Diffuse Dermal Angiomatosis of the Breast

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Background: Diffuse dermal angiomatosis is rare and usually considered a variant of reactive angioendotheliomatosis. It generally involves the extremities of patients with severe vascular disease and other comorbidities. Two patients with breast involvement have been described; however, neither had a relevant medical history or a vaso-occlusive disorder, but both had large pendulous breasts, and 1 was positive for IgM anticardiolipin and antinuclear antibodies.

Observations: A 53-year-old woman had a reticulated, erythematous plaque with superficial ulceration and underlying tender nodules on her left breast. She had a history of cardiovascular disease and was a heavy smoker. Biopsy of the lesion showed diffuse proliferation of additional endothelial cells and small bland vessels within the papillary and upper reticular dermis. Angiography showed almost complete occlusion of the subclavian artery proximally. Diffuse dermal angiomatosis was diagnosed. With isotretinoin therapy, the lesions improved. One month later, after percutaneous subclavian arterial revascularization, the lesion resolved completely. A literature review suggested that a history of heavy smoking, in addition to a history of vascular disease, may be important in the pathogenesis of diffuse dermal angiomatosis.

Conclusions: Clinical acumen is crucial to diagnose diffuse angiomatosis of the breast. Appropriate treatment to alleviate hypoxia may improve the patient's condition.

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The results were within normal limits.

A punch biopsy specimen was obtained from the lesional area of the left breast. Examination of the specimen showed diffuse proliferation of additional endothe-

Table. Summary of the Clinical Features and Presentation of Reported Cases of Diffuse Dermal Angiomatosis

<table>
<thead>
<tr>
<th>Source</th>
<th>Patient No./ Sex/Age, y</th>
<th>Location of Lesion</th>
<th>Clinical Presentation</th>
<th>Comorbidities</th>
<th>Smoking Habit</th>
<th>Treatment</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sommer et al, 2004</td>
<td>1/F/59</td>
<td>Forearm</td>
<td>Solitary, erythematous, indurated, centrally ulcerated plaque</td>
<td>End-stage renal failure and S/P brachiobasilic fistula</td>
<td>Yes</td>
<td>Prednisolone, 40 mg/d</td>
<td>Completely healed after 2 mo</td>
</tr>
<tr>
<td>Kim et al, 2002</td>
<td>2/F/58</td>
<td>Thigh</td>
<td>Large, ulcerated, red-violaceous plaque</td>
<td>Hypertension, IDDM, and intermittent claudication of both legs, with no palpable peripheral pulses</td>
<td>Yes</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>PICKADO et al, 2002</td>
<td>3/F/47</td>
<td>Breast</td>
<td>Painful ulcers on both breasts</td>
<td>No relevant medical history, large pendulous breasts, and positive for anticardiolipin and antinuclear antibodies</td>
<td>NA</td>
<td>Daily baby aspirin and pentoxifylline (Trental)</td>
<td>Improved</td>
</tr>
<tr>
<td>McLaughlin et al, 2001</td>
<td>4/F/28</td>
<td>Breast</td>
<td>Violaceous, nonhealing, ulcerating macules on both breasts</td>
<td>No relevant medical history and large pendulous breasts</td>
<td>Yes</td>
<td>Isotretinoin</td>
<td>Completely resolved after 2 mo</td>
</tr>
<tr>
<td>Kimyai-Asadi et al, 1999</td>
<td>5/F/57</td>
<td>Thigh and inner ankle</td>
<td>Large, painful, blanchable, reticulated, erythematous plaques</td>
<td>Hypertension, CRI, and debilitating bilateral leg claudication; angiography showed complete occlusion of left renal artery and infrarenal aorta</td>
<td>Yes</td>
<td>Aortobifemoral bypass surgery</td>
<td>Completely cleared after 6 wk</td>
</tr>
<tr>
<td>Requena et al, 1999</td>
<td>6/F/73</td>
<td>Forearm, distal to AV fistula</td>
<td>Purpuric plaque</td>
<td>CRI and on hemodialysis</td>
<td>NA</td>
<td>Removal of AV fistula</td>
<td>Lesion resolved after fistula removed Resolved after 1 mo</td>
</tr>
<tr>
<td>Krell et al, 1994</td>
<td>7/F/47</td>
<td>Thigh</td>
<td>Ulcerated plaques with hyperpigmented border surrounded by diffuse erythema</td>
<td>Hypertension and severe PVD, S/P BKA, antinuclear antibody negative, and DLE treated with steroids and hydroxychloroquine sulfate (Plaquenil sulfate); angiography showed complete occlusion of aorta, below renal arteries</td>
<td>NA</td>
<td>Axillary-femoral bypass surgery</td>
<td>Resolved after 1 mo</td>
</tr>
<tr>
<td>Krell et al, 1994</td>
<td>8/F/83</td>
<td>Thigh</td>
<td>Painful ulcerated plaque surrounded by dusky erythema</td>
<td>Severe PVD, occlusion of previous femoral grafts and bilateral iliac arteries, and no palpable pulses on involved lower extremities</td>
<td>Yes</td>
<td>Second vascular operation for revision of occluded graft</td>
<td>Completely cleared after 1 mo</td>
</tr>
</tbody>
</table>

Abbreviations: AV, arteriovenous; BKA, below-knee amputation; CRI, chronic renal insufficiency; DLE, discoid lupus erythematosus; IDDM, insulin-dependent diabetes mellitus; NA, not available; PVD, peripheral vascular disease; S/P, status post.

Figure 1. A, Left medial breast lesion; B, the lesion has a reticulated erythematous indurated plaque and ulceration with scar formation. Deeper tender nodules are also present.

kocyte count, with mild lymphocytosis, and a slight increase in the erythrocyte sedimentation rate, all results were within normal limits.
Diffuse proliferation of spindle-shaped endothelial cells with focal small, bland vessel formation in full thickness of the dermis, extending to superficial panniculus (hematoxylin-eosin); B, higher magnification shows proliferating endothelial cells (hematoxylin-eosin); and C and D, CD31 staining highlights diffuse proliferating endothelial cells in the dermis (original magnification x40 [A] and x200 [B-D]).

Because of her angina pectoris and left arm claudication, angiography was performed and showed almost complete occlusion of the left subclavian artery proximally, with a subclavian "steal" phenomenon (Figure 3A). A stent was placed in the proximal left subclavian artery, and circulation was restored (Figure 3B). One month after the procedure, the lesion on the left breast completely resolved.

COMMENT

Although DDA was described initially in 1994 as a variant of reactive cutaneous angioendotheliomatosis, it was recently recognized as a distinct clinical pathologic entity in the spectrum of cutaneous reactive angiomatoses. All the reported cases of DDA have involved women (age range, 28-63 years), with most of them in their 50s (Table). At presentation, lesions vary from a solitary erythematous patch to an indurated plaque surrounded by dusky erythema. Ulceration and tenderness are common. The sites most affected are the extremities, especially the upper thigh area. Comorbid conditions in-
clude cardiovascular disease, hypertension, and diabetes mellitus. Severe peripheral vascular disease has been noted in most cases.

The distinctive histopathologic feature of DDA is diffuse proliferation of endothelial cells between collagen bundles, instead of within the vascular lumina, which is often observed in reactive angioendotheliomatosis. Small vascular lumina formed by spindle-shaped endothelial cells with vacuolated cytoplasm occur throughout the full thickness of the dermis. The histopathologic differential diagnosis includes benign conditions such as acroangiodermatitis and malignant conditions such as Kaposi sarcoma and low-grade angiosarcoma. A recent study 

Involvement of the breast by DDA is rare. Thus far, 2 cases have been described that demonstrated typical histologic features of DDA. However, both of the patients involved lacked a relevant medical history, including a history of a vaso-occlusive disease process. It is possible, as suggested by some authors, that both patients had traumatic ulcerations of fat-rich areas in their large pendulous breasts and that subsequent angiogenesis was responsible for a DDA-like histologic picture. The case report of DDA by Kutzner et al lends support to this hypothesis. They described a 43-year-old woman who had a brownish, livid, rapidly evolving lesion of DDA above a surgical scar. The lesion had developed after 20 kg of fatty tissue had been removed from the lower abdominal wall. It regressed within 12 weeks, and the patient was disease free 4 years later. Potentially, other mechanisms may be involved in the evolution of DDA. It is possible that along with vaso-occlusive disease, an underlying coagulopathy may have a role in pathogenesis. Thus far, 1 patient with DDA-like lesions has been described who was positive for antinuclear and IgM anticardiolipin antibodies.

Our patient had the classic medical history for DDA, including a personal and family history of coronary artery disease and a medical history of triple bypass surgery, hyperlipidemia, and peripheral vascular disease. The management of DDA requires improving underlying tissue hypoxia and ischemia status. The most efficient method for accomplishing this improvement is revascularization of the affected area. Corticosteroid therapy was used in 1 patient, and the lesion completely resolved after 2 months. Our patient had noted improvement with isotretinoin therapy, which was reported to be effective in 1 patient, possibly because of its antiangiogenesis effect. After the blockage of the subclavian artery was identified and treated with percutaneous stent placement in our patient, her skin lesions resolved entirely.

It is notable that our patient and nearly all the others described in the literature had a history of heavy smoking. Smoking is a well-recognized risk factor for cardiovascular disease. Free radicals in cigarette smoke are responsible for endothelial dysfunction, decreased levels of high-density lipoprotein, increased levels of low-density and very-low-density lipoproteins, and abnormal platelet function. Cigarette smoking is one of the most
important factors for the development of peripheral arterial disease.\textsuperscript{11} Smoking increases the risk of peripheral arterial disease by several-fold and is a more influential pathogenetic factor for this disease than for coronary artery disease. In an animal study, smoking increased vascular endothelial growth factor gene expression in pulmonary arteries.\textsuperscript{12} Our patient had a history of familial type II dyslipidemia, which also may have contributed to the vascular endothelial cell proliferation of her skin condition.

In summary, we describe a distinctive case of DDA involving the breast. Diffuse dermal angiomatosis is a rare condition in the spectrum of reactive angiomatoses. Many comorbid conditions exist in patients with DDA. Accurate clinical evaluation of a patient’s vascular status and education about smoking cessation are critical, because appropriate treatment to alleviate hypoxia may be therapeutically effective.

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Financial Disclosure: None.

REFERENCES


ARCHIVES Web Quiz Winner

Congratulations to the winner of our December challenge, Nagwa Abd El Aal. The correct answer was \textit{actinomycetoma}. For a complete discussion of this case, see the Off-Center Fold section in the January ARCHIVES (Fields KS, Florell SR. Chronic foot infection in a Mexican immigrant. Arch Dermatol. 2006;142:101-106).

Be sure to visit the Archives of Dermatology Web site (http://www.archdermatol.com) to try your hand at the interactive quiz. We invite visitors to make a diagnosis based on selected information from a case report or other feature scheduled to be published in the following month’s print edition of the ARCHIVES. The first visitor to e-mail our Web editors with the correct answer will be recognized in the print journal and on our Web site and will also receive a free copy of \textit{The Art of JAMA II}.

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