

BRIEF ARTICLE

Diffuse Dermal Angiomatosis of the Breasts: A Case Series of 8 Patients

Landon K. Hobbs, BS¹, Darren Guffey, MD¹, R. Hal Flowers, MD¹

¹Department of Dermatology, University of Virginia School of Medicine, Charlottesville, VA

ABSTRACT

Background: Diffuse dermal angiomatosis (DDA) is a rare, reactive vascular disorder of the skin. Association with vascular disease, smoking, and large pendulous breasts has been reported. No standard of care exists but benefit from various with medications and reduction mammoplasty has been reported.

Methods: We report a case of a 49-year-old obese female with a history of smoking who presented with DDA that improved with smoking cessation and pentoxifylline prior to reduction mammoplasty. We also performed a retrospective chart review of all patients with DDA seen at our institution between 2010 and 2020.

Results: Eight female patients with DDA affecting the breasts were evaluated at our institution. The mean age was 49.5 years. Five of the patients noted symptoms at presentation. Obesity was seen in 7 (87.5%) patients and 5 (63%) had a smoking history. There was no significant difference between symptomatic and asymptomatic groups in regard to age, $t_4=-0.63$, $p=0.56$, but BMI trended higher in the symptomatic group, $t_6=2.27$, $p=0.06$. Three patients (38%) were noted to have fibromyalgia. All symptomatic patients saw improvement in their symptoms with treatments including reduction mammoplasty (1 patient), aspirin (1 patient), pentoxifylline (3 patients), smoking cessation (2 patients), and/or weight loss (1 patient).

Conclusions: Our series is the second largest series of DDA of the breasts and confirms many reported associations including obesity, smoking, and large pendulous breasts. We report the first known case of improvement with weight loss as a sole intervention, as well as identify a novel

INTRODUCTION

Diffuse dermal angiomatosis (DDA) is a rare, benign, acquired reactive vascular disorder of the skin first described in 1994 most commonly affecting middle-aged females.¹⁻³ As of early 2016, only 73 patients with DDA had been reported to date.³ Most case reports and series describe an association with hypoxic conditions such as vascular disease, calciphylaxis, and

smoking, as well as other comorbid conditions including obesity and diabetes. DDA can present as early as three years after significant weight gain.^{1,3-6} The condition has also been reported as more common in females with large pendulous breasts.^{1,3,4} DDA typically presents with multiple erythematous to violaceous purpuric patches and plaques that may progress to necrosis and painful ulceration. Although breast involvement was once considered rare in DDA, recent studies suggest that the

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breasts may be the most common site.^{3,4,7,8} Histology is typically characterized by extensive proliferation of CD31 and CD34 positive endothelial cell proliferation around collagen bundles.^{2,3,5-7,9,10} Although there is currently no standard of care, improvement in comorbidities including smoking cessation (if applicable), medical therapy (including corticosteroids, isotretinoin, aspirin, and pentoxifylline), and reduction mammoplasty have all been reported to be effective.^{1-4,7,8,10}

CASE PRESENTATION

A 49-year-old female with a one pack-year history of smoking and obesity (body mass index 45) presented to clinic with a 10-month history of painful plaques on bilateral breasts refractory to oral antibiotics. Recent mammogram was normal. Physical exam revealed large pendulous breasts, with prominent small telangiectasias and crusted ulcerations at the inferior aspects and an active ulcer on the left medial breast and scars from prior ulcers (Figure 1).



Figure 1. Right breast. Prominent small telangiectasias, crusted ulcerations, and scars from prior ulcers.

The patient reported allergy to aspirin, but was counseled on smoking cessation,

referred for reduction mammoplasty, and started on pentoxifylline. At follow up three months later, her pain was drastically improved, all prior ulcers were healed, and she had no new ulcers. She had maintained abstinence from smoking but had only taken the pentoxifylline for two months due to cost. The patient eventually underwent bilateral reduction mammoplasty nine months later with full recovery and has not had any recurrence of her symptoms.

METHODS

After obtaining IRB approval, we performed a retrospective chart review of all patients with DDA seen at our institution between 2010 and 2020. We obtained a list of patients from the MC Research Analytics team, who did an electronic medical record (EPIC) search of “diffuse dermal angiomatosis.” We compiled data on demographics, clinical presentation, relevant co-morbidities including body mass index (BMI), smoking history, biopsy and lab results, and any treatments used with described outcomes. Basic statistical analyses, including t-tests of unequal variance, were performed to further describe clinical characteristics including BMI and age.

RESULTS

Our initial review identified 17 patients with potential DDA. Nine patients were excluded due to a more likely alternative diagnosis or incomplete medical record. Of the eight patients determined to have DDA (Table 1), all were female and five were symptomatic. All eight of the patients had DDA of the breasts without involvement of any other location. The mean age was 49.5 years.

Table 1. Clinical data of patients in the series

Patient	Demographics	Location of DDA	Symptoms	Co-morbidities	BMI	Macromastia	Smoking History? (PY at presentation)	Treatment and Outcome
1	47F, White	Bilateral breasts	Pain, itching	FM, HLD, HTN	33.1	Yes ^a	Yes (10)	Repeat reduction mammoplasty → Resolution
2	23F, Black	Bilateral breasts	Pain, purulent drainage	HTN	50.3	Yes	Yes (2)	ASA + Pentoxifylline + smoking cessation → Improvement
3	63F, White	Left breast	Pain, itching	HLD, HTN, HypoT, Factor V Leiden	70.4	Yes	Yes ^b (33)	Weight loss ^c → Resolution
4	51F, White	Bilateral breasts	Pain	FM, HypoT, Cirrhosis	41.8	Yes	Yes (35)	Pentoxifylline → Improvement
5	49F, Black	Bilateral breasts	Pain, purulent drainage	Ameloblastoma	45.7	Yes	Yes (1)	Smoking cessation + Pentoxifylline → Improvement ^d
6	34F, White	Bilateral breasts	-	-	37.3	N/S ^a	No	None
7	63F, White	Bilateral breasts	-	-	33.5	N/S	No	None
8	66F, White	Bilateral breasts	-	FM, HLD, HTN, HypoT	25.7	N/S	No	None

^aHistory of prior breast reduction mammoplasty

^bPatient endorsed quitting smoking five years prior to presenting with DDA

^cPatient's lesions resolved as BMI decreased to 55.9 over two years

^dUnderwent reduction mammoplasty for macromastia after DDA had improved with smoking cessation and pentoxifylline

ASA – aspirin; BMI – body mass index; DDA – diffuse dermal angiomas; F – female; FM – fibromyalgia; HLD – hyperlipidemia; HTN – hypertension; HypoT – hypothyroidism; N/S – not specified; PY – pack years.

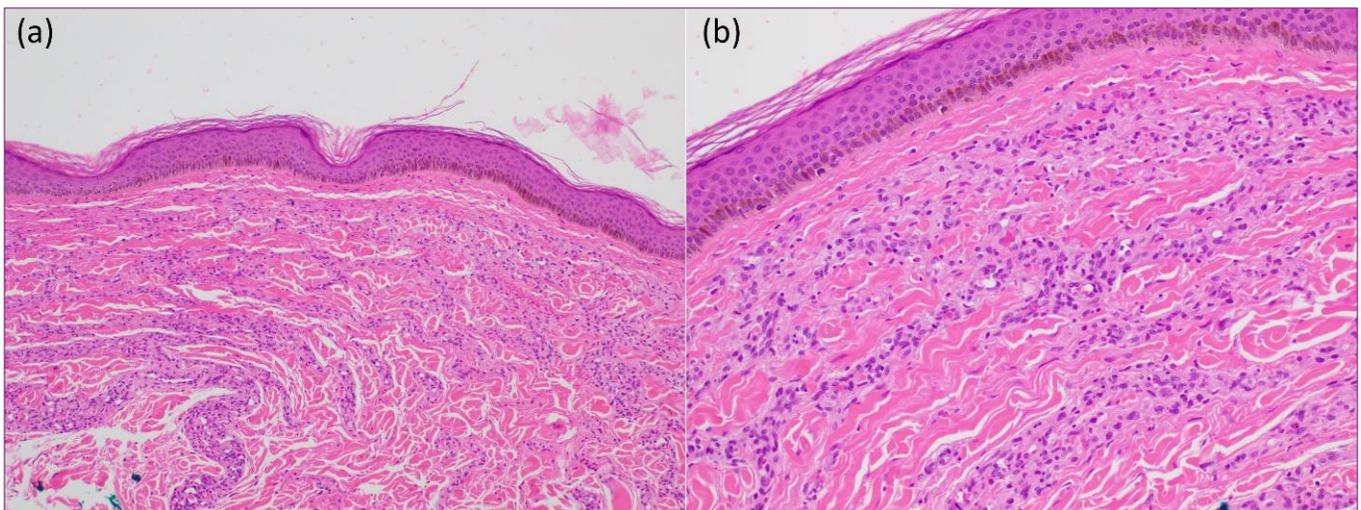


Figure 2. A biopsy specimen from a patient in the series shows diffuse proliferation of capillary vessels in superficial and mid dermis between collagen bundles. (H&E, a: 10x; b: 20x)

The symptomatic cohort consisted of three white and two black females with a mean age of 46.6 years (SD=14.6). Of these five patients, all had histories of obesity (BMI: M=48.3, SD=13.9), macromastia, and smoking. Other common co-morbidities included hypertension (3 patients), hyperlipidemia (2 patients), fibromyalgia (2 patients), and hypothyroidism (2 patients). Histologic specimens obtained from three symptomatic patients were consistent with DDA with proliferation of superficial dermal vessels (Figure 2). All patients saw improvement in their symptoms with reduction mammoplasty (1 patient), aspirin (1 patient), pentoxifylline (3 patients), smoking cessation (2 patients), and/or weight loss (1 patient). By last follow up, two of the four patients who were smoking at initial presentation had quit and had seen improvement in symptoms.

In the asymptomatic group, all three were white females and the mean age was similar to that in the symptomatic group (54.3 ± 17.7 , $t_4 = -0.63$, $p = 0.56$). None of the patients had a history of smoking and BMI was lower than in the symptomatic group (BMI: M=32.2, SD=5.9, $t_6 = 2.27$, $p = 0.06$). Patient 6 had undergone reduction mammoplasty years prior to being seen by dermatology; macromastia was not noted on dermatologic evaluation. Biopsy was deferred in all asymptomatic cases and the diagnoses were made on clinical grounds alone. The patients remained clinically stable at last follow up.

DISCUSSION

Our series of eight patients represents the second largest cohort of patients with DDA of the breasts, and third largest cohort of DDA overall. The case series of 22 patients with DDA of the breasts by Reusche et al. is

the largest to date.⁴ Ten of their patients were diagnosed with DDA clinically while twelve were confirmed with biopsy. Other notable case series include: nine patients with concomitant calciphylaxis and DDA but only one with involvement of the breasts⁵, seven patients with DDA found in a case series of patients with calciphylaxis but none involving the breasts⁶, and five patients with DDA of the breasts⁷.

Our case series confirmed many recognized characteristics and co-morbidities of DDA. Five of the eight (62.5%) patients experienced moderate-to-severe mastalgia. However, three patients (37.5%) were asymptomatic and not treated. In their series, Reusche et al. similarly reported that 50% (11/22) had no documentation of treatment, including three patients with biopsy-confirmed DDA.⁴ We also found high prevalence of comorbidities reported to be associated with DDA including obesity (7/8), hypertension (4/8), and hyperlipidemia (3/8), very similar to prior reports. The difference in BMI between the symptomatic and asymptomatic groups was on the threshold of significance, likely affected by small sample size ($n=8$). All of the symptomatic patients in our series had a history of smoking, consistent with the reported association between DDA and smoking. Reusche et al. reported that 50% (11/22) patients identified as former or current smokers, with 58.3% (7/12) of patients with biopsy-confirmed DDA having a smoking history. Interestingly, all 3 asymptomatic patients were non-smokers. Our confirmation of this association is notable as other series have contested the link between smoking and DDA.⁴

Prior to our series only a single patient with concomitant DDA and fibromyalgia (FM) had been reported.¹ Our series of DDA patients includes three patients diagnosed with FM

(38%). The prevalence of FM in the United States is approximately 2%, thus it would not be unreasonable that this observation represents mere coincidence. However, the two disease processes may be linked by a common association, specifically obesity.¹¹ Alternatively, there may be an under recognition of DDA as a diagnosis and significant cause of pain, which may be misattributed to FM by non-dermatologists.

Diffuse dermal angiomatosis occurring after reduction mammoplasty has been reported in five patients.^{2,4,7} Reusche et al. reported one patient in their series with recurrence of macromastia and DDA following breast reduction 30 years prior.⁴ Adams et al. reported one case of DDA in a female who had undergone reduction mammoplasty over 20 years prior.² Tollefson et al. reported three of five patients in their series had undergone breast reduction mammoplasty six weeks to 30 years prior to presenting with DDA.⁷ In our series, two patients had undergone reduction mammoplasty years prior to developing DDA. Despite positive outcomes reported after reduction mammoplasty for patients with DDA of the breasts, these reports of DDA in patients with previous reduction mammoplasty suggest that the surgery is not curative since macromastia may still recur with time. The above literature provides support for the proposed causative association between macromastia and DDA. Macromastia is believed to result in tissue hypoxemia due to subclinical torsion, compression, and increased venous hydrostatic pressure.⁸ Mastectomy may lead to full resolution^{4,9} but should be considered only after exhausting all more conservative approaches.

We report the first case of DDA that improved with weight loss as the primary intervention (Patient 3, BMI decreased from 70.4 to 55.9). In the literature one patient

with DDA was reported to improve with the combination of weight loss and smoking cessation¹⁰, however another patient did not see substantial improvement despite reducing smoking and losing weight.⁸ Furthermore, there are reports of DDA presenting after or worsening with weight gain.^{1,3,4,8} In the series, we saw a trend of greater BMI among symptomatic patients compared to asymptomatic patients. Higher BMI would likely result in larger pendulous breasts, a risk factor for DDA of breasts. Our observation of DDA improving with weight loss as the sole intervention provides further evidence that obesity may be a primary etiologic factor in this rare disease.

CONCLUSION

In summary, our series confirms many of the previously reported associations with DDA including obesity, smoking, and large pendulous breasts. Our series identified a novel potential association between DDA and fibromyalgia which warrants further investigation. Finally, we report the first known case of improvement of DDA with weight loss as a sole intervention and recommend weight reduction be considered alongside other first line interventions for this rare disease.

Conflict of Interest Disclosures: None

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Corresponding Author:
Landon K. Hobbs, BS
Department of Dermatology
University of Virginia School of Medicine
1215 Lee Street
Charlottesville, VA 22903

Phone: 434-924-5115
 Fax: 434-244-4504
 Email: lkh6k@virginia.edu

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