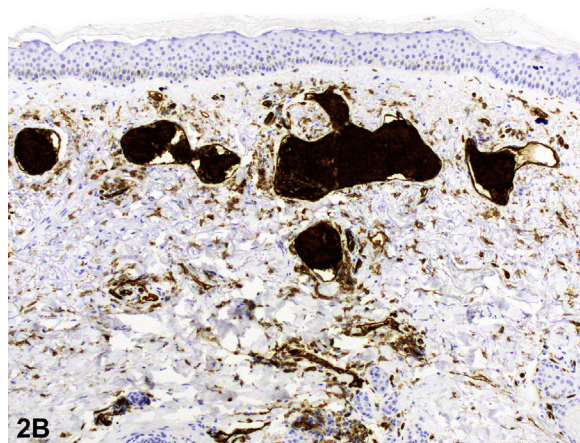
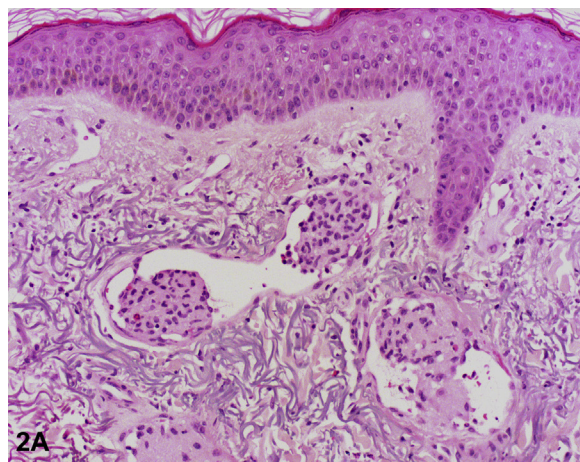


## Purpuric plaques in a patient with breast cancer



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**Key words:** antiphospholipid syndrome; metastatic breast cancer; purpura; reactive angioendotheliomatosis.



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Funding sources: Supported by Brigham and Women's Hospital Department of Dermatology.

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Conflicts of interest: None disclosed.

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JAAD Case Reports 2020;6:1228-30.

2352-5126

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<https://doi.org/10.1016/j.jidcr.2020.09.013>

## CASE PRESENTATION

A 55-year-old woman with a recent history of metastatic breast cancer to bone presented with a purpuric rash on her jaw, neck, and chest (Fig 1). A hypercoagulability evaluation revealed an elevated activated partial thromboplastin time as well as lupus anticoagulant and anticardiolipin antibodies. The patient had no symptoms indicating infection. A lesional skin biopsy was performed and revealed ectatic, although not atypical, vascular spaces in the dermis, some of which were filled with clusters of cells in direct contact with the vessel walls (Fig 2, A). These cells stained intensely positive for CD31 (Fig 2, B) and focally for PU-1 and CD163.

### Question 1: What is the most likely diagnosis?

- A. Intravascular histiocytosis
- B. Glomeruloid hemangioma
- C. Papillary endothelial hyperplasia
- D. Reactive angioendotheliomatosis
- E. Cutaneous angiosarcoma

### Answers:

**A.** Intravascular histiocytosis — Incorrect. Intravascular histiocytosis, which presents as erythematous plaques on the extremities, is a benign proliferation of histiocytes (which stain for CD68, CD163, and PU-1) within the lumina of cutaneous vessels. Immunostaining of endothelial cells with podoplanin demonstrates that cases are typically intralymphatic.<sup>1</sup>

**B.** Glomeruloid hemangioma — Incorrect. These are benign vascular lesions associated with polyneuropathy, organomegaly, endocrinopathy, myeloma protein, and skin changes, also known as POEMS syndrome, with histopathology showing capillaries in glomeruloid formations.

**C.** Papillary endothelial hyperplasia — Incorrect. Papillary endothelial hyperplasia is a reactive proliferation of endothelial cells with papillary formations related to thrombi formation. This painful benign lesion on the head, neck, or upper extremities presents as a solitary nodule located within a dilated dermal, subcutaneous, or submucosal vein.

**D.** Reactive angioendotheliomatosis — Correct. Reactive angioendotheliomatosis (RAE) is a rare cutaneous disease that may present as erythematous or violaceous papules, nodules, or plaques, which can be ulcerated; involved areas may be painful, pruritic, or asymptomatic.<sup>2,3</sup> RAE has been observed in patients with a variety of conditions, including infections, pregnancy, malignancy, connective tissue disease, antiphospholipid syndrome, and cryoglobulinemia. RAE typically resolves with the treatment of the underlying condition.<sup>2</sup> Our patient's cutaneous lesions started to recede after a

cycle of cytotoxic chemotherapy and improved significantly with subsequent rounds. The patient was not treated with anticoagulants.

**E.** Cutaneous angiosarcoma — Incorrect. Cutaneous angiosarcoma is an aggressive malignancy showing atypical, anastomosing vessels dissecting through the dermis and often presents as red to purple patches or plaques on the head and neck in the elderly.<sup>4</sup>

### Question 2: Which of the following best describes the histopathologic findings of reactive angioendotheliomatosis?

**A.** Hyperplastic endothelial cells, sometimes spindled, diffusely infiltrating the papillary and reticular dermis, and sometimes forming small vascular lumina.

**B.** Tightly packed cells surrounding endothelium-lined ramifying vessels and exhibiting poorly-defined cell boundaries with round or oval nuclei.

**C.** Endothelial cells ranging from flattened to columnar in shape, with irregular vascular channels in the dermis and subcutis.

**D.** Vascular proliferation and endothelial cell hyperplasia within the lumina and around dermal vessels, without significant cellular atypia.

**E.** Proliferation of capillary-sized vessels with compact deep lobules and cells with occasional mitotic figures.

### Answers:

**A.** Hyperplastic endothelial cells, sometimes spindled, diffusely infiltrating the papillary and reticular dermis, and sometimes forming small vascular lumina — Incorrect. This is characteristic of acroangioidermatitis, also known as pseudo-Kaposi sarcoma, which is a benign angioproliferative disorder arising in the setting of chronic venous insufficiency. When human herpesvirus-8 staining is negative, Kaposi sarcoma can be excluded.<sup>5</sup>

**B.** Tightly packed cells surrounding endothelium-lined ramifying vessels and exhibiting poorly-defined cell boundaries with round or oval

nuclei — Incorrect. This is characteristic of hemangiopericytomas, which are rare neoplasms derived from pericytes.

**C.** Endothelial cells ranging from flattened to columnar in shape, with irregular vascular channels in the dermis and subcutis — Incorrect. This is characteristic of endovascular papillary angioendothelioma (Dabska tumor), a low-grade angiosarcoma that typically arises in children. These lesions may appear either as diffuse swelling or as an intradermal tumor.<sup>5</sup>

**D.** Vascular proliferation and endothelial cell hyperplasia within the lumina and around dermal vessels, without significant cellular atypia — Correct. Histopathologically, RAE is characterized by dermal vascular proliferation and endothelial cell hyperplasia within the lumina and around dermal vessels, without significant cellular atypia. Intravascular mononuclear cells are typically labeled by vascular markers CD31, CD34, or ERG (a transcription factor that serves as a highly sensitive marker for vascular differentiation) and demonstrate weak or negative staining for histiocytic markers, such as CD68, CD163, or PU-1. Microthrombi and occluded vessels are often present.<sup>2</sup>

**E.** Proliferation of capillary-sized vessels with compact deep lobules and cells with occasional mitotic figures — Incorrect. This is the pathologic description of a pyogenic granuloma.

**Question 3: Which of the following is not associated with reactive angioendotheliomatosis?**

- A.** Intravascular large cell lymphoma
- B.** Rheumatoid arthritis
- C.** Antiphospholipid syndrome
- D.** Chronic lymphocytic leukemia
- E.** Renal disease

**Answer:**

**A.** Intravascular large cell lymphoma — Correct. Intravascular large cell lymphoma was previously referred to as malignant angioendotheliomatosis because histopathology of this condition

demonstrates intraluminal proliferation of large atypical cells. However, these cells are not derived from endothelial cells but rather lymphoid in origin, the majority of which are B-cell proliferations.<sup>5</sup>

**B.** Rheumatoid arthritis — Incorrect. There have been literature reports of patients with rheumatoid arthritis developing RAE.<sup>3</sup>

**C.** Antiphospholipid syndrome — Incorrect. There have been cases reported in the literature, similar to the current case, in which RAE was discovered in a patient with laboratory-confirmed antiphospholipid antibodies. In our case, antiphospholipid syndrome was confirmed with repeated antiphospholipid antibody tests remaining positive after a recheck at 12 weeks.<sup>3</sup>

**D.** Chronic lymphocytic leukemia — Incorrect. Several case reports have demonstrated an association between chronic lymphocytic leukemia and RAE.<sup>3</sup>

**E.** Renal disease — Incorrect. Renal disease has been associated with RAE. In one study of 15 patients, six patients had renal disease, including three who had undergone renal transplant.<sup>3</sup>

**Abbreviation used:**

RAE: reactive angioendotheliomatosis

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