Concurrent diffuse dermal angiomatosis and granuloma inframammary adultorum of the breast

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Abstract

Diffuse dermal angiomatosis (DDA) is a cutaneous reactive angiomatosis. Typically presenting as ulcerated, erythematous, violaceous, or purpuric plaques on the breast or lower extremities, DDA is believed to be a reaction to tissue ischemia. Granuloma inframammary adultorum (GIA) is a type of irritant dermatitis of multifactorial etiology, clinically presenting as papules and nodules. Herein, we report an interesting rash presenting as fungiform papulonodules overlying a large violaceous plaque on the left breast. Biopsy revealed an exuberant epidermal proliferation and a diffuse and deep dermal proliferation, consisting of small slit-like blood vessels in between collagen bundles. In light of these clinical and histopathologic findings in the setting of an indurated plaque on a pendulous breast of a woman with multiple risk factors for local tissue ischemia, a diagnosis of concurrent diffuse angiomatosis of the breast (DDAB) and GIA was rendered. This case highlights the critical importance of clinicopathologic correlation in the diagnosis of multiple diagnostic entities.

Keywords: adultorum, angiomatosis, breast, carcinoma, cell, dermal, diffuse, dermatosis, erosive, granuloma, inframammary, papulonodular, squamous

Introduction

Diffuse dermal angiomatosis (DDA) is a rare pathology categorized as a cutaneous reactive angioendotheliomatosis [1]. Although cases involving the extremities have been more commonly documented, recently there have been multiple reported cases of DDA of the breast (DDAB). On presentation, DDA varies in appearance from an erythematous, violaceous patch to an indurated plaque with multiple ulcers [2]. Histologically, the disease is seen as a diffuse interstitial proliferation of CD31-positive endothelial cells within the papillary or reticular dermis [3]. Pathogenesis of the disease is believed to be the result of tissue ischemia with known risk factors such as hypercoagulable states, smoking, hypertension, hyperlipidemia, vasculitis, and macromastia [2,4,5].

Erythema inframammary adultorum is a type of erosive papulonodular dermatosis (EPND). The more common form of EPND is erythema gluteal adultorum that occurs in the diaper region, related to prolonged contact with urine or feces as a result of infrequent change of diapers. Granuloma inframammary adultorum (GIA) is a less common form of EPND, and is believed to have multifactorial etiology including topical cream or ointment application, occlusive effect of tight fitting clothes, perspiration in hot weather, and infrequent cleaning. Granuloma inframammary adultorum typically presents as granulomatous-appearing papules and nodules [6,7].

Case Synopsis

A 45-year-old woman with a past medical history of smoking, alcoholism, hypertension, hyperlipidemia, and gastroesophageal reflux presented to the emergency department for altered mental status. Brain MRI revealed multifocal small acute infarcts

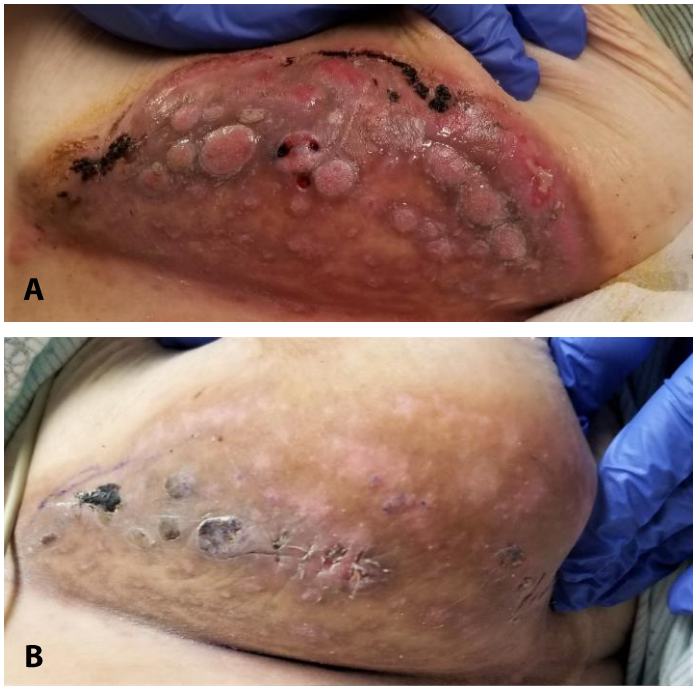

Figure 1. ***A)*** *Left breast lesion on day one of hospital stay.* ***B)*** *Left breast lesion on day 13 following heparin, aspirin, and smoking cessation.*

suggestive of embolic disease. On admission, she was started on aspirin 81mg daily and prophylactic anticoagulation with heparin, as well as smoking cessation. On examination, there was a large well-demarcated indurated erythematous-to-violaceous plaque on the inferior aspect of the left breast measuring 20cm×7cm. This plaque had a mamillated surface, scattered nodules, erosions, and ulcerations with fibrinous exudate (**Figure 1A**). It was unclear when the patient first noticed the breast lesion, although she recalled that it had been draining some yellowish exudate for a month prior to admission. There was no history of breast cancer or radiation therapy. The other breast was unremarkable on clinical examination. There was no known history of use of any topical cream or ointment. Mammography revealed skin thickening of left inferior breast and left axillary lymph node thickening and excluded the presence of a dominant mass, suspicious calcification, or architectural distortion in both breasts. A biopsy of left axillary lymph node was negative for malignancy. The initial skin biopsy showed a well differentiated squamous proliferation composed of anastomosing cords of squamous cells with nuclear atypia and abundant glassy-pink cytoplasm. The histologic differential diagnosis was pseudoepitheliomatous hyperplasia (PEH) and well differentiated squamous cell carcinoma. Special stains and cultures for microorganisms, including bacteria, fungi, and mycobacteria, were negative. Antigen-based serology for deep fungal infections such as aspergillosis, blastomycosis, coccidioidomycosis, and histoplasmosis were also negative.

The atypical epidermal proliferation initially noted was again observed on repeat incisional biopsy (**Figure 2A**, **B**) performed a week after admission. On closer examination, routine sections showed a diffuse and deep proliferation of small slit-shaped blood vessels (**Figure 2C**) present between collagen bundles in the dermis that was better highlighted by CD31 immunohistochemistry (**Figure 2D**). The endothelial cells lacked atypia or mitotic figures and were negative for Human Herpes Virus 8 (HHV8), thus excluding the diagnoses of angiosarcoma and Kaposi sarcoma, respectively. Cytokeratin AE1/AE3 was negative, ruling out an occult carcinoma. There was a mixed inflammatory dermal infiltrate and red blood cell extravasation.

As part of the patient's work-up for altered mental status in the setting of multifocal brain infarcts, hypercoagulability studies were performed and revealed heterozygosity for *Factor V* Leiden R506Q variant mutation. After about two weeks of low dose daily aspirin, routine prophylactic anticoagulation, and smoking cessation since admission, almost complete resolution of the breast plaque and its associated violaceous erythema was observed (**Figure 1B**).

Case Discussion

Diffuse dermal angiomatosis is a rare skin condition, classified as a form of reactive vascular proliferation that manifests clinically within a spectrum of lacy, erythematous, violaceous patches-to-indurated, purpuric plaques with overlying ulceration. When it presents on the breasts, DDA is typically bilateral in

distribution. Currently, the pathogenesis is believed to relate to an upregulation of pro-angiogenic factors such as vascular endothelial growth factor coagulation in the form of heterozygosity for *Factor V* Leiden R506Q variant. However, the clinical picture did not entirely fit this entity.

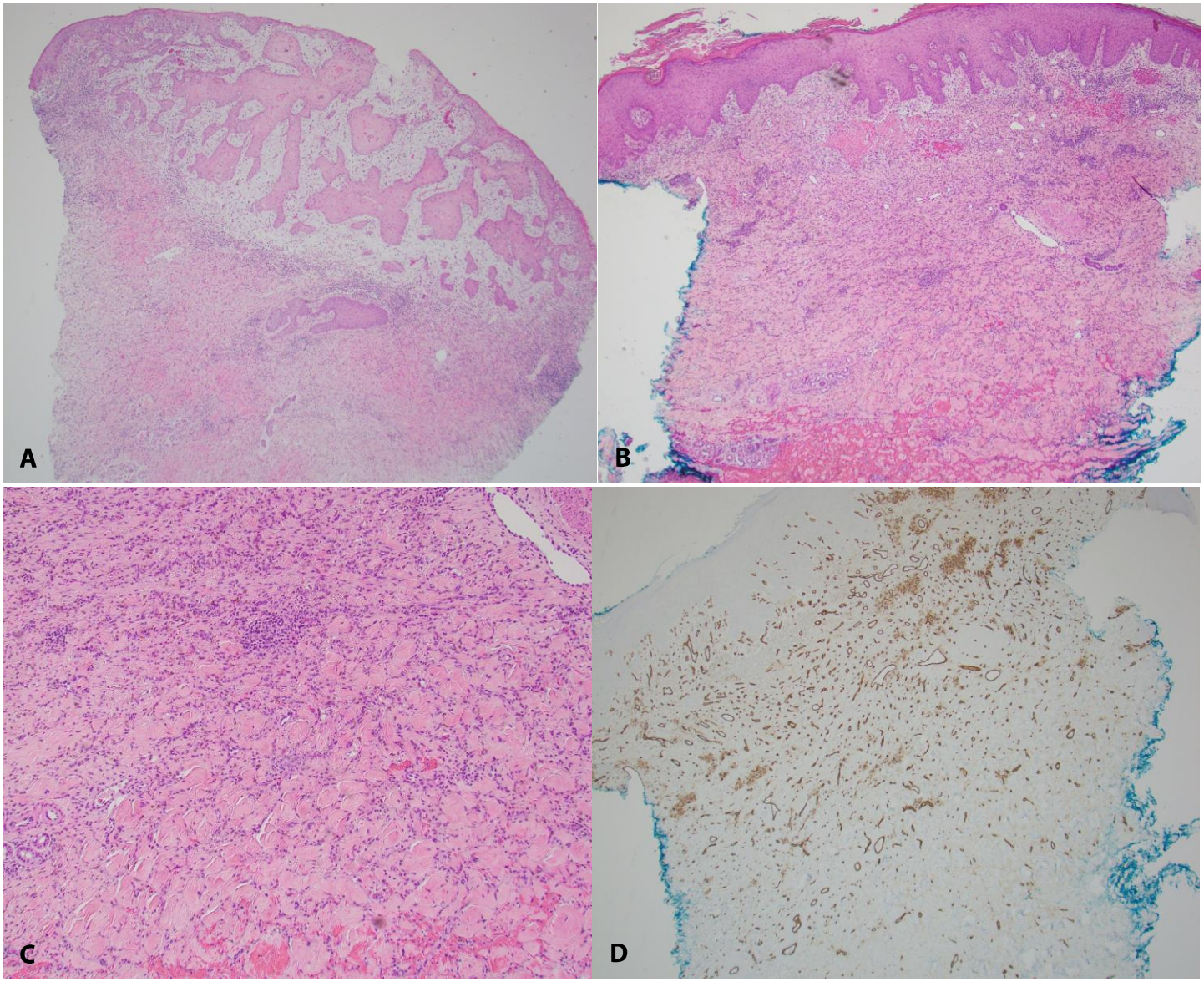

Figure 2. *H&E pathology showing atypical epidermal proliferation and diffuse dermal vascular proliferation.* ***A), B)*** *40×;* ***C)*** *100×.* ***D)****. Immunohistological stain for CD31 better highlights the diffuse dermal vascular proliferation, 40×.*

owing to chronic hypoxia or ischemia in the local tissue [8]. As follows, documented risk factors for DDA appear to be similar to those relevant to other vascular disorders. Noted risk factors include smoking history, elevated body mass index, hypertension, hyperlipidemia, underlying hypercoagulability, vasculitis, and macromastia [2,4,5]. In our case, the patient exhibited many of these risk factors such as a heavy smoking history, hypertension, hyperlipidemia, and increased risk of

Granuloma inframammary adultorum, a variant of EPND, can infrequently occur at this site. The etiology is usually topical corticosteroid cream or ointment, occlusion by clothing, contact with wet clothing due to perspiration, and infrequent cleaning [6]. The entity presents with granulomatous-appearing papules, nodules, and ulcers [6,7]. Our case closely mimicked EPND clinically, although there was no known history of topical cream or ointment use in our patient.

Upon review of histologic features described in the literature, EPND has epidermal acanthosis, dermal edema, proliferation of dermal capillaries, red blood cell extravasation, plump endothelial cells, and mixed inflammatory infiltrate [6,7,9-14]. In our case, we did have similar superficial features, but based on the degree and depth of vascular proliferation, a concurrent diagnosis of GIA and DDA was made. Presence of DDA was supported by the presence of a hypercoagulability disorder, profuse and deep dermal vascular proliferation, and resolution of the lesion on anticoagulation therapy. Whether the occurrence of these two entities was coincidental or related is not clear.

The mainstay of treatment for EPND is discontinuation of the triggering factors [6,7]. Current treatment strategies for DDA focus on improving the local tissue ischemia or hypoxia by targeting control of the patient's vascular status and risk factors. Recent literature suggests that revascularization is the most effective form of treatment, particularly when there is clear evidence of vaso-occlusive disease [2,3,15-17]. Others suggest that the mainstay of treatment is control of cardiovascular risk factors through smoking cessation, antihypertensive treatment, and dyslipidemia treatment [5,18]. Other options that have shown efficacy include antiangiogenic medications such as isotretinoin and systemic corticosteroids [2,16]. Reduction mammoplasty has also been associated with complete resolution of recurrent cases of DDAB [19].

Conclusion

This case highlights the importance of clinicopathologic correlation in rendering the most accurate diagnosis. When the clinical picture does not entirely fit the pathologic findings, a combination of entities should be suspected.

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Potential conflicts of interest

The authors declare no conflicts of interest.

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