

CORRESPONDENCE

Stewart-Treves syndrome arising in patients with lymphaticovenular anastomosis for chronic lymphedema of the leg

Case 1. A 51-year-old woman presented with lymphedema of the left leg in 2000, without past history of surgery or radiation. She underwent lymphaticovenular anastomosis twice for her left lymphedema in 2003 and 2006. The skin incision was made at the thigh, knee and ankle. However, the surgery was unsuccessful, and conservative pressure therapy was continued. In 2010, she was referred to our department with a one-year history of a purplish lesion on her left lower leg. Examination revealed a slightly indurated, ecchymotic lesion, measuring 8 × 7 cm on the lymphedematous lower leg (*figure 1A*). A biopsy specimen of the lesion showed some vascular channels lined by atypical endothelial cells with an extravasation of erythrocytes and scattered atypical cells in the dermis (*figure 1C*). Double immunofluorescence analysis showed that tumor cells were positive for podoplanin and negative for von Willebrand factor (*figure 1D*), indicating the development of lymphangiosarcoma. FDG PET/CT imaging showed a mottled, abnormal accumulation in the left lower leg (*figure 1B*). She was treated with X-ray at a dose of 60 Gy and eight courses of monthly docetaxel. There has been no evidence of local recurrence or metastases 13 months after the radiation.

Case 2. A 71-year-old woman, who was treated for cervical carcinoma in 1996, undergoing a hysterectomy and radiotherapy, developed chronic lymphedema of both legs. She underwent lymphaticovenular anastomosis twice in 2000 and 2001. However, the lymphedema gradually progressed, accompanied by hyperkeratotic papules of lymphangiectases. In 2010, she was referred to our department for further evaluation regarding a two-month history of a hemorrhagic lesion on her right buttock with high uptake of FDG as determined by PET/CT (*figure 1E*). Physical examination revealed hemorrhagic nodules on the right buttock and lower abdomen (*figure 1F*). Under a diagnosis of STS, she was treated by electron beams at a total dose of 60 Gy, followed by intravenous injections of interleukin-2 for five weeks. However, she developed several recurrences on her buttock and died of sepsis.

Stewart-Treves syndrome (STS) is a rare form of lymphangiosarcoma that occurs as a complication of lymphedema. The lymphedematous region becomes an immunologically vulnerable area that is predisposed to malignancy. Lymphedema in the extremities is troublesome for patients and conventional therapies are not always satisfactory. Lymphaticovenular anastomosis is a novel treatment of

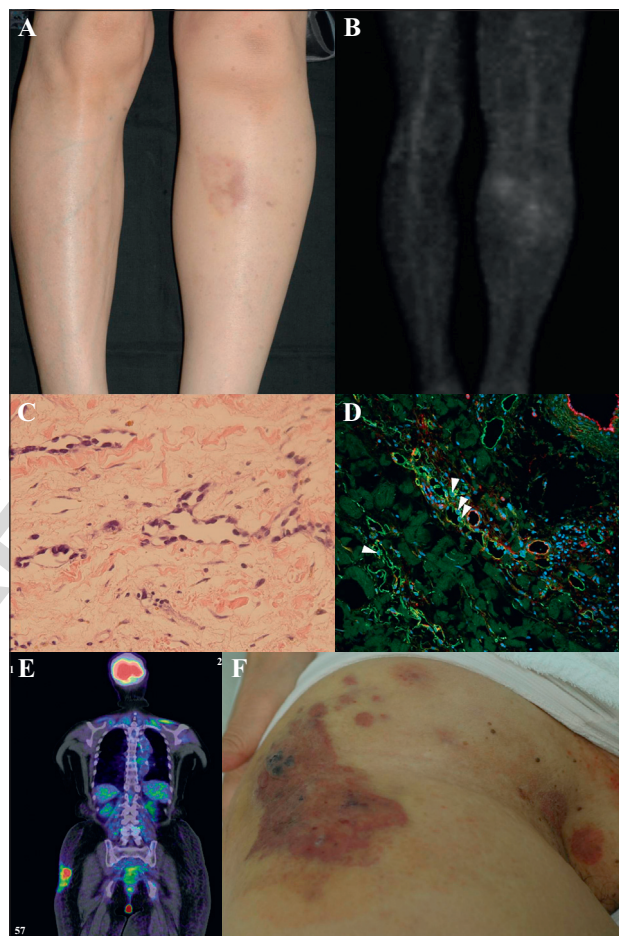


Figure 1. **A)** An ecchymotic lesion with lymphedema of the left lower leg. **B)** FDG PET/CT imaging shows a mottled, abnormal accumulation in the left lower leg. **C)** Angiolymphatic spaces lined by atypical endothelial cells. **D)** Double immunofluorescence analysis. Green, podoplanin for lymphatic vessels; Red, von Willebrand factor for blood vessels; light blue, DAPI for nuclei; arrowheads, tumor cells. **E)** FDG PET/CT image showing abnormal accumulation in the right buttock. **F)** Hemorrhagic nodules on the right buttock and lower abdomen.

lymphedema in the extremities [1]. The supermicrosurgical anastomosis of a lymphatic collector and a subdermal venule is performed through two or three incisions. This surgery has good results in most patients with upper extremity lesions and in about half of those with lower extremity lesions [2].

In the present cases, chronic lymph stasis might predispose the onset of the lymphangiosarcoma. The association between lymphangiosarcoma and lymphaticovenular anastomosis is unclear. A history of prior trauma and surgery has been noted in some studies on cutaneous angiosarcoma. However, Holden *et al.* [3], found no definitive predisposing factors in any of 72 patients reviewed. We previously reported a case of metastatic angiosarcoma in a skin graft donor site associated with the Koebner phenomenon, and proposed that this phenomenon may be involved in the pathogenesis of angiosarcoma [4]. Furthermore, a few cases of angiosarcoma have occurred in post-transplant patients with arteriovenous fistula (AVF) [5, 6]. Oscillatory blood flow in AVF causes shear stress at the endothelium, providing a pro-inflammatory stimulus to upregulate growth peptides, and enhances the activity of the DNA transcription regular NFkB by phosphorylation [5]. Similarly, the aberrant flow through lymphaticovenular anastomosis may be one of the factors contributing to the tumorigenesis of STS. The prognosis is poor despite aggressive treatment. Therefore, we should be aware of the possible occurrence of this condition during the treatment and follow-up of chronic lymphedema. ■

Disclosure. *Financial support: none. Conflict of interest: none.*

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doi:10.1684/ejd.2012.1726

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