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Original Article

Rare High-Grade Malignant Myxofibrosarcoma and Postoperative Recurrence: A Case Report

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Abstract:
This article reports a rare case of high-grade malignant myxofibrosarcoma (MFS) located in the left proximal thigh and its postoperative recurrence. Myxofibrosarcoma is a relatively uncommon subtype of soft tissue sarcoma, with high-grade variants being exceptionally rare. The patient experienced recurrence following surgical resection. Investigation into the recurrence mechanisms revealed that the aggressive invasiveness of tumor cells, supportive tumor microenvironment (TME), and the presence of cancer stem cells (CSCs) might be critical factors contributing to recurrence. Tumor cells secrete proteases such as matrix metalloproteinases (MMPs) to degrade the extracellular matrix (ECM), facilitating invasion and metastasis. Immune cells and fibroblasts within the TME provide favorable conditions for tumor survival and growth. CSCs, possessing self-renewal and multidifferentiation capabilities, allow residual cells to persist and proliferate post-surgery. A deeper understanding of these mechanisms is crucial for optimizing therapeutic strategies and improving survival rates in MFS patients.

Keywords: Myxofibrosarcoma; High-grade malignancy; Local recurrence; Wide excision; Adjuvant radiotherapy

Introduction

Myxofibrosarcoma (MFS) is a subtype of soft tissue sarcoma, with a relatively low incidence, and highly malignant myxofibrosarcoma is even rarer[1]. This tumor has unique histological features and is composed of a myxoid stroma and fibroblast-like cells in varying proportions. Although surgical resection is the main treatment method, the postoperative recurrence rate is relatively high, which seriously affects the prognosis of patients[2-4]. Understanding its recurrence mechanism is crucial for formulating effective treatment plans. This article reports a recurrent case of a patient with highly malignant myxofibrosarcoma in the left inguinal region, a rare case. By combining molecular pathological and imaging features, this article deeply explores its recurrence mechanism, providing a basis for optimizing treatment.

2. Case Report

The patient is a 56-year-old married male who was admitted to the hospital due to "a skin mass on the left thigh that has been growing and enlarging for one year". The patient reported that approximately one year prior to admission, without any apparent precipitating factors, a subcutaneous mass the size of a broad bean was noticed at the root of the left thigh. At that time, the patient did not attach much importance to it and did not seek further medical treatment.

Subsequently, the aforementioned mass gradually increased in size at a moderate growth rate. After the patient self-administered topical ointment for treatment (the specific medication and dosage were unspecified), the mass significantly enlarged, and its growth rate became notably faster than before. Additionally, the mass gradually protruded from the skin surface, exhibiting protuberant growth, accompanied by local pain. Currently, the patient presented to the outpatient department of our hospital for further diagnosis and treatment. After a thorough examination of the patient, the outpatient physician admitted the patient to our department with a diagnosis of "skin tumor at the root of the left thigh". Throughout the course of the illness, the patient did not experience symptoms such as fever, rigors, nausea, chest distress, cough, or sputum production.Recently, the diet has been acceptable, the sleep is average, the bowel movements and urination are normal, and there has been no obvious weight loss recently. Physical examination upon admission: body temperature is 36.6℃, respiratory rate is 18 breaths per minute, heart rate is 74 beats per minute, blood pressure is 115/85 mmHg, and the pain score is 4. The breath sounds of both lungs are clear, and no dry or moist rales are heard; the heart rhythm is regular, and no pathological murmurs are heard in each valve area; the abdomen is soft, without tenderness, and the liver and spleen cannot be palpable below the costal margin.Specialty Findings: A skin mass measuring 10 cm × 7 cm × 5 cm is visible in the area near the groin of the left thigh root (Picture 1).

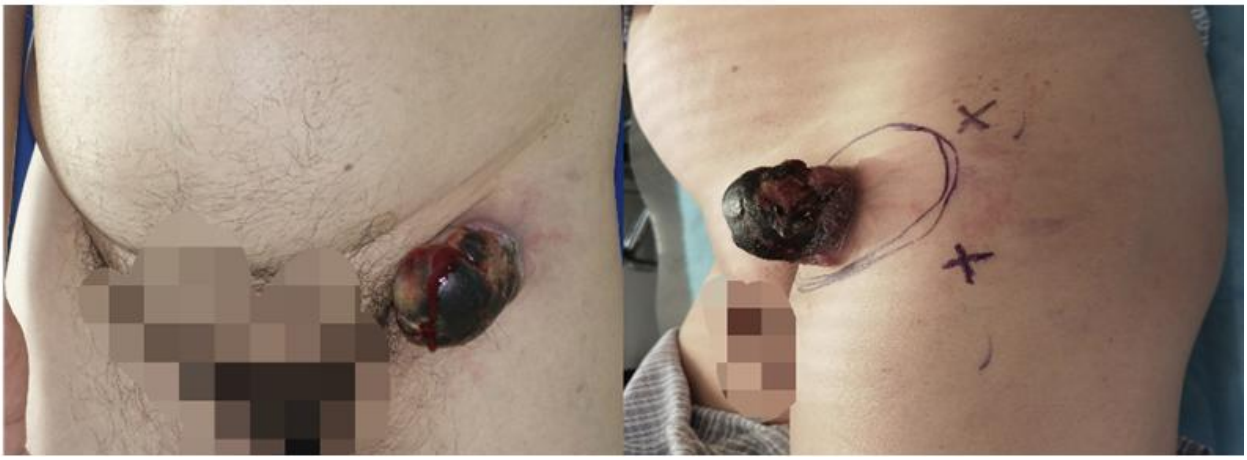

Figure 1 | A skin mass with a size of 10 cm × 7 cm × 5 cm can be seen in the area near the groin at the root of the left thigh.

The mass is hard in texture and reddish-brown in color. A few tortuous blood vessels can be seen beneath the mass. There is local ulceration on the surface of the mass, with the formation of a blood scab. It bleeds when touched. The mass invades the deep subcutaneous tissue, and there is positive tenderness. A swollen lymph node measuring 2 cm × 1.5 cm can be palpated in the left inguinal region. No abnormal mass or swollen lymph node is palpable on the right side. Upon admission, electrocardiogram and chest X-ray show no obvious abnormalities. Color Doppler ultrasound of the inguinal lymph nodes indicates: 1. Swelling of the left inguinal lymph nodes, considered to be reactive hyperplastic lymph nodes; 2. The right inguinal lymph nodes are visible (Picture 2).

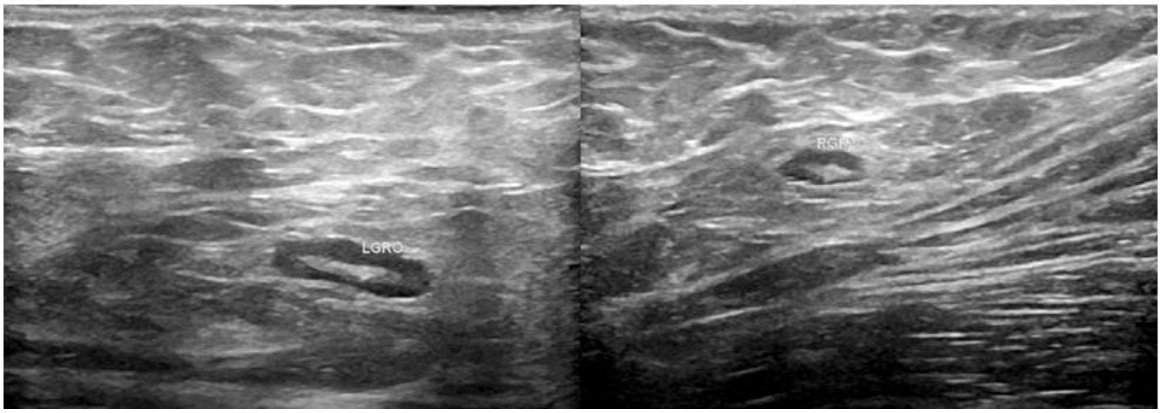

Figure 2 | Comparative scanning of bilateral inguinal regions: Several hypoechoic areas were detected respectively in the left and right inguinal regions. They have clear boundaries, regular shapes, and the internal echoes are slightly inhomogeneous. The sizes of one of them are 1.7 cm × 1.5 cm and 0.8 cm × 0.4 cm respectively. No abnormal color flow was observed.

Pelvic MRI shows: 1. A mass in the subcutaneous soft tissue near the groin of the left thigh root, most likely a mesenchymal-derived malignant tumor; exudation in the subcutaneous fat layer of the left thigh root; 2. Multiple enlarged lymph nodes in the left inguinal region and the areas along the course of the bilateral iliac blood vessels (Picture 3).

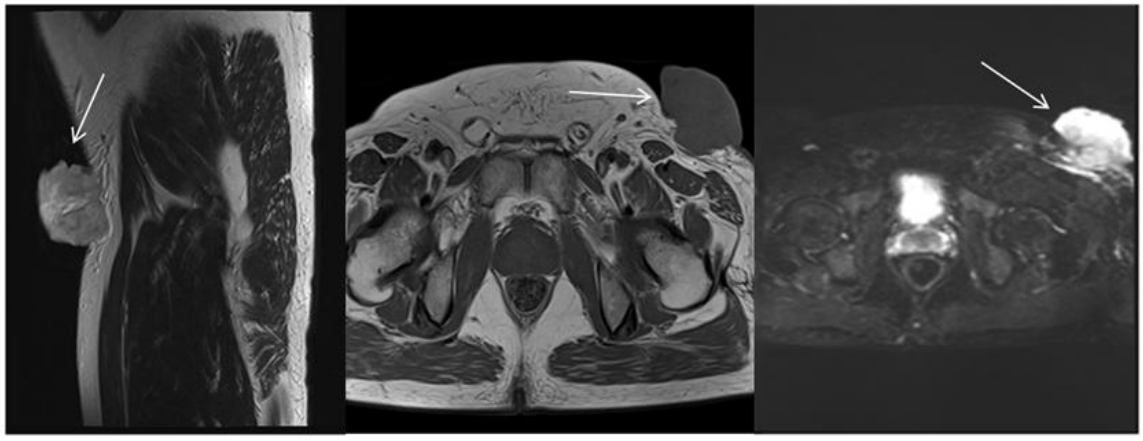

Figure 3 | An abnormal signal mass approximately 5.1 cm * 7.1 cm is seen within the subcutaneous soft tissues in the area near the inguinal region at the root of the left thigh. It shows long T1 and long T2 signal shadows. On DWI, it presents a high signal, and on the ADC map, it shows a slightly high signal. The outline of the lesion is relatively smooth, the boundary is clear, and it protrudes outside the contour of the thigh. Flaky and flocculent exudative shadows are observed within the subcutaneous fat layer at the root of the left thigh. The white arrow points to the location of the mass.

On the third day of hospitalization, the patient underwent resection of the skin mass on the left thigh and local skin flap transfer surgery under general anesthesia. After successful intubation under general anesthesia, the patient was placed in the supine position. The left thigh and the inguinal region were disinfected twice with 0.5% povidone-iodine, and sterile towels and drapes were applied. Findings during the operation: A skin mass measuring 10 cm × 7 cm × 5 cm was visible near the inguinal region at the root of the left thigh. The mass was hard in texture and reddish-brown in color. A few tortuous blood vessels could be seen beneath the mass. There was local ulceration on the surface of the mass, and a blood scab had formed. When touched, it bled. The mass invaded the deep subcutaneous tissue. A swollen lymph node measuring 2 cm × 1.5 cm could be palpated in the left inguinal region.The surgical site was alternately and repeatedly irrigated with 1.5% hydrogen peroxide solution and normal saline, three times each. A scalpel was used to incise the skin and subcutaneous tissues 2 cm outside the edge of the wound surface. The

mass and the enlarged inguinal lymph nodes were completely excised in the fat layer on the surface of the fascia, and a frozen pathological examination was performed. After hemostasis of the secondary wound by electrocoagulation, wet dressing was applied. The report of the intraoperative frozen pathological examination showed: 1. (Left thigh) Mesenchymal-derived malignant tumor; 2. (Left inguinal) No tumor metastasis was found in the lymph nodes (Picture 4).

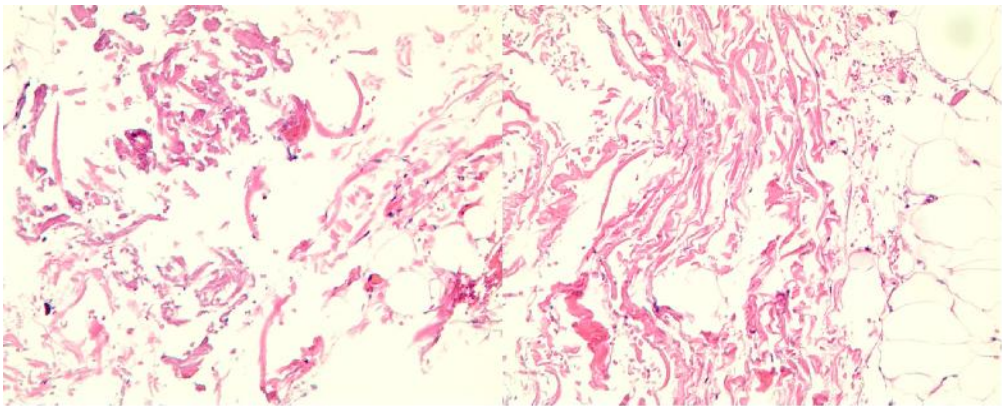

Figure 4 | The pathological diagnosis shows that the tissue samples from the left thigh are abundant fibrous adipose tissues, with a small amount of inflammatory cell infiltration, and no tumor tissue is found.

The scalpel was used to re-excise the remaining adipose tissue at the base of the wound surface, and the adipose tissue at the base was excised on the surface of the muscle and sent for postoperative pathological examination. The bleeding points within the wound surface were coagulated for hemostasis by electrocoagulation.The secondary wound was measured to be approximately 14 cm × 8 cm. Since the secondary wound of the patient was located in the groin and the wound cavity could not be closed by pulling together and suturing the free margins of the skin on both sides, it was decided during the operation to repair the wound with a perforator flap of the lateral circumflex femoral artery. Taking the tensor fasciae latae muscle as the center, the upper boundary was the edge of the iliac crest, the lower boundary was 5 cm above the plane of the knee joint. The anterior and posterior longitudinal incisions were along the anterior and posterior edges of the tensor fasciae latae muscle. A flap with a size of approximately 14 cm × 8 cm was designed. The scalpel was used to incise the skin, subcutaneous tissue and deep fascia along the inner edge of the flap, and the incision was extended downward. The flap was separated at the deep fascia layer. The perforating blood vessels were carefully searched for. The lateral circumflex femoral artery was found on the lateral side of the wound and the lateral side of the thigh. Blunt dissection was carefully performed at the site where the blood vessel entered the flap. It was traced that the source artery was the transverse branch of the lateral circumflex femoral artery, which was protected. The lower segment of the flap tissue was completely freed at the infiltrated fascia layer with tissue scissors, and the irrelevant blood vessels were ligated with sutures. The pedicle of the flap was located at the transverse branch of the lateral circumflex femoral artery. The subcutaneous tissue at the pedicle was retained, and the flap was fully elevated. The flap was pulled towards the secondary wound to cover the wound. It was checked that the blood supply of the flap was good. The scattered bleeding points were electrocoagulated for hemostasis. The flap and the marginal tissue of the skin were intermittently sutured with 2-0 absorbable sutures. The subcutaneous tissues on both sides of the donor site were freed to form two random flaps. The free flaps on both sides were pulled together, and the intradermal tension-reducing suture was intermittently performed with 2-0 absorbable sutures. The skin was intermittently sutured with No. 0 sutures. One negative pressure drainage tube was placed under the flap. The wound was covered with iodophor gauze, sterile dry gauze and wound stickers, and the drainage tube was properly fixed (Figure 5).

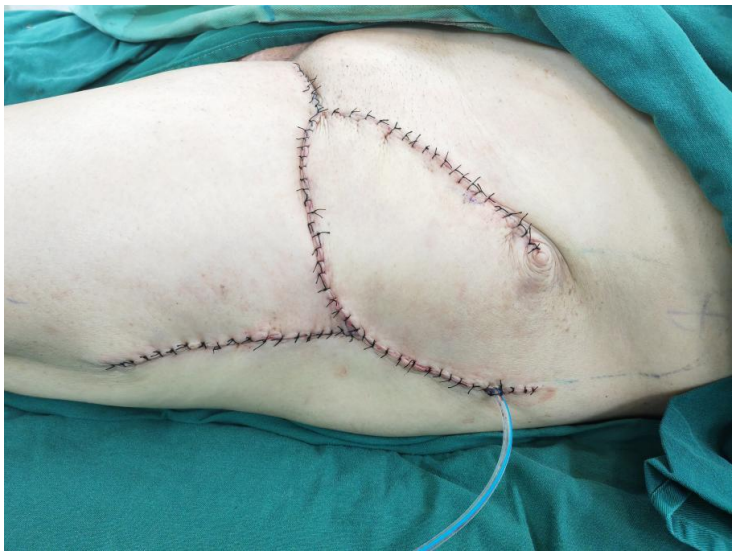

Figure 5 | After the resection of the mass

The operation was completed. After the patient was sent to the recovery room and became conscious, the patient was safely returned to the ward. The anesthesia during the operation was satisfactory, the operation was smooth, the bleeding was approximately 150 ml, and no blood transfusion was given. The patient was conscious after the operation and was safely returned to the ward. Two months after discharge, the patient came for a follow-up examination at the outpatient clinic of our department. A piece of skin and subcutaneous tissue from the left thigh was sent for examination. The pathological report diagnosis was: (Left thigh) In combination with the medical history, it was consistent with the recurrence after the operation of a highly malignant myxofibrosarcoma (Figure 6).

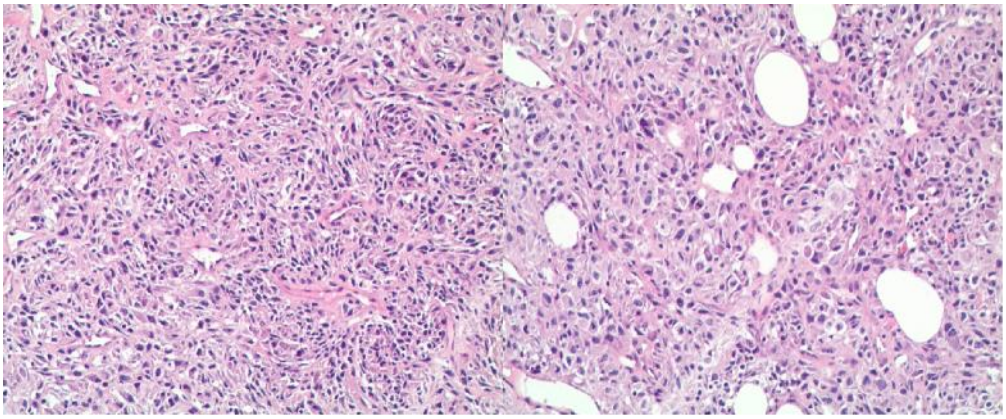

Figure 6 | Pathological examination during the outpatient reexamination after two months. Microscopic findings: The tumor tissue is composed of spindle cells and polygonal cells.

3. Discussion

In this case, the patient experienced a recurrence of highly malignant myxofibrosarcoma (MFS) in the groin area of the thigh in the short term after surgery. The mechanism of recurrence is complex and involves multiple factors such as the biological characteristics of tumor cells, the regulation of the tumor microenvironment, the activity of cancer stem cells, and the thoroughness of surgical resection[5]. Firstly, the invasiveness of highly malignant MFS cells is an important factor contributing to postoperative recurrence. MFS has a unique infiltrative growth pattern. Especially in the superficial form, tumor cells will infiltrate the surrounding soft tissues at both microscopic and macroscopic levels along the planes of normal tissues (such as the fascial plane and vascular plane)[6, 7]. This invasiveness makes it difficult to completely remove tumor cells during surgery, and the remaining cells become the source of recurrence [8]. At the same time, MFS cells are

able to secrete a variety of proteases, such as matrix metalloproteinases (MMPs). These enzymes can degrade components of the extracellular matrix (ECM), including collagen and laminin, thus disrupting tissue structure and providing a pathway for the migration and spread of tumor cells.In addition, adhesion molecules such as integrins on the surface of tumor cells can interact with the extracellular matrix (ECM), further promoting the adhesion and migration of tumor cells. In this case, the tumor cells are closely adhered to the surrounding muscle tissue, indicating their strong invasiveness, which may be one of the key factors leading to postoperative recurrence[9] . Secondly, the tumor microenvironment plays an important role in the recurrence of MFS. The tumor microenvironment is an important basis for the growth, proliferation, and metastasis of tumor cells, and it contains various cellular components, such as immune cells, fibroblasts, and endothelial cells, etc[10].In the MFS, tumor cells are capable of regulating the functions of immune cells, causing them to shift from an anti-tumor state to a pro-tumor state. Tumor-Associated Macrophages (TAMs) can secrete a variety of cytokines, such as Transforming Growth Factor-β (TGF-β). This cytokine not only inhibits the activity of immune cells but also promotes the metabolic reprogramming of tumor cells through the activation of the HIF1α/TRIB3 signaling pathway, thereby driving tumor progression. In addition, cytokines such as TGF-β and IL-10 secreted by TAMs can inhibit the activation and proliferation of effector T cells, further weakening the immune system's attack on tumor cells[11, 12]. Cancer-Associated Fibroblasts (CAFs) secrete growth factors (such as TGF-β, IL-6, etc.) and extracellular matrix (ECM) components, remodeling the tumor microenvironment and providing support and nutrients for tumor cells. TGF-β secreted by CAFs can induce the differentiation and activation of immunosuppressive cells (such as regulatory T cells), while inhibiting the infiltration of cytotoxic T cells. Moreover, the cytokines secreted by CAFs can also promote the transformation of TAMs from the anti-tumor M1 type to the pro-tumor M2 type [13].In addition, the presence of cancer stem cells is also one of the important mechanisms for the recurrence of MFS after surgery. Cancer stem cells are a small subset of tumor cells that have the ability of self-renewal and multi-directional differentiation, and they are resistant to traditional radiotherapy and chemotherapy. After tumor treatment, these cancer stem cells can survive and continue to proliferate, leading to tumor recurrence. Studies have shown that there may be cancer stem cells expressing specific surface markers (such as CD133) in MFS. In this case, although the patient received surgical resection, radiotherapy and chemotherapy, the tumor still recurred, suggesting the possible existence of cancer stem cells, which allowed the tumor cells to remain and continue to grow[14]. Finally, the thoroughness of surgical resection also has a significant impact on the recurrence of MFS. MFS is characterized by strong adhesiveness and unclear boundaries, and tumor cells may infiltrate into the surrounding tissues, making it difficult to completely remove the tumor during surgery[15]. In this case, there may have been an incomplete resection during the patient's initial surgery, and the remaining tumor cells became the source of recurrence. Therefore, precise preoperative assessment of the tumor scope, meticulous intraoperative operation, and close postoperative follow-up are crucial for reducing the risk of MFS recurrence.

4. Conclusion

This article reports a rare case of postoperative recurrence of a highly malignant myxofibrosarcoma (MFS) in the root of the left thigh of a 56-year-old male, and explores its complex recurrence mechanism. The patient experienced recurrence just 2 months after wide resection combined with the repair of the lateral circumflex femoral artery perforator flap. Pathological examination confirmed it was a highly malignant MFS. The study shows that the recurrence mechanism involves multiple factors: highly malignant MFS cells degrade the extracellular matrix by secreting matrix metalloproteinases (MMPs), showing significant invasiveness; immunosuppressive cells in the tumor microenvironment (such as tumor-associated macrophages (TAMs) secreting transforming growth factor-β (TGF-β)) and tumor-promoting fibroblasts form a supportive niche; the CD133+ cancer stem cell population is resistant to treatment and maintains regenerative potential; in addition, the invasive nature of the tumor margin leads to incomplete surgical

resection. This case suggests that a multimodal treatment strategy should be adopted: accurate imaging evaluation of the extent of tumor invasion before surgery, extended resection during the operation combined with intraoperative frozen pathological monitoring of the surgical margin, and postoperative radiotherapy targeting residual lesions. At the same time, novel targeted therapies for the regulation of cancer stem cells and the tumor microenvironment are also needed. This study provides an important clinical basis for optimizing the individualized comprehensive treatment of highly malignant MFS.

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Authors' Contributions

Wang Xin (WX) and Ma Chenghu (MCH)conceptualized the study, conducted the investigation, analyzed data, and wrote the manuscript. Mei Song (SM) assisted in reviewing and editing the manuscript. Jiahuan Li (LJH), Qian Tang (TQ), and Jianing Wang (WJN) participated in data collection and supervised manuscript drafting. All authors read and approved the final manuscript.

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Data and Materials Availability

All data generated or analyzed during this study are included in this published article.

Declarations

Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee of the 940th Hospital of the Joint Logistics Support Force of the Chinese People's Liberation Army. We confirm that this study adhered to the 1964 Helsinki Declaration and its subsequent amendments. Written informed consent was obtained from all individuals for the publication of any potentially identifiable images or data.

Competing Interests

The authors declare no competing interests.

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