Reactive Angioendotheliomatosis

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HISTORY OF PRESENT ILLNESS: 60 year-old Caucasian male presents with a lesion on his left thigh for three months. The lesion is initially a pink plaque described to be the size of a lemon with subsequent progression in size, pain and central crusting. He has no history of similar lesions elsewhere. Patient was recently evaluated by vascular surgery and was found to have stenosis as well as occlusion of the left iliac arteries via ultrasound. He is also noted to have had a stroke, myocardial infarction, and pancreatitis within the last three months.

MEDICAL HISTORY/SURGICAL HISTORY: Deep venous thrombosis of left distal lower extremity, cholecystectomy, colonoscopy, stroke, hyperlipidemia, hypertension, myocardial infarction, and pancreatitis

MEDICATIONS: Atorvastatin, duloxetine, levothyroxine, trazodone, clopidogrel, metoprolol, oxycodone-acetaminophen

PREVIOUS TREATMENTS: Triamcinolone 0.1% ointment twice daily as needed

CURRENT TREATMENT: Left common femoral endarectomy with bovine patch per vascular surgery, local wound care

PHYSICAL EXAMINATION: Pink to red large plaque on the left medial thigh with a small amount of scale. More centrally, there is firm white induration of the plaque with dark brown scale crust. The right leg is clear.

LABORATORY DATA: Hemoglobin 11.7 g/dL (12.0-17.0), platelets 418 thousand s/uL (149-390), fibrinogen 503 mg/dL (227-495), and erythrocyte sedimentation rate 36 mm/hr (0-11)

STUDIES: Vascular study of abdominal aorta and iliac arteries reveals aorta to be patent and normal in caliber with mild diffuse arterial occlusive disease noted, elevate velocities suggest a 50 to 75% stenosis in the mid right external iliac artery with stent, high grade stenosis versus occlusion of the left iliac artery with reconstitution of the distal external iliac artery.

BIOPSY: *Cleveland Clinic (S18-27479, 2/27/2018)* Left thigh: "poorly-demarcated dermal-based proliferation of poorly formed slit like vascular spaces which percolate through reticular collagen bundles, surround adnexal structures and extend into the subcutis. The vascular spaces are lined with flattened, bland endothelial cells without cytologic atypia or mitotic activity. CD31 and 34 stains reveal a patchy proliferation of capillaries scattered throughout the dermis. HHV8 stain, to rule out Kaposi 's sarcoma, is negative."

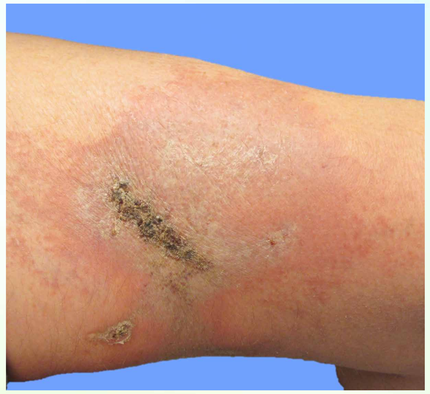

Figure A. Clinical presentation of left thigh.

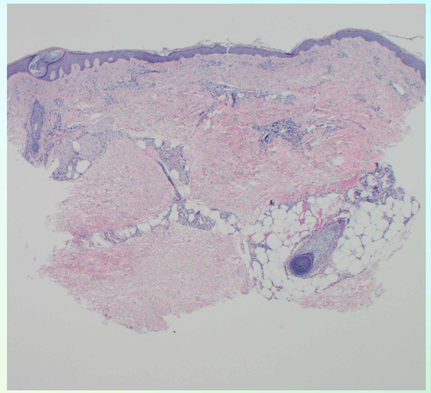

Figure B. H&E at 4x. Dermal based proliferation of spindle cells.

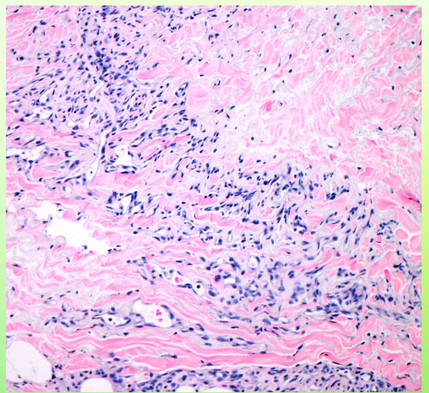

Figure C. H&E at 20x. Flattened endothelial cells without cytologic atypia or mitotic activity.

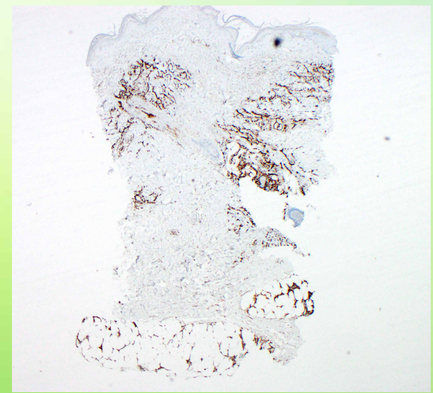

Figure D. CD34 stain showing patchy proliferation of capillaries throughout the dermis.

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Reactive Angioendotheliomatosis (RAE) is a rare, benign condition that presents with a cutaneous vascular proliferation with secondary intravascular thrombi leading to necrosis and infarction of the skin. RAE tends to occur in patients with coexistent systemic diseases. Clinical presentation demonstrates erythematous macules, purpuric papules, and purpuric plaques, which can be ulcerated. Lesions can affect the face or trunk, but tend to target the limbs. The condition favors middle-aged adults with no gender predilection. Patients may experience constitutional symptoms, such as fevers and weight loss. Many patients also have an elevated erythrocyte sedimentation rate. Other laboratory abnormalities can include thrombocytopenia, anemia, and leukocytosis. Coexistent diseases are broad in the literature and include infectious diseases, systemic disease, blood disorders, monoclonal gammopathies, and vascular abnormalities, including severe peripheral vascular atherosclerotic disease.

While the pathogenesis is unknown, changes in portal and systemic hemodynamics as well as a response to local hypoxia have been reported. This is further supported by the cases of RAE that improve after arterial bypass procedures, corroborating the notion that local tissue hypoxia may have been an inciting agent leading to induction of angiogenesis. Another theory is that deposition of complement and immunoglobulins may induce vascular injury. Furthermore, association with underlying systemic infections suggest that RAE can represent a hypersensitivy response of endothelial cells to foreign antigens. This hypersensitivity response leads to deposition of immunoglobulins in capillaries in the skin leading to thrombi and ensuing local hypoxia.

On histopathology, the individual lesions can vary. Histopathologic examination shows dilated vessels in the dermis and upper subcutaneous fat, filled with cells and fibrin, sometimes leading to vascular occlusion. There may be proliferation of pericytic myoepithelial cells. The intravascular cells are positive for CD31, and CD34 but negative for HHV-8. In addition, intravascular cells will be positive for *Ulex Europeus* and factor VIII-associated antigen supporting an endothelial origin.

Other important clinical entities to consider include Kaposi's Sarcoma and angiosarcoma. Prognosis of RAE is generally good and characterized by self-limited disease. Therapy, if needed, is directed at the underlying systemic disease. However, no specific treatment is currently available. Consideration can be made for antibiotics for infections and systemic steroids for their suppressive role on neoangiogenesis when no apparent cause can be found. In all, RAE is a rare disease related to a reactive endothelial proliferation in response to an unknown stimulus.

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