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## Cutaneous angiosarcoma in a patient with systemic sclerosis: First case from India

Sir,  
Cutaneous angiosarcoma is a rare malignant vascular tumor, which has been reported seldom with systemic sclerosis.<sup>1-4</sup> We are reporting a case of cutaneous angiosarcoma (face) occurring over the sclerodermoid skin in a patient with systemic sclerosis. To the

best of our knowledge, this has not been previously reported from the Indian subcontinent.

A 56-year-old female, already diagnosed with systemic sclerosis and interstitial lung disease since the last 6 years, presented with a



**Figure 1:** Bluish red plaque with hemorrhagic blister over the sclerodermoid skin of the scalp and forehead



**Figure 2:** Bluish red plaque with hemorrhagic blister over the sclerodermoid skin of the scalp and forehead

rapidly progressing, painful, bluish red and hard swelling over the left side of the forehead since 1 month. Cutaneous examination revealed generalized sclerosis and a large well-defined, bluish-red, woody hard, tender plaque (7 × 5 cm) with multiple hemorrhagic vesicles and bullae was noted over the left temporoparietal area with extensions over the forehead, zygomatic, and maxillary areas [Figures 1-4]. Differential diagnoses of angiosarcoma and mycetoma were considered. Investigations showed elevated erythrocyte sedimentation rate (34 mm/h), positive antinuclear antibodies (3+), Scl-70 (3+) and SS-A antibodies (+). Computed tomography scan of the head showed edema in the subcutaneous plane.

Fine needle aspiration cytology from the plaque showed clusters of malignant cells with mitotic figures, suggestive of a malignant pathology. Incisional skin biopsy from the same site revealed a few branching vascular channels in the dermis, lined by a single row of flat to plump endothelial cells [Figure 5]. The individual cells had scant eosinophilic cytoplasm with enlarged round to oval nucleus [Figure 6]. Atypical cells were positive for CD34 and CD31 [Figures 7 and 8],

strongly positive for Ki67, and negative for leukocyte common antigen (LCA). A final diagnosis of cutaneous angiosarcoma was made. No improvement was seen even after six cycles of chemotherapy.

Angiosarcoma is a rare, malignant vascular tumor that is localized to the skin or superficial soft tissue. It is known to occur in three different clinical settings – idiopathic cutaneous angiosarcoma of the head and neck (most common), angiosarcoma complicating lymphedema and post-irradiation angiosarcoma. The cancerous lesion rapidly progresses and has a fulminant course.

Histologically, low-grade angiosarcoma is composed of irregular vascular channels dissecting dermal collagen, lined by atypical endothelial cells. In a few cases, tumor can show high grade differentiation with vascular anastomosing channels lined by atypical endothelium, resembling high-grade sarcoma and carcinoma. Immunohistochemistry with endothelial specific antibodies (Ulex europaeus agglutinin, antibody to factor VIII related, and CD31 and 34 antigens) helps in confirming the diagnosis.

The exact mechanism responsible for tumorigenesis in systemic sclerosis patients is still unknown. Multiple mechanisms have been proposed; such as endothelial cell damage through ischemia, growth modulatory mediators released from inflammatory cells and platelets, genetic susceptibility, decline in the number of natural killer T cells, therapeutically induced immunosuppression and vascular endothelial growth factor (VEGF) overexpression.<sup>5</sup>

Shah *et al.*<sup>6</sup> investigated 23 systemic sclerosis patients with malignancy and concluded that patients with RNA polymerase III



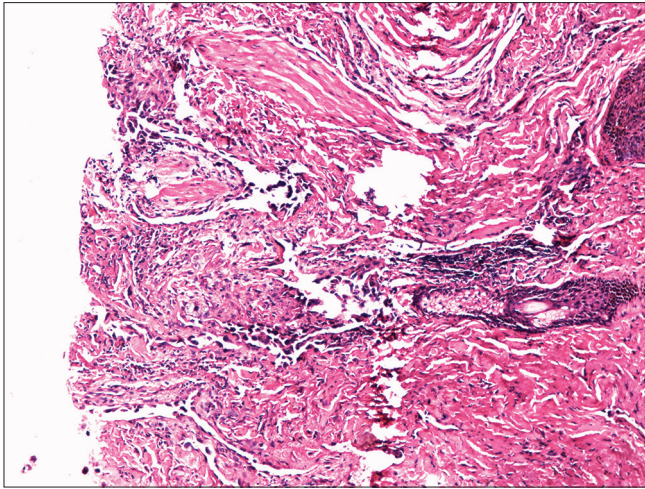
**Figure 3:** Rapid extension of the lesion with crusting and erosion over the surface on day 3 of admission



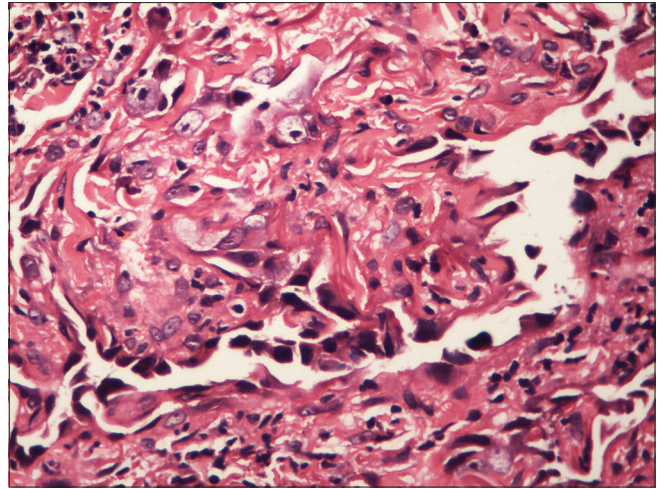
**Figure 4:** Rapid extension of the lesion with crusting and erosion over the surface on day 3 of admission

**Table 1: Demographic details and clinical features of reported cases of cutaneous angiosarcoma with systemic sclerosis**

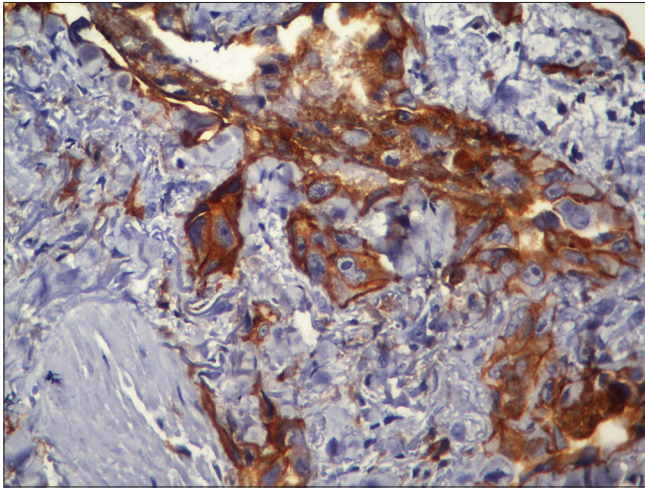
Case reports	Age (years)/sex	Ethnicity	Duration of systemic sclerosis (years)	Site
Puizina-Ivic <i>et al.</i> , 2005	77/female	Caucasian	8	Left temporal area, forehead, and face
Fonder and Douglas 2008	40/male	Black	5	Scalp
Kubota <i>et al.</i>	67/female	Japanese	17	Scalp
Carter <i>et al.</i>	58/female	African-American	Unknown	Right elbow
Our case	56/female	Indian	6	Left temporal area, forehead, and face



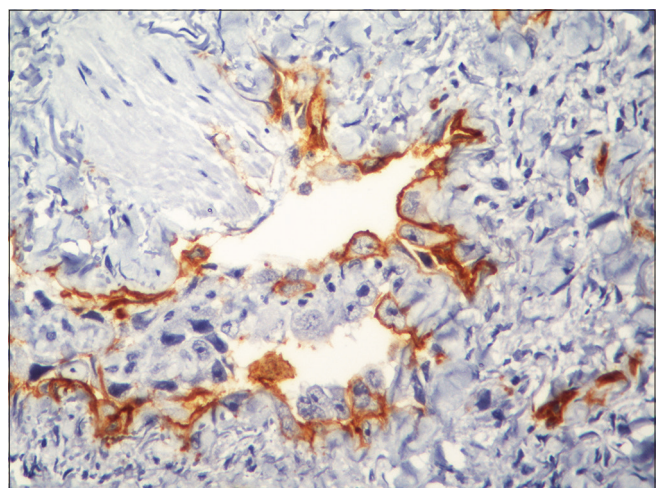
**Figure 5:** Dermis showing irregular anastomosing vascular channels (H and E, ×100)



**Figure 6:** Magnified view of vascular channels in the dermis lined by endothelial cells (H and E, ×100)



**Figure 7:** Immunohistochemistry showing CD31 positive cells (immunohistochemistry, ×400)



**Figure 8:** Immunohistochemistry showing CD34 positive cells (immunohistochemistry, ×400)

antibodies had a uniquely close temporal relationship with cancer diagnosis and systemic sclerosis onset.

The site of angiosarcoma was similar to the earlier reported cases of systemic sclerosis with angiosarcoma [Table 1]. Levels of anti-RNA polymerase 3 antibodies and VEGF could not be assessed. It would be interesting to evaluate the levels of serum VEGF in systemic sclerosis and to determine its cut-off levels to predict the risk of developing angiosarcoma in the subset of patients who have higher/very high levels of VEGF. Treatment with anti-VEGF monoclonal antibodies (Bevacizumab) in this subset of patients might help in arresting the neoplastic process.

Angiosarcoma can pose diagnostic challenges as it can mimic other benign vascular lesions. Immunohistochemistry and detailed neuroimaging studies can minimize the delay in diagnosis. To the best of our knowledge, this case is the fifth reported case of angiosarcoma in association with Systemic sclerosis.

#### Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for

her images and other clinical information to be reported in the journal. The patient understands that her name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Nil.

#### Conflicts of interest

There are no conflicts of interest.

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