

## Stewart Treves Syndrome of the Lower Extremity after Cervical Uterine Neoplasm

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### Abstract

### Case Report

The Stewart-Treves syndrome is a rare and deadly entity, which is defined as cutaneous angiosarcoma arising in the setting of chronic lymphedema. It is typically a result of post-mastectomy lymphoedema, it also develops in Milroy disease, idiopathic, congenital, traumatic and filarial lymphoedema. It is extremely uncommon in the lower extremities as a result of idiopathic chronic lymphedema or secondary of radiotherapy for cervix cancer. The pathophysiology is poorly understood, and the treatment of Stewart-Treves syndrome is complex. Surgery remains the key to manage it. Unless the treatment, its prognosis is poor. We report a case of cutaneous angiosarcoma of the lower extremity in a patient with chronic lymphoedema secondary of radiotherapy and surgery for cervix cancer. The body scan didn't show any metastatic lesions. The patient underwent acetabulum disarticulation with free margin, but she relapsed three months later. To the best of our knowledge, there are very few cases reported in the literature.

**Keywords:** angiosarcoma, Stewart-Treves syndrome, lymphedema, radiotherapy, cervical uterine neoplasm.

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## INTRODUCTION

Stewart-Treves syndrome (STS) is a rare cutaneous angiosarcoma associated with chronic lymphedema. It was first reported by Fred Stewart and Norman Treves [1] in 1948. The pathophysiology is poorly understood. It may be as a result of the accumulation of protein-rich interstitial fluid in a chronically swollen limb [2]. This fluid alters the local immune environment of the chronically edematous limb and promotes lymphangiogenesis. It also exacerbates the locally immunocompromised state to easily presented malignancy.

The prognosis of Stewart-Treves syndrome is poor. The aggressive nature of this disease requires radical resection, often forequarter amputations. Because of its aggressiveness and poor prognosis, early detection and surgical management are considered the main factors survival.

## CASE REPORT

We present the case of a 66-year-old female patient with bulky squamous-cell cervical carcinoma classified as stage IIB of FIGO.

She underwent concomitant radiochemotherapy. She received a cisplatin-based chemotherapy regimen weekly at 40 mg/m<sup>2</sup>/week. The radiotherapy regimen consisted of pelvic irradiation (45 Gy total dose) in 25 fractions over 5 weeks days, in a dose of 1.8 Gy per session, followed by high dose rate high brachytherapy in a dose of 15 Gy. Then, the patient underwent radical hysterectomy with bilateral pelvic lymphadenectomy in 2005. Since then she has developed chronic bilateral lower extremity lymphedema.

Twelve years after, she developed multiple coalescing, hemorrhagic and necrotic elevated purple-black papules in the right lower extremity. These lesions extend back to the anterior face of the thigh (Figure 1). These lesions were associated with 2cm inguinal lymphadenopathy.



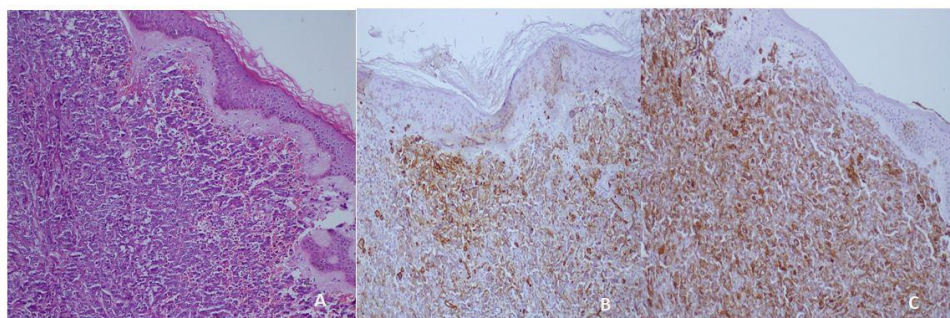
**Fig-1: Lower right extremity of the patient, multiple coalescing, hemorrhagic and necrotic elevated purple-black papules**

Punch biopsies were performed and histology results confirmed an angiosarcoma, invading the dermis, without ulcerating the epidermis, made of a diffuse layer of vaguely epithelial cells, with a prominent nucleus, richly mitotic with images of abnormal mitoses (Figure 2).

Immunohistochemical studies revealed that the tumor cells were positive for CD31 and CD34 (Figure 2). The human herpesvirus-8 (HHV8), P63, HMB45, PS100, and cytokeratin showed no immunoreactivity. Based on the morphology, immuno-profile, and clinical presentation, the patient was diagnosed with Stewart-Treves syndrome (STS).

The CT body scan didn't show any metastatic lesion. The patient underwent acetabulum disarticulation, with a 100 mm macroscopic safety margin. The definitive histological exam showed a microscopic free margin at 11 mm and a metastatic inguinal lymph node.

Three months later, locoregional recurrence in the amputation scar and pubis was noted. Local excision was performed, and the anatomopathological study confirmed the recurrence with free margins. The patient was lost from sight after.



**Fig-2: A, Cutaneous angiosarcoma: anastomosing vascular channels lined by atypical endothelial cells (H&E section x200). B: Cutaneous angiosarcoma: heterogeneous expression of tumor cells with CD34 (x200). C: Cutaneous angiosarcoma: diffuse marking of tumor cells for the CD31 antigen (x200).**

## DISCUSSION

STS is defined by the appearance of lymphangiosarcoma in a location affected by chronic lymphedema [1, 3]. STS is a rare tumor and accounts for approximately 5% of all angiosarcoma [2]. About 400 cases of angiosarcoma related to the STS have been reported in the English literature. The upper limb is the site involved in 90% of cases, usually in 5 to 15 years after radical mastectomy with axillary lymph node dissection for the treatment of breast cancer [3]. There are many causes of lymphedema, such as trauma, infectious (filariasis), venous stasis, morbid obesity, leg ulcerations, and surgery of the groin, legs, or pelvis.

Etiopathology of angiosarcoma is not clear and controversial. One theory is that chronic lymphedema causes local immunodeficiency, hence promoting

oncogenesis [4, 5]. The local immune response within the affected limb is altered by protein-rich interstitial fluid and the lymphatic channels enriched with growth factors, all stimulating lymphangiogenesis and the development of collateral vessels [6]. Also, the fluids in the lymphatic channels are rich in growth factors [5].

Besides chronic lymphedema, additional factors such as radiation therapy may increase the risk. Among patients receiving radiation therapy, the relative risk of developing angiosarcoma is 15.9% [10]. The incidence of Stewart Treves syndrome has significantly declined with the improvement of operative and radiation therapy techniques and the use of chemotherapy [7].

Three phases in the development of STS have been distinguished in the literature: (1) prolonged lymphedema, (2) angiomatosis, and subsequently (3) angiosarcoma [3]. Prolonged lymphedema is observed in Kaposi sarcoma as well as angiosarcoma, resulting in localized immunosuppression and vascular oncogenesis in the presence of human herpesvirus 8 (HHV-8) infections and immunosuppression [5].

The clinical presentation of angiosarcoma is either a cutaneous or subcutaneous mass or a poorly healing pressure sore with recurrent bleeding. In later advanced stages, multiple red-blue and confluent macules or nodules were observed, with ulceration and necrosis.

The histologic findings of angiosarcoma in STS show heterogeneous morphology with areas dominated by hemangiosarcoma and lymphangiosarcoma structures [8].

Because it is a poorly differentiated neoplasm, it requires confirmation by immunohistochemistry. Diagnostically practical stains include CD34, FLI-1, Von Willebrand factor, factor VIII, and CD31, the latter being the one with higher sensitivity and specificity [3, 4].

The most important differential diagnosis of Stewart Treves Syndrome is Kaposi sarcoma (KS). Immunohistochemical testing for the presence of HHV-8 is the primary way to differentiate STS from KS [3].

The treatment of STS is complex. Surgery remains the key to manage STS. The role of chemotherapy and radiotherapy is uncertain [9]. Grobmyer *et al.* reported no significant difference in the survival of patients treated with chemotherapy versus amputation/disarticulation or wide local excision of the affected limb in localized disease, which offers the best chance of long-term survival. Wide local excision is not beneficial over amputation. Even when a 2–3-cm wide margin of resection is obtained at the primary surgery, a high local recurrence rate is observed [11].

However, regardless of the approach applied, the overall prognosis of STS is poor, with a high rate of local recurrence and metastatic disease [3, 4]. The median survival is 2.5 years after diagnosis, with most patients dying from metastatic disease within two years [3, 4]. The long-term survivorship is rare. Untreated patients usually live for 5–8 months after diagnosis [3].

We have presented a female patient with angiosarcoma of the lower extremity complicating chronic lymphedema, 12 years after treatment of cervix cancer. Our case is unusual to the rarity of this syndrome. Despite a rare complication, it should be considered in patients presenting with chronic

lymphedema as the early diagnosis may be crucial to improving survival.

Preventative measures should be encouraged, given the disappointing treatment results. These combine treatment of chronic lymphedema, weight loss, pressure garments, physiotherapy, compressive devices and furthermore, microsurgery, and laser therapy [3, 5].

## CONCLUSION

The oncologist must be aware and think about this rare but aggressive entity in patients with chronic lymphedema secondary to cancer treatment. Biopsy confirmed the diagnosis after the immunohistochemical tests. CT scan and MRI should be performed for evaluating the extent of disease and for guiding treatment strategies. Surgery stills the main key of treatment.

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