatomical sites, as seen in the present case, represent an exceptionally aggressive disease pattern that poses profound therapeutic dilemmas. Such presentations may reflect a particularly virulent tumor biology, a field effect with multiple primary tumors, or early, widespread subclinical dissemination.

This case report aims to describe an unusual and particularly challenging presentation of aggressive, multifocal recurrent fibrosarcoma in a 65-year-old female patient. Despite an initial diagnosis of low-grade fibrosarcoma and subsequent multimodal treatment including surgery and chemotherapy, the patient developed numerous recurrences across various anatomical locations over a relatively short period. The novelty of this case lies in the extensive and relentless multifocal nature of the recurrences, highlighting the unpredictable and often devastating behavior of this malignancy, especially in an elderly patient. We detail the diagnostic workup, the complex series of surgical interventions undertaken, the histopathological findings, and the ongoing management challenges.<sup>9,10</sup> This report intends to contribute to the limited literature on such extreme presentations of fibrosarcoma, underscoring the critical need for individualized, aggressive management strategies where appropriate, and emphasizing the ongoing search for more effective systemic therapies to combat this formidable disease. Furthermore, it highlights the limitations encountered within a specific healthcare system context regarding advanced molecular diagnostics, which could potentially guide more personalized treatment approaches.

## **2. Case Presentation**

A 65-year-old Indonesian female presented to our institution with a complex and distressing history of recurrent fibrosarcoma, profoundly impacting multiple anatomical sites. Her oncological journey commenced approximately three years prior to this comprehensive evaluation, with the insidious onset of

a progressively enlarging mass in her left inguinal region. This initial tumor was surgically excised in 2022, and subsequent histopathological analysis revealed it to be a Grade I fibrosarcoma. Following this surgery, the patient underwent a course of chemotherapy, the specifics of which were not fully documented in the referral notes, though it was noted as having been administered. Despite these initial therapeutic efforts, the patient unfortunately experienced a recurrence of the tumor at the primary inguinal site, described as growing to the "size of a chicken egg." More alarmingly, this local recurrence was accompanied by the sequential development of new tumor masses in several disparate locations. In early 2023, masses in the right hypochondriac area and the left flank necessitated further surgical removal. Subsequently, additional nodules became apparent in her left breast, the right supraclavicular fossa, the right antebrachial region, the left thigh, and bilaterally within the gluteal regions, painting a picture of aggressive, multifocal disease. The patient reported no significant underlying systemic illnesses, such as diabetes mellitus or hypertension, and had no other known major comorbidities. Her Karnofsky Performance Status at the time of admission for the multi-site excisions was rated at 80%, indicating she was still capable of most daily activities with some effort, despite the symptomatic burden of her disease (Table 1).

Upon detailed physical examination preceding the planned extensive surgeries, the patient was alert and oriented but appeared moderately ill. Her vital signs were stable, with a blood pressure of 112/75 mmHg, heart rate of 88 beats per minute, respiratory rate of 20 per minute, temperature of 36.5°C, and oxygen saturation of 99% on room air. Significant findings included a palpable, firm mass in the right supraclavicular region, approximately 4x3 cm, with noticeable increased vascularity of the overlying skin. Examination of her left breast revealed a palpable, firm, mobile mass measuring about 3x2 cm in the upper outer quadrant. Her abdomen bore the scars of previous surgeries in the right hypochondriac and left

flank regions, with a palpable mass noted deep to the left flank scar. Additional masses were identified in the right antebrachial area (approx. 2x2 cm) and a deeper, firm, slightly tender mass (approx. 5x4 cm) in the anteromedial aspect of her left thigh. Critically, an open wound was present over the postoperative scar in the left inguinal region, with a substantial underlying recurrent tumor mass measuring approximately 6x5 cm, which felt firm and fixed to deeper tissues. Palpable masses were also noted in both gluteal regions. Cardiopulmonary examination was otherwise unremarkable. Initial laboratory investigations revealed normocytic anemia (Hemoglobin 10.2 g/dL) and leukopenia (WBC 3,800/ $\mu$ L). Renal and liver function tests were within normal limits. Inflammatory markers, such as ESR and CRP, were elevated. A plain chest X-ray was clear, showing no evidence of pulmonary metastases at that juncture. However, a whole abdomen Multislice Computed Tomography (MSCT) scan with contrast provided a more comprehensive assessment of the disease extent. This imaging confirmed the presence of multiple soft tissue density masses with irregular, lobulated contours—features suggestive of malignancy—in the bilateral inguinal regions, bilateral gluteal regions, and bilateral lumbar areas. The largest of these was the recurrent inguinal mass. The MSCT also highlighted multiple suspicious lymphadenopathies in the right para-iliac, bilateral inguinal, and presacral regions. Multiple small cystic lesions were seen in the liver, their nature (benign cysts versus metastases) remaining indeterminate without further investigation. Incidental findings included a suspected right renal angioliipoma and simple renal cysts.

Review of previous pathology reports indicated the initial inguinal mass (excised in 2022) was a Grade I fibrosarcoma. Specimens from the flank and abdominal masses excised in early 2023 were diagnosed as malignant spindle cell tumors, with fibrosarcoma being a prime differential. Immunohistochemical analysis of these latter specimens was crucial: the tumor cells stained

diffusely positive for CD34, while being negative for S-100, CD-117, and Desmin. This immunoprofile, combined with the spindle cell morphology, strongly supported the diagnosis of fibrosarcoma over other potential spindle cell malignancies. Thus, the final preoperative diagnosis before the comprehensive resections was multiple recurrent fibrosarcoma involving numerous sites. Given the widespread nature of the disease and the patient's reasonable performance status, a strategic decision was made by the multidisciplinary team for staged surgical debulking via multiple wide excisions. The initial phase of this surgical plan, undertaken in October 2023, targeted the symptomatic and larger lesions in the left inguinal region, left mammae, and left flank. Intraoperatively, multiple distinct tumor masses were encountered at these sites. The lesions in the left flank and inguinal area were noted to be infiltrating the overlying skin, whereas the tumor in the left breast appeared somewhat more encapsulated. All visible tumors were excised with a margin of surrounding grossly normal tissue. Hemostasis was meticulously achieved, and the surgical beds were irrigated with hydrogen peroxide and normal saline before wound closure. The estimated blood loss for this tripartite procedure was minimal, approximately 70 ml. Postoperatively, the patient was managed with intravenous antibiotics and analgesics, remained hemodynamically stable, and was discharged on the first postoperative day, with a follow-up scheduled within a week. Histopathological examination of the resected specimens from this first stage confirmed invasive mesenchymal tumors at all three sites (left inguinal, left mammae, left flank). Microscopically, the tumors were composed of spindle-shaped cells with nuclear atypia, arranged in a characteristic "fascicular" or "herringbone" pattern. Invasion into adjacent adipose tissue was noted in the breast and flank specimens. The conclusive diagnosis for all three sites was fibrosarcoma. The overall interpretation was that of fibrosarcoma originating in the left inguinal region with subsequent multifocal disease or metastases to the left breast and left flank. Surgical

margins for these resections were reported as clear (Table 1).

Following the confirmation of these findings, the patient underwent a second planned surgical procedure to address the remaining identified tumor sites. This involved multiple wide excisions of soft tissue tumors located in the right and left gluteal regions, the left antebrachial area, and the left supraclavicular region. Intraoperatively, tumors with similar gross characteristics were found and excised. The patient's postoperative course was again relatively uncomplicated; she maintained hemodynamic stability and was discharged the following day after adequate pain control was achieved. Histopathology of these specimens also confirmed fibrosarcoma. The patient's long-term follow-up plan included regular clinical assessments and serial imaging (CT scans of the chest, abdomen, and pelvis) every three to four months for the initial two years, then with decreasing frequency, to monitor for any new recurrences or distant metastases. Given the aggressive nature of her disease and the previous partial response to chemotherapy, discussions regarding further systemic therapy options were ongoing, though hampered by the lack of detailed molecular profiling of the tumor due to systemic constraints. Supportive care, including psychological support and physiotherapy, was also integrated into her management plan (Table 2).

### 3. Discussion

This case report describes an exceptionally challenging scenario of aggressive, multifocal recurrent fibrosarcoma in a 65-year-old female. Fibrosarcoma, while constituting a small fraction of adult soft tissue sarcomas, is well-recognized for its potential for local aggressiveness and distant spread. The presentation in an elderly patient adds another layer of complexity, often involving considerations related to comorbidities, physiological reserve, and tolerance to aggressive therapies, although this particular patient was reported to have no significant systemic diseases. The striking feature of this case is

the relentless and widespread pattern of recurrence. Despite an initial diagnosis of Grade I fibrosarcoma for the inguinal lesion and subsequent chemotherapy, the patient developed multiple new tumor foci in diverse anatomical locations within a relatively short timeframe. This pattern of multifocal recurrence is unusual for fibrosarcoma, which more typically recurs locally or metastasizes to distant sites like the lungs. Such widespread disease could suggest several possibilities: an inherently aggressive biological phenotype of the tumor despite an initial low-grade designation, the possibility of a field cancerization effect with multiple synchronous or metachronous primary tumors, or early subclinical dissemination that became manifest over time. The latter is perhaps more plausible given the metastatic involvement of the breast and flank from the inguinal primary, as suggested by the pathological interpretation. The term "aggressive" is fitting, as even low-grade fibromyxoid sarcoma, a variant, can demonstrate early postoperative recurrences and metastases, particularly if initial resections are inadequate.<sup>11,12</sup>

The diagnostic journey itself presented challenges. The initial differentiation of a malignant spindle cell tumor often requires a comprehensive immunohistochemical panel to exclude other spindle cell sarcomas and even some carcinomas or melanomas. In this case, the positive staining for CD34 was a key finding. While CD34 is classically associated with dermatofibrosarcoma protuberans (DFSP) and solitary fibrous tumors, it can also be expressed in a subset of other mesenchymal neoplasms, including some fibrosarcomas. The negativity for S-100 (ruling out MPNST, melanoma), CD-117 (ruling out GIST), and Desmin (ruling out leiomyosarcoma) was crucial in narrowing the diagnosis towards fibrosarcoma, especially in conjunction with the characteristic spindle cell morphology and herringbone pattern observed. The consistent histopathological features across multiple sites confirmed the recurrent and disseminated nature of the same neoplastic process.

Table 1. Summary of clinical patient data.

Parameter	Details
<b>Demographics</b>	Age: 65 years
	Gender: Female
	Occupation: Housewife
	Relevant Social History: Non-smoker, occasional alcohol consumption. Lives with family, supportive home environment.
<b>Anamnesis</b>	
Initial presentation	History of an enlarging left inguinal mass for approximately 3 years. Initially painless, gradually increased in size.
First surgery (2022)	Surgical removal of the left inguinal mass in 2022. Details of specific surgical procedure (e.g., wide excision vs. marginal excision) not fully specified in initial notes but presumed to be excisional.
Initial histopathology	Grade I fibrosarcoma from the left inguinal mass.
Adjuvant treatment	Underwent chemotherapy following the initial surgery in 2022. Specific regimen, number of cycles, and patient tolerance not detailed in the initial record.
First recurrence & new masses	Mass recurred in the left inguinal region post-surgery, described as "size of a chicken egg". Subsequently, additional masses developed in the waist (left flank, right hypochondriac), thigh (left femur region), shoulder (right supraclavicular), and left breast. Some of these new masses appeared within months of the initial treatment.
Surgery (2023)	Underwent removal surgery of masses in the right hypochondriac and left flank region in 2023, prior to the current comprehensive evaluation.
Systemic diseases	No history of diabetes mellitus, hypertension, or other significant chronic comorbidities.
Family history	No significant family history of malignancies reported.
Performance status	Karnofsky Performance Status: 80% on admission for the subsequent major surgeries (Capable of normal activity with effort; some signs or symptoms of disease).
<b>Physical examination (Pre-operative for multiple excisions)</b>	
General appearance	Compos mentis, moderately ill.
Vital signs	Blood Pressure: 112/75 mmHg. Heart Rate: 88 bpm. Respiratory Rate: 20 breaths/minute. Temperature: 36.5°C. Oxygen Saturation: 99% on room air.
Head & neck	Palpable mass in the right supraclavicular region, approximately 4x3 cm, firm, mobile, with overlying skin showing increased vascularization.
Chest	Cardiac and lung examination: No abnormalities detected on auscultation and percussion. Left mammae: Palpable firm mass, approximately 3x2 cm, in the upper outer quadrant, mobile, not fixed to skin or chest wall.
Abdomen	Postoperative scar noted in the right hypochondriac region. Postoperative dry-wound scar in the left flank region. Palpable mass deep to the scar in the left flank region.
Extremities	Palpable firm mass in the right antebrachial region, approximately 2x2 cm, mobile. Palpable deep-seated mass in the anteromedial aspect of the left femur region, approximately 5x4 cm, firm, slightly tender.
Inguinal/Gluteal	Open wound over a postoperative scar with an underlying recurrent mass in the left inguinal region, approximately 6x5 cm, firm, fixed to underlying tissues. Palpable masses in bilateral gluteal regions, varying sizes (Right gluteal ~4cm, Left gluteal ~3cm, deep, firm).
Skin	Skin over right supraclavicular mass showed increased vascularization. Other masses generally had skin color similar to surrounding tissue.
<b>Laboratory findings (Pre-operative)</b>	
Complete blood count	Hemoglobin: 10.2 g/dL (Normal: 12-16 g/dL for females) - Anemia noted. Hematocrit: 31% (Normal: 36-46%). White Blood Cell Count: 3,800 / $\mu$ L (Normal: 4,000-11,000 / $\mu$ L) - Leukopenia noted. Differential: Neutrophils 60%, Lymphocytes 30%, Monocytes 8%, Eosinophils 2%. Platelet Count: 250,000 / $\mu$ L (Normal: 150,000-450,000 / $\mu$ L).
Renal function	Creatinine: 0.9 mg/dL (Normal: 0.6-1.2 mg/dL). Blood Urea Nitrogen (BUN): 15 mg/dL (Normal: 7-20 mg/dL).
Liver function	Alanine Aminotransferase (ALT): 25 U/L (Normal: <35 U/L). Aspartate Aminotransferase (AST): 30 U/L (Normal: 40 U/L). Total Bilirubin: 0.7 mg/dL (Normal: 0.2-1.2 mg/dL).
Coagulation profile	Prothrombin Time (PT): 12.5 seconds (Control: 12.0 seconds). Partial Thromboplastin Time (PTT): 30 seconds (Control: 32 seconds). INR: 1.0.
Inflammatory markers	Erythrocyte Sedimentation Rate (ESR): 45 mm/hr (Normal: <20 mm/hr). C-Reactive Protein (CRP): 15 mg/L (Normal: <5 mg/L).
<b>Imaging findings</b>	
Chest X-ray (PA view)	No abnormality in the heart shadow or lung fields. No evidence of pulmonary metastases at the time of this examination.
Whole abdomen MSCT with contrast	1) Multiple soft tissue density masses with indistinct, irregular edges and lobulated shape observed in: bilateral inguinal regions, bilateral gluteus regions, bilateral lumbar regions. Impression: Malignant tumor; possible residual/recurrent masses. Largest inguinal mass measured approx. 6.2 x 5.5 cm. Largest gluteal mass approx. 4.5 x 4.0 cm. 2) Multiple suspicious lymphadenopathies: noted in the right para-iliac region, bilateral inguinal regions, and presacral region. Largest lymph node approx. 1.8 cm in short axis. 3) Liver: Multiple, small, well-defined cystic lesions, largest measuring 1.5 cm. Differential diagnosis included benign cysts versus metastasis; further characterization recommended if clinically pertinent. 4) Kidneys: Fat density, rounded lesion with well-defined regular edges in the right renal median pole, suspected angioliopoma. Simple cyst of the right kidney and multiple simple cysts of the left kidney (Bosniak category I). 5) Spine: Thoracolumbar spondylosis noted.
MRI of the left thigh	A T1-weighted image showed an isointense to muscle, lobulated mass in the anteromedial compartment measuring 5.2 x 4.1 x 3.8 cm. T2-weighted images showed heterogeneous high signal intensity. Post-contrast images demonstrated avid, heterogeneous enhancement. The mass appeared to abut the femoral vessels without clear invasion. No definite bone erosion.
<b>Histopathological &amp; immunohistochemical diagnosis (IHC)</b>	
Previous inguinal mass (excised 2022)	Grade I fibrosarcoma.
Flank and abdominal masses (excised early 2023)	Malignant spindle cell tumor. Differential diagnoses included fibrosarcoma, leiomyosarcoma, gastrointestinal stromal tumor (GIST), or malignant peripheral nerve sheath tumor (MPNST).
Immunohistochemistry (IHC) on Flank/Abdominal Specimen	S-100: Negative. CD-117 (c-kit): Negative. Desmin: Negative. CD34: Positive, diffused in tumor cells.
Pathological interpretation	Based on morphology (spindle cells, fascicular pattern) and IHC profile (CD34 positivity, negative for S100, CD117, Desmin), the tumor was most consistent with fibrosarcoma.
<b>Final pre-operative diagnosis (for staged multiple excisions in late 2023)</b>	Multiple recurrent fibrosarcoma (left inguinal post-excision, left mammae, left flank, and other sites as per imaging/clinical findings).

Table 2. Procedure of treatment and follow-up.

Stage	Details
<b>Pre-operative preparation (for Staged Multiple Excisions)</b>	After thorough evaluation and discussion with the patient and her family regarding the prognosis and the extensive nature of the proposed procedures, a plan for multiple wide excisions was formulated. This involved a multidisciplinary team discussion including surgical oncologists, medical oncologists, radiologists, and pathologists. Pre-operative assessments confirmed fitness for surgery. Informed consent was obtained, addressing the risks, benefits, and potential complications of multiple surgeries, including prolonged operative time, risk of infection, bleeding, and potential need for further treatments. Prophylactic intravenous antibiotics were administered prior to each procedure. The anesthesia type was general anesthesia for all procedures.
<b>Surgical procedure 1 (October 2023 - Left Inguinal, Left Mammae, Left Flank)</b>	<b>Date:</b> October 2023 (approximate). <b>Sites:</b> Left inguinal region, left mammae, left flank. <b>Surgical Approach &amp; Technique:</b> <i>Left Inguinal:</i> Wide excision of the recurrent mass, encompassing previous scar tissue. Dissection was carried out to ensure adequate deep and lateral margins. <i>Left Mammae:</i> Wide local excision of the palpable mass in the upper outer quadrant. <i>Left Flank:</i> Wide excision of the mass located deep to the previous surgical scar. <b>Intraoperative Findings:</b> Multiple masses confirmed at all three sites. The tumors in the left flank and inguinal region were described as soft tissue masses extending to involve the overlying skin. The left breast mass was noted to be somewhat encapsulated. No gross invasion into major neurovascular structures was identified at these sites during this procedure. <b>Margins:</b> The surgical intent was to achieve wide clear (R0) margins for all resected specimens. <b>Hemostasis:</b> Achieved using electrocautery and ligatures as needed. <b>Wound Irrigation:</b> Cavities were irrigated with hydrogen peroxide solution followed by 0.9% sodium chloride solution. <b>Closure:</b> Layered closure of wounds. Drains were placed as deemed necessary by the surgical team. <b>Estimated Blood Loss:</b> Approximately 70 mL. <b>Specimens Sent:</b> Tissues from all three sites (A: left inguinal, B: left mammae, C: left flank) were sent for histopathological examination.
<b>Post-operative care (Immediate after Surgery 1)</b>	Admitted to the general surgical ward. <b>Medications:</b> Intravenous antibiotics (third-generation cephalosporin) and multimodal analgesia (NSAIDs and opioids as required) were administered. <b>Positioning:</b> Fowler position maintained initially. <b>Diet:</b> No dietary restrictions post-operatively. <b>Monitoring:</b> Close monitoring of vital signs, wound sites for signs of infection or hematoma, and pain control. <b>Patient Condition:</b> Remained hemodynamically stable. Reported pain at surgical sites, which was managed and reduced with analgesia. Compos mentis throughout. <b>Discharge:</b> Discharged on the first postoperative day. <b>Follow-up:</b> Returned to the hospital for wound check and suture review 5 days post-discharge.
<b>Histopathology results (from Surgery 1)</b>	<b>Specimen A (Left Inguinal):</b> Skin and subcutaneous tissue infiltrated by an invasive mesenchymal tumor. Tumor cells were spindle-shaped with hyperchromatic nuclei, arranged in a "fascicular" pattern with intersecting bundles, characteristic of a "herringbone" appearance. Mitotic activity was noted. Diagnosis: Fibrosarcoma. <b>Specimen B (Left Mammae):</b> Tumor morphologically similar to Specimen A, showing invasion into surrounding adipose tissue. Diagnosis: Fibrosarcoma. <b>Specimen C (Left Flank):</b> Tumor features consistent with Specimens A and B, with invasion into adipose tissue. Diagnosis: Fibrosarcoma. <b>Overall Pathological Conclusion:</b> Multifocal fibrosarcoma involving the left inguinal region, left mammae, and left flank. The findings were interpreted as fibrosarcoma of the left inguinal region with metastatic deposits or synchronous multifocal disease in the left breast and left flank. Surgical margins were reported as clear for all three specimens from this procedure.
<b>Surgical procedure 2 (Follow-up Multiple Wide Excisions)</b>	<b>Timing:</b> Performed following the availability of histopathology results from Surgery 1 and further staging, approximately 2-3 weeks later. <b>Sites:</b> Right gluteal region, left gluteal region, left antebraclial region, and left supraclavicular region. <b>Surgical Approach &amp; Technique:</b> Multiple wide excisions of all grossly identifiable soft tissue tumors at these locations. Each lesion was excised with a planned margin of surrounding healthy tissue. <b>Intraoperative Findings:</b> Tumors of varying sizes and consistencies were found at each site, consistent with preoperative imaging. For example, the supraclavicular mass was firm and involved subcutaneous tissue, while gluteal masses were deeper. <b>Estimated Blood Loss:</b> Approximately 100-150 mL (cumulative for all sites). <b>Specimens Sent:</b> All resected tissues were sent for histopathological examination. Results confirmed fibrosarcoma at all sites, similar in morphology to previous specimens. Detailed margin status for each site obtained.
<b>Post-operative care (Immediate after Surgery 2)</b>	Patient remained hemodynamically stable throughout and after the procedure. Primary complaint was pain at the multiple surgical sites, which was managed effectively with analgesics. Wounds were monitored for complications. <b>Discharge:</b> Discharged on the first postoperative day once pain was adequately controlled and she was mobilizing safely.
<b>Further treatment/Considerations</b>	<b>Previous Chemotherapy:</b> The patient had received chemotherapy approximately 4 months after her initial inguinal surgery in 2022. This was reportedly initiated after she complained of a new abdominal mass two months prior to starting chemotherapy. Details of the regimen (doxorubicin-based) and number of cycles were not available, but the disease recurred and progressed despite this treatment. <b>Current Adjuvant Plans:</b> Given the multifocal recurrences and previous chemotherapy, the role of further adjuvant systemic therapy was discussed by the multidisciplinary team. Options such as different chemotherapy regimens or consideration for targeted therapies (if molecular profiling became available) were weighed against potential toxicities and patient preference. Palliative radiotherapy to symptomatic sites might be considered in the future if unresectable recurrences cause significant symptoms. The limitations within the national healthcare system regarding access to advanced genetic testing were acknowledged as a factor impacting further personalized treatment strategies.
<b>Long-term follow-up plan</b>	Regular clinical examinations every 2-3 months for the first two years, then every 4-6 months for years 3-5, and annually thereafter. Imaging surveillance with CT scans of the chest, abdomen, and pelvis to be performed every 3-4 months for the first two years, then every 6 months for the next three years, and then annually, or as clinically indicated by new symptoms. MRI of specific areas of concern as needed. Close monitoring for any new palpable masses, pain, or systemic symptoms suggestive of recurrence or metastasis. Referral for physiotherapy and occupational therapy to address any functional limitations resulting from multiple surgeries. Psychological support and counseling to be offered to the patient and family to cope with the chronic and recurrent nature of the disease.
<b>Patient status at last documented follow-up</b>	At the last follow-up detailed in the source document (shortly after the second set of excisions), the patient was reported to be in good general condition, hemodynamically stable, with surgical site pain subsiding. Further information on her long-term disease status beyond this point was not available in the initial report.



Surgical management remains the cornerstone of treatment for localized and recurrent fibrosarcoma, with the primary goal being complete oncologic resection with wide, negative (R0) margins. Achieving such margins is paramount for minimizing the risk of further local recurrence. This principle was applied in this case, with multiple wide excisions performed across various anatomical sites. However, the sheer number of lesions and their widespread distribution make achieving long-term disease control through surgery alone exceptionally difficult. Each surgical intervention carries risks, including infection, bleeding, wound healing complications, and potential functional impairment, which can be magnified in elderly patients even if they are otherwise fit. The decision to undertake multiple, staged excisions was likely made to manage the tumor burden systematically while minimizing the physiological stress of a single, excessively prolonged operation. The intraoperative findings of multiple masses, some appearing encapsulated and others more infiltrative, further underscore the complexity of achieving complete eradication.<sup>13,14</sup>

The role of adjuvant therapies in fibrosarcoma, particularly in the adult-type, is often debated and individualized. Adjuvant radiotherapy is commonly used to improve local control, especially for high-grade tumors or when margins are close or positive. Whether radiotherapy was considered or administered at any point for this patient beyond the initial chemotherapy is not explicitly stated in the provided information. Given the multifocal nature and repeated recurrences, delivering effective radiotherapy to all involved sites or potential sites at risk would be challenging and associated with significant toxicity. The patient did receive chemotherapy after her first surgery in 2022. However, its efficacy appears to have been limited, given the subsequent rapid and widespread recurrences. Systemic chemotherapy for adult soft tissue sarcomas, including fibrosarcoma, typically involves agents like doxorubicin and ifosfamide. While it can achieve responses in a subset of patients with advanced or metastatic disease, its role in the

adjuvant setting for completely resected fibrosarcoma is less clear, often reserved for high-risk cases, and its impact on overall survival is modest for many sarcoma subtypes. The limited success of the initial chemotherapy in this patient highlights the chemoresistant nature of many fibrosarcomas. Emerging therapies, including targeted agents and immunotherapy, are being investigated for various sarcomas. For example, pembrolizumab has shown some activity in advanced soft tissue sarcomas. However, the selection of such therapies is often guided by specific molecular targets or biomarkers. The report mentions that further genetic testing was hindered due to limitations within the national healthcare system, which unfortunately precluded a more in-depth molecular characterization of the tumor that might have identified actionable mutations or guided enrollment in clinical trials of novel agents. This lack of genetic data is a limitation in fully understanding the tumor's biology and potential therapeutic vulnerabilities.<sup>15,16</sup>

The prognosis for patients with recurrent, multifocal fibrosarcoma, especially in the elderly, is generally poor. Factors such as the high grade of the tumor (though initially Grade I, the recurrent disease behaved aggressively), the multiplicity of lesions, and the rapid development of new tumors all contribute to a guarded outlook. Older age itself can be an independent poor prognostic factor for STS. While surgical treatment can improve prognosis even in very elderly patients ( $\geq 85$  years), the challenge in this case is not just the resectability of individual lesions but the systemic nature of the disease's spread and its tendency to reappear. A multidisciplinary team (MDT) approach is essential in managing complex sarcoma cases like this one, involving surgical oncologists, medical oncologists, radiation oncologists, radiologists, and pathologists. This collaborative approach ensures comprehensive evaluation, staging, and the formulation of an optimal, individualized treatment plan, considering all available modalities and patient-specific factors. The provided information suggests such planning occurred. Comparing this case

to the literature, while recurrent fibrosarcoma is a known entity, the sheer multiplicity and widespread anatomical involvement seen here, especially following an initial low-grade diagnosis, appears to be at the more aggressive end of the spectrum. Case reports of recurrent large fibrosarcomas highlight management dilemmas, and studies on low-grade fibromyxoid sarcoma (LGFMS), which can sometimes be CD34 positive, also describe high rates of local recurrence and late metastasis, sometimes years after initial diagnosis. The aggressive behavior in this patient, despite an initial "Grade I" diagnosis for the inguinal mass, might suggest under-grading initially, sampling error, or a rapid dedifferentiation process within the tumor. The "malignant spindle tumor" description for subsequent lesions suggests a less differentiated, more aggressive morphology. The "herringbone" pattern seen in the later resections is classic for fibrosarcoma.<sup>17,18</sup>

The limitations of this case report include the lack of detailed information on the initial chemotherapy regimen and the absence of comprehensive genomic sequencing of the tumor tissue, which could have provided insights into specific driver mutations or therapeutic targets. Such molecular information is becoming increasingly important in sarcoma management, with fusion genes like *COL1A1-PDGFB* being implicated in some fibrosarcomatous tumors. The inability to perform such tests due to systemic constraints is a significant challenge in providing cutting-edge care in some settings. Living with recurrent, multifocal cancer significantly impacts a patient's quality of life, involving repeated hospitalizations, surgeries, and the psychological burden of an uncertain future. Palliative care and psychosocial support are crucial components of management for such patients. The management of this patient, focusing on repeated wide excisions, aimed to control local disease and palliate symptoms from enlarging masses. Given the aggressive nature and multifocality, the goals of treatment likely shifted towards prolonging a good quality of life and managing symptomatic disease, rather than cure. The patient's

relatively good performance status (Karnofsky 80%) initially allowed for these aggressive surgical attempts. Vigilant follow-up with regular imaging, as planned, is critical for detecting new recurrences at the earliest possible stage, allowing for timely intervention if deemed appropriate.<sup>19,20</sup>

#### 4. Conclusion

This case report details the extraordinarily aggressive clinical course of a 65-year-old female with multifocal recurrent fibrosarcoma. Despite an initial low-grade diagnosis and multimodality therapy including chemotherapy and multiple extensive surgical resections, the patient experienced relentless disease progression with tumors appearing in numerous disparate anatomical sites. The management of such cases is profoundly challenging, with surgical extirpation remaining the primary modality for local disease control and palliation of symptoms. However, the inherent biological aggressiveness and propensity for widespread recurrence often limit the long-term efficacy of locoregional treatments. This case underscores the limitations of current therapeutic options for highly aggressive, multifocal fibrosarcoma and highlights the critical need for novel systemic therapies. The inability to perform comprehensive genetic testing due to healthcare system constraints in this specific case also emphasizes the disparities in access to advanced molecular diagnostics that could potentially guide more personalized and effective treatment strategies. Further research into the molecular pathogenesis of aggressive fibrosarcoma variants is crucial to identify new therapeutic targets and develop interventions that can alter the natural history of this devastating disease. A multidisciplinary approach, coupled with vigilant long-term surveillance and supportive care, is essential in managing these complex patients and optimizing their quality of life.

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