Diffuse Dermal Angiomatosis of the Breast: A Case Presentation and Discussion

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Abstract

Diffuse dermal angiomatosis (DDA), a rare dermatological disorder and variant of reactive cutaneous angioendotheliomatosis, is characterized clinically by the presence of erythematous and violaceous lesions that have the potential to ulcerate. Although it classically presents in the extremities, a few cases have been reported of DDA involving the breast (DDAB). DDA has often been linked to vaso-occlusive and cardiac co-morbidities, and treatment has therefore usually targeted these underlying conditions. This case presents a patient with DDAB who was successfully treated with isotretinoin therapy, supporting previous reports of its benefit in the management of this patient population.

Introduction

In 1994, Krell et al. initially recognized diffuse dermal angiomatosis (DDA) as a rare but distinct variant of reactive cutaneous angioendotheliomatosis.[1,2] Clinically, it presents as erythematous, violaceous, indurated plaques that are often ulcerated and tender. It generally involves the lower extremities, although only a total of 14 cases of DDA have been cited in the current literature to date.[1,2] A form of DDA has also been reported that is localized to the breast (DDAB). Only five documented cases of DDAB have been cited.[1] Patients with DDAB often present with intractable breast pain along with these cutaneous lesions.[1,3,4]

Due to its rarity, the pathogenesis of the disease is not fully understood, but it is thought to be a result of tissue ischemia.[1] Numerous studies have reported an association with severe peripheral vascular disease among other co-morbidities.[2,5,6] Histologically, diffuse dermal vascular- and endothelial-cell proliferation between collagen bundles is seen, and uniform positivity is achieved with immunoperoxidase stains CD31 and CD34, vascular markers characteristic of DDA.[1,4,5]

The management of DDA and DDAB is centered on improving the underlying ischemia and achieving revascularization. The modalities in current practice include the use of oral corticosteroids, isotretinoin, reduction mammoplasty, and stent placement in extreme cases of vaso-occlusive disease.[1,8] In this case report, we present an adult patient with a classic presentation of DDAB who was successfully treated with isotretinoin for a duration of four months.

Case Report

A 60-year-old Caucasian female presented with a three-month history of exquisitely tender, ulcerating and bleeding breasts, with a tremendous amount of exuded material bilaterally. This eruption started approximately six weeks after cardiac surgery. During the procedure, the patient received heparin, but was not placed on coumadin. She denied exacerbating or alleviating factors. Past medical history was significant for cardiovascular disease, transient ischemic attack, hypertension, and hypercholesterolemia. The patient was a smoker when she was evaluated for this eruption. Her medications upon evaluation included atorvastatin, clopidogrel, lisinopril, metoprolol, and topical lidocaine. Family history was noncontributory. All labs were found to be within normal limits.

Physical exam revealed livedo reticularis on the breasts, bilaterally. The left breast (**Figure 1**) was much more affected than the right (**Figure 2**), with associated healed punctuate ulcerations and changes of healed infarcts. The rest of her

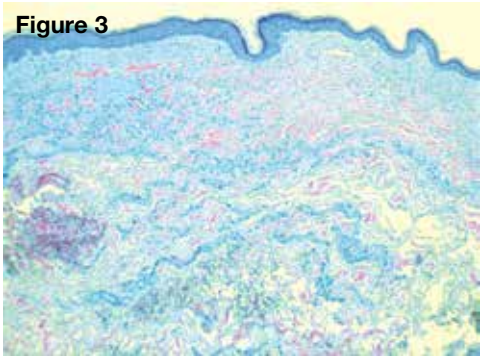
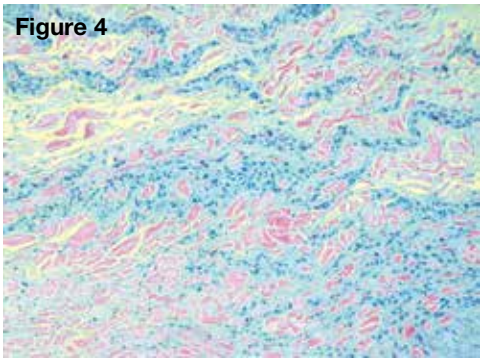


Figure 3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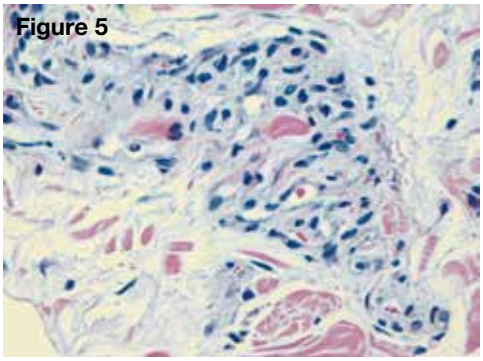
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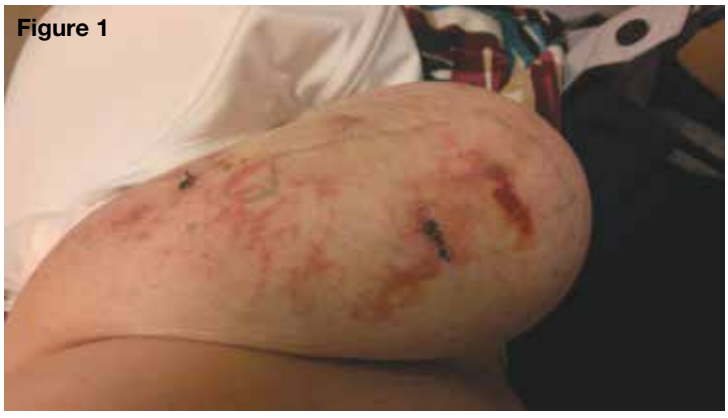
Figure 1

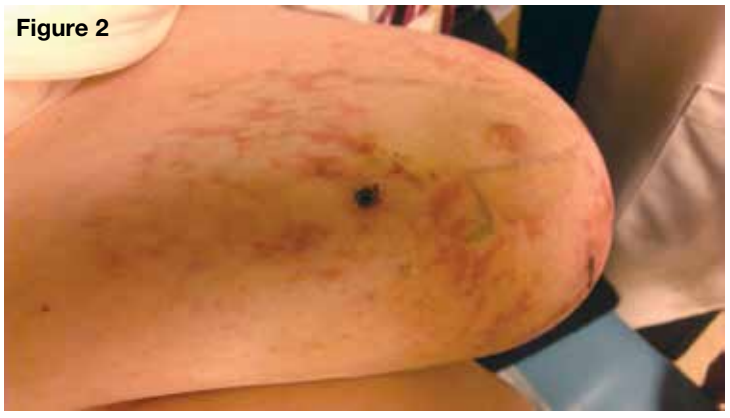
Figure 2

cutaneous exam was negative.

Histologic sections of a punch biopsy from the left breast revealed a diffuse capillary proliferation within the dermis and extending into the subcutis in a patchy distribution (**Figures 3** [5x], **4** [10x], **5** [20x] **p. 33**). There was no evidence of vasculitits or a thrombotic vasculopathy to suggest either coumadin or heparin necrosis. There was also no evidence of endothelial atypia or malignancy. This pattern was consistent with diffuse dermal angiomatosis, a form of reactive angioendotheliomatosis. Treatment included pain control and isotretinoin at a dose of 40 mg PO twice daily for a duration of four months, to which the patient responded positively.

Discussion

First described in 1994 by Krell et al., diffuse dermal angiomatosis (DDA) is a rare skin condition primarily affecting females and characterized by erythematous, violaceous, indurated plaques that are often ulcerated and tender and are commonly localized to the lower extremities.[1-3] Although the pathogenesis is unknown, it is often noted in patients with severe peripheral vascular disease among other co-morbidities.[2,5] A few authors have reported a correlation between DDA and trauma, namely from surgery.[1] While DDA is rare, with 14 total cases reported, involvement of the breast is even less frequently diagnosed.[1,2] To date, only five cases of DDA of the breast (DDAB) have been described.[1] Although often affecting large pendulous breasts bilaterally, these patients presented in an otherwise atypical fashion without relevant medical history or vaso-occlusive disorder.[2] Histologically, however, they demonstrated diffuse dermal vascular and endothelial cell proliferation between collagen bundles and uniform positivity with immunoperoxidase stains CD31 and CD34, vascular markers characteristic of DDA.[1,4,5] HHV-8 is also often used to aid in diagnoses and is uniformly negative in DDA.[1]

The exact process underlying the development of DDA has yet to be determined, but tissue ischemia is often cited.[1] According to Bauer et al., the current hypotheses regarding the pathogenesis of the disease are as follows: "1) atherosclerotic plaques may embolize to distal small vessels and create endothelial hyperplasia; (2) vascular steal syndromes can give rise to ischemic necrosis with subsequent ulceration; or (3) ischemia leads to increased vascular endothelial growth factor and subsequent endothelial proliferation."[6] Given this understanding, it is believed that reversing ischemia and achieving revascularization can be beneficial in improving the clinical signs of disease.[6] Several associations have been made between DDA and other co-morbid conditions. Many authors have reported associations between DDA and peripheral vascular atherosclerosis, arteriovenous fistulas, anticardiolipin antibodies, hypercoagulable states, and breast ulceration.[2,6,7] The most common and widely accepted association, however, has been with vascular occlusive disease.[6] Smoking and DDA have also been found to be strongly associated, with patient's often having a significant clinical history of long-term tobacco use. Hypertension has also been reported to be associated with DDA.[1,4]

As noted previously, the management of DDA and DDAB is centered on improving the underlying ischemia and achieving revascularization. Many modalities have been implemented in the treatment of DDA and DDAB, including the use of oral corticosteroids, isotretinoin, reduction mammoplasty, and stent placement in extreme cases of vaso-occlusive disease.[1,8] Morimoto et al., as well as other authors, have described successful revascularization procedures facilitating the healing of DDA ulcers.[9] In this case report, we describe successful treatment with isotretinoin at a dose of 40 mg PO twice daily for a duration of four months. Isotretinoin is a retinoid compound most often used to treat severe acne. Its antiangiogenic properties, however, have proved to be beneficial in the treatment of DDAB as well.[10] A similar response to isotretinoin therapy was reported by Mclaughlin et al. This study found that treatment with a dose of 1 mg/kg of isotretinoin over two months resulted in complete resolution of the ulceration in this patient with DDAB.[5] Although the exact mechanism of action of isotretinoin in the treatment of DDAB is unknown, it has been postulated that it may involve the inhibition of angiogenesis and/or protease production, stimulation of fibrinolysis, and possibly enhancement of keratinocyte migration.[5,10]

Although the use of isotretinoin in the treatment of DDAB has proved promising, the drug is not without risk. It must be highly regulated due to its effect as a teratogen. Other possible side effects include dry skin, chapped lips, epistaxis, cheilitis, severe depression, and suicidal ideation. Therefore, although found to be effective in this patient population, all the risks and benefits of isotretinoin therapy must be thoroughly considered on a case-by-case basis.[10]

Conclusion

DDA is a rare variant of reactive cutaneous angioendotheliomatosis, classically described on the lower extremities but occasionally involving the breast (DDAB) and presenting as unbearable breast pain. Although few cases of DDAB have been reported, its recognition and discussion is paramount in identifying the appropriate treatment for this patient population. Evaluation of these patients should be focused on symptoms and relevant medical history, with particular emphasis on vaso-occlusive and hypercoagulable co-morbidities. Management should be patient-dependent, and we believe that isotretinoin therapy should be considered in patients with a classical clinical and histological presentation of DDAB. In addition, due to the strong correlation of DDA and tobacco use, smoking cessation should always be encouraged in conjunction with medical treatment and strict control of cardiovascular risk factors.

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