Diffuse dermal angiomatosis of the breast

Nicholas Nguyen^a, Annika S. Silfvast-Kaiser, MD^b , Jillian Frieder, MD^b, Marcus Zaayman, MD^b and Alan Menter, MD^b

^aTulane University, New Orleans, Louisiana; ^bDivision of Dermatology, Baylor Scott & White, Dallas, Texas

ABSTRACT

Diffuse dermal angiomatosis of the breast can be a painful, irritating, and persistent inflammatory condition. It tends to present in middle age and is associated with a number of risk factors, mainly relating to tissue hypoxia. There are no standard treatment guidelines, and current treatment focuses on mitigating tissue hypoxia by addressing atherosclerosis through lifestyle changes and medical and/or surgical intervention. Herein, we present a case of diffuse dermal angiomatosis of the breast, describing the condition and current treatment approaches and the likelihood that this diagnosis is more common than previously believed.

KEYWORDS Breast; cutaneous reactive angioendotheliomatosis; diffuse dermal angiomatosis of the breast; reactive angioendotheliomatosis; vascular proliferation

Diffuse dermal angiomatosis (DDA) is a benign, cutaneous vascular disorder. It was first described as a subtype of reactive angioendotheliomatosis (RAE) in 1994 by Krell et al.¹ More recently, DDA has been recognized as a distinct, rare variant of RAE associated with smoking, trauma, underlying vaso-occlusion, and hypercoagulability.^{1–3} Clinically, DDA manifests with tender, violaceous-to-erythematous ulcerated plaques and purpuric papules.^{1,4} Lesions may also have central ulceration with surrounding tissue necrosis. Lesions tend to persist and progressively enlarge.^{5–8} While the extremities are the most commonly reported location, there have been several reported cases of DDA of the breast (DDAB), indicating that DDAB is likely more prevalent than previously thought.^{5,9–13} Herein, we report a case of bilateral DDAB and review the management strategies utilized for this disease to date.

CASE DESCRIPTION

A 33-year-old black woman presented with a 1-year history of pruritic, painful, nonhealing lesions on both breasts that would occasionally bleed and drain. The lesions first appeared on her left breast and subsequently involved her right breast as well. Prior failed treatments included topical antibiotic ointment, antifungal cream, zinc oxide, and petroleum jelly. The patient was a daily cigarette smoker, drank alcohol occasionally, and denied any illicit drug use.

Overall, she was obese (body mass index >30 kg/m²) but reported good general health, with no personal or family history of heart disease, stroke, peripheral vascular disorder, or coagulopathy. She was not taking any regular medications. Vital signs were within normal limits and review of systems showed only her breast lesions.

Examination revealed large, pendulous breasts with four well-demarcated, exquisitely tender, indurated, violaceous-to-erythematous plaques with central ulceration and crusting on the left breast, with one similar lesion on the lateral portion of the right breast, surrounded by reticulate erythema (*Figure 1*). A 4 mm punch biopsy was performed on the left breast. Histopathological examination revealed a proliferation of vessels with hyperplastic endothelial cells within the dermis and small vascular lumina consistent with DDA (*Figure 2*). Erythroblast transformation-specific related gene (ERG) and cluster of differentiation 31 (CD31) immunostaining was positive, highlighting vascular proliferation. The specimen was negative for human herpesvirus 8.

DISCUSSION

DDA is a unique variant of RAE commonly reported on the lower extremities and, more recently, in women with large, pendulous breasts.^{1,2} DDAB tends to affect individuals aged 40 to 60 years who have multiple risk factors for atherosclerosis (i.e., hypertension, hyperlipidemia, diabetes mellitus, chronic smoking history, previous heart disease,

Corresponding author: Alan Menter, MD, Division of Dermatology, Baylor Scott & White, 3900 Junius Street, Suite 145, Dallas, TX 75246 (e-mail: amderm@gmail.com)

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Figure 1. Large, pendulous breasts showing reticulate, erythematous-to-violaceous plaques with central ulceration.

Figure 2. Skin biopsy of the left breast.

and stroke).^{10,13} The differential diagnosis includes acroangiokeratosis, Kaposi sarcoma, and low-grade angiosarcoma. Histologically, a proliferation of endothelial cells and microscopic capillaries in the dermis is seen, in contrast to the intraluminal proliferation of endothelial cells seen in classic RAE.^{2,14} CD31, CD34, and ERG stains are positive, underscoring benign dermal endothelial cell proliferation. Human herpesvirus 8 testing is negative.^{3,9,14–16} Although the pathogenesis of DDA remains unclear, it is postulated that angiogenesis is due to up-regulation of vascular endothelial growth factor, secondary to chronic ischemia and hypoxia.⁴

DDA has been linked to underlying chronic and focal hypoxia secondary to multiple etiologies including severe peripheral vascular disease, subclavian artery stenosis, hypercoagulable states like antiphospholipid syndrome, monoclonal gammopathy, “steal syndrome” from arteriovenous fistula, calciphylaxis, smoking, obesity, and large pendulous breasts (see *Table 1*).^{5,7–9,13,16–25} Risk factors shared by most reported patients include large pendulous breasts, elevated body mass index, and smoking history.²⁴ Large, pendulous breasts (which tend to occur along with obesity) are thought to contribute to chronic hypoxia of focal breast tissue via subclinical torsion, compression, repeated micro trauma, and increased pressure.^{5,9,24} Smoking is known to impair wound healing, with persistent use contributing to atherosclerosis and peripheral arterial disease.¹⁰ Severe atherosclerosis can manifest as peripheral arterial disease with occlusion of major vasculature, causing diminished blood flow in the legs and breasts of women.^{1,9,11,12,17,21,23} As DDA can be an indicator of severe atherosclerosis, patients with relevant risk factors should undergo appropriate workup.

There are no standardized treatment guidelines for DDAB. Targeting tissue hypoxia is the main goal, with primary preventive measures aiming to reduce risk factors associated with

Table 1. Etiologies linked to chronic and focal hypoxia in diffuse dermal angiomas

- Severe peripheral vascular disease
- Subclavian artery stenosis
- Hypercoagulable states (e.g., antiphospholipid syndrome)
- Monoclonal gammopathy
- Steal syndrome from arteriovenous fistula
- Calciphylaxis
- Smoking
- Obesity
- Large, pendulous breasts

atherosclerosis.^{5,6,9,13} Definitive treatment response has been seen with revascularization, reduction mammoplasty, and excision of the lesion(s).^{5,6,9,13,15} In most patients with vascular disease, DDA lesions resolved after necessary revascularization procedures.^{6,7,9,11,24} Conservative treatment with isotretinoin, oral corticosteroids, or pentoxifylline/aspirin has shown variable degrees of success.^{4–6,9,11,13,15,16,19,21,23,26} Spontaneous resolution has also been reported.⁹

Similar to case reports by McLaughlin et al⁴ and Song et al²⁷ our patient had no history of ischemia or vascular disorders. This patient’s risk factors for the development of DDAB were obesity, large, pendulous breasts, and chronic smoking history, but she was otherwise healthy. Despite our patient’s tobacco use and obesity, her young age and lack of risk factors made severe atherosclerosis an unlikely factor. Since her diagnosis of DDAB, she was counseled to quit smoking. She is considering breast reduction surgery, as this procedure has resulted in resolution of DDAB in previously reported patients.^{5,6,9,11,13,27}

In conclusion, DDA involving the breast is likely more common than previously thought. It is often associated with severe atherosclerosis in older individuals. With increased reports of DDAB in women under age 40, atherosclerosis is unlikely to be the sole risk factor. The sheer mass of large, pendulous breasts leading to vascular compression, torsion, and ultimately tissue hypoxia is likely the main causative factor, especially in younger women. DDAB should be included in the differential diagnosis of young women with purpuric, nonhealing lesions of the breast.^{5,6} Although no standardized treatment guidelines currently exist, the most successful management strategies of DDAB reported to date include revascularization, smoking cessation, treatment with systemic corticosteroids, isotretinoin, and reduction mammoplasty.^{5,6,9,11,13,27}

ORCID

Annika S. Silfvast-Kaiser <http://orcid.org/0000-0003-3397-0946>

Marcus Zaayman <http://orcid.org/0000-0003-1531-8313>

Alan Menter <http://orcid.org/0000-0002-9314-0007>

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