Title: Eruptive Disseminated Porokeratosis Associated with Corticosteroid-Induced Immunosuppression

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Eruptive Disseminated Porokeratosis

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Eruptive Disseminated Porokeratosis

Abstract

Eruptive disseminated porokeratosis (EDP) is a disease clinically presenting with sudden onset of erythematous papules and plaques, with a ridge-like border histologically represented by a cornoid lamella. We report a case of EDP occurring in a 39-year-old woman three days after completing a two-week course of oral corticosteroid therapy for an acute asthma exacerbation. Our patient was treated with emollients and sun protection. Unlike the more chronic disseminated superficial (actinic) porokeratosis (DSP), EDP secondary to immunosuppression from corticosteroid therapy is very rarely reported in the dermatologic literature.

Introduction

Porokeratosis is a clonal disorder of keratinocytes characterized by annular atrophic plaques surrounded by ridge-like borders that expand centrifugally, with the histological feature of cornoid lamella, a column of parakeratotic cells. Five clinical variants of porokeratosis have been described: Mibelli disease, disseminated superficial (actinic), porokeratosis palmaris et plantaris disseminata, linear, and punctate porokeratosis.[1] Porokeratosis lesions result from the peripheral expansion of an abnormal mutant clone of epidermal keratinocytes, which may be triggered by light, trauma, infection, or immunosuppression.[2] In immunosuppressed patients, it is usually the disseminated superficial (actinic) porokeratosis (DSP) variant that is seen, typically appearing on extremities symmetrically and less often the trunk.[3-4]

Immunosuppression-induced DSP has been reported in the literature in the context of transplantation, hematological malignancy, HIV infection, electron beam irradiation, immunosuppressive chemotherapy and systemic corticosteroids.[3] While DSP is almost always asymptomatic and insidious, Schena *et al*[4] reported only sixteen worldwide cases of an acute,

pruritic variant of DSP known as eruptive disseminated porokeratosis (EDP). We describe a rare case of EDP, only the second of which can be most attributable to corticosteroid-induced immunosuppression.

Case Report

A 39-year-old Caucasian woman presented with multiple scattered, erythematous, blanchable, well-defined papules and plaques with atrophic centers. The lesions appeared suddenly on her lower legs, forearms, and upper chest. Initially asymptomatic, they soon became pruritic. She had signs of actinic damage including solar lentigines on her face, chest, back, and upper extremities; however, she denied recent sun exposure. She also denied any personal or family history of previous rashes. The patient had a past medical history of well-controlled asthma and treated histoplasmosis ten years prior. She gave a history of vomiting and diarrhea of one day's duration a month prior and a twenty-four pound weight loss since this episode due to lack of appetite. Furthermore, she had a non-productive, persistent cough with periodic shortness of breath and wheezing that was not ameliorated by a week-long course of levofloxacin.

She was treated with a prednisone taper two weeks prior to presentation for suspected asthma flair secondary to viral infection, after extensive work-up and rule out of active histoplasmosis, tuberculosis, or underlying pulmonary malignancy. Her taper started at 60 mg daily for one week, reduced by 20 mg every three days thereafter. The rash appeared three days following cessation of oral steroids (two days after completing levofloxacin).

Close examination with light and magnification revealed a peripheral, keratotic rim characteristic of porokeratosis. Punch biopsy obtained from representative lesions on the left leg revealed peripheral perifollicular dyskeratotic basal cells with cornoid lamella as well as focal absence of

the granular cell layer in these areas with sparse superficial perivascular lymphocytic infiltrate in the dermis, confirming the diagnosis of porokeratosis. Sun protection, emollients, and observation for signs of malignant degeneration were discussed. Two months later the patient displayed continuing improvement of the lesions, resolution of the cough with inhaled corticosteroids, and weight gain.

(Insert figure 1)

(Insert figure 2)

(Insert figure 3)

Discussion

EDP is characterized by a sudden onset of small monomorphic erythematous plaques on the trunk, arms, and legs that are typically pruritic. While DSP is a chronic skin disorder usually clinically defined by a slow onset developing over years, EDP is unique in that the disseminated lesions appear within a few days to months. Schena *et al*[4] presented this concept of EDP as a new variant of porokeratosis that clinically resembles DSP with lesions similarly distributed but with different time evolution. EDP has previously been described in patients with cancer of the liver, colon, and pancreas, organ transplant, diabetes mellitus, herpes simplex infection[4], bone marrow transplant[3], myelodysplastic syndrome[5], and both immunosuppressant[6,7] and nonimmunosuppressant[8,9] drug therapy. Only one other case of EDP due directly to systemic corticosteroid immunosuppression, a 75-year-old man treated with betamethasone for DSP[7], has been previously reported.

In concordance with EDP as a paraneoplastic syndrome[4], as pulmonary malignancy was ruled out, the trigger for EDP in our patient was likely due to immunosuppression secondary to systemic corticosteroid therapy. Also included in the differential is EDP secondary to an idiosyncratic drug reaction to the antibiotic she had recently taken, akin to a recent report citing a similar presentation suggestive of perioperative flucloxacillin and/or gentamicin causing EDP in a 63-year-old man.[9] However, the disparity in lesion resolution time and classes of antibiotics used between the cases makes this less likely. In fact, there are reports of other drugs causing EDP such as anti-TNF therapy[6] and sumarin[8] that, while not directly applicable in our patient, should be considered in future cases. As our patient's asthma attack was questionably viral in etiology, one could argue that this infection was the nidus for the EDP episode; however, as testing for viral serology is not clinically indicated in such a setting, one could only speculate this potentially contributing. Since our patient had a history of diarrhea, conceivably she may have always had DSP and developed enterovirus-associated eruptive pseudoangiomatosis (EP) in these areas that made the lesions manifest; however, we consider this much less likely based off the history, clinical and histopathological findings, and probability of having a rare disease like EP in conjunction with DSP.

The mechanisms by which immunosuppression results in EDP are currently unclear. In DSP, immunosuppression may trigger expression of a mutant clone of epidermal cells either directly or by disrupting the growth dynamics of the epidermis. The cornoid lamella correlates with the border between normal epidermis and this clone of mutant keratinocytes. Immune surveillance that might otherwise attack the mutant clone would be impaired in the setting of immunosuppression.[10] We speculate immunosuppression caused by corticosteroids acts

similarly to cause the acute variant EDP, probably with other unknown pathways also contributing.

After thorough literature review, we can affirm our case is indeed the second case of EDP most likely related to corticosteroid-induced immunosuppression. Skin lesions of EDP in our patient have gradually improved after discontinuing oral steroid therapy with no other directly implemented therapy. In summary, we describe a case of EDP following systemic corticosteroid therapy immunosuppression, which is only the second case described in the literature.

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Learning Points

- Eruptive disseminated porokeratosis (EDP) is a recently described and characterized form of porokeratosis involving the sudden onset of erythematous pruritic papules and plaques.
- A high percentage of EDP cases occurred in the context of internal malignancy and immunosuppression.
- Corticosteroid use can induce EDP.
- EDP should alert the physician to strongly consider underlying immunosuppression and malignancies.
- EDP may now be added as the sixth variant of the Porokeratoses.

Learning objective: To demonstrate knowledge of eruptive disseminated porokeratosis and risk factors surrounding it.

1. Which of the following is characteristic only of eruptive disseminated porokeratosis (EDP) versus the more classic disseminated superficial (actinic) porokeratosis (DSP/DSAP)?
    a. Cornoid lamella
    b. Acute onset (weeks to months)
    c. Potentially underlying immunosuppression
    d. Monomorphic papules and plaques

e. Involvement of keratinocytes

Answer to question 1

a. Incorrect- Cornoid lamella is a histological feature of all porokeratoses.
b. Correct- EDP is characterized by its acute onset (weeks to months), whereas the more classic DSP/DSAP has a chronic onset (develops over years).
c. Incorrect- Both EDP and DSP/DSAP can develop in the context of immunosuppression
d. Incorrect- Both EDP and DSP/DSAP typically manifest as these types of lesions
e. Incorrect- expansion of an abnormal mutant clone of keratinocytes is thought to drive both processes

2. Which health state has been suggested in the literature to induce EDP?
    a. High blood pressure
    b. Heart attack
    c. Underlying cancer/malignancy
    d. Tick bite
    e. Pregnancy

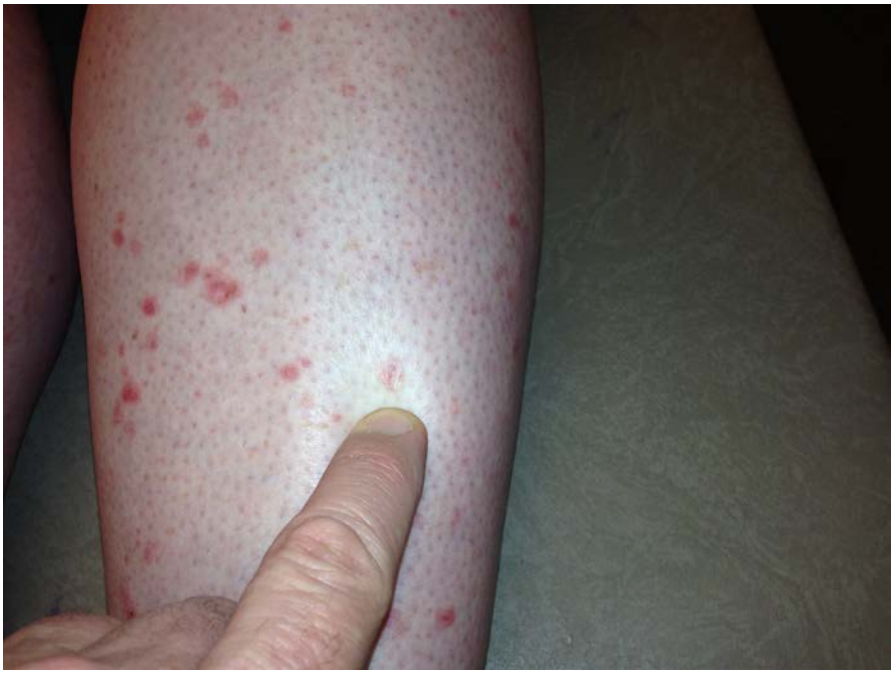
Answer to question 2

a. Incorrect- High blood pressure (hypertension) has not been previously reported or suggested to cause EDP.
b. Incorrect- Heart attack/myocardial infarction has not been previously reported or suggested to cause EDP.

c. Correct- Underlying cancer/malignancy has been reported multiple times in the literature, and it is suggested that EDP may be a paraneoplastic syndrome of underlying malignancy.
d. Incorrect- Tick bites and the diseases they can cause have not been previously reported or suggested to cause EDP.
e. Incorrect- Pregnancy has not been previously reported or suggested to cause EDP.

Eruptive Disseminated Porokeratosis

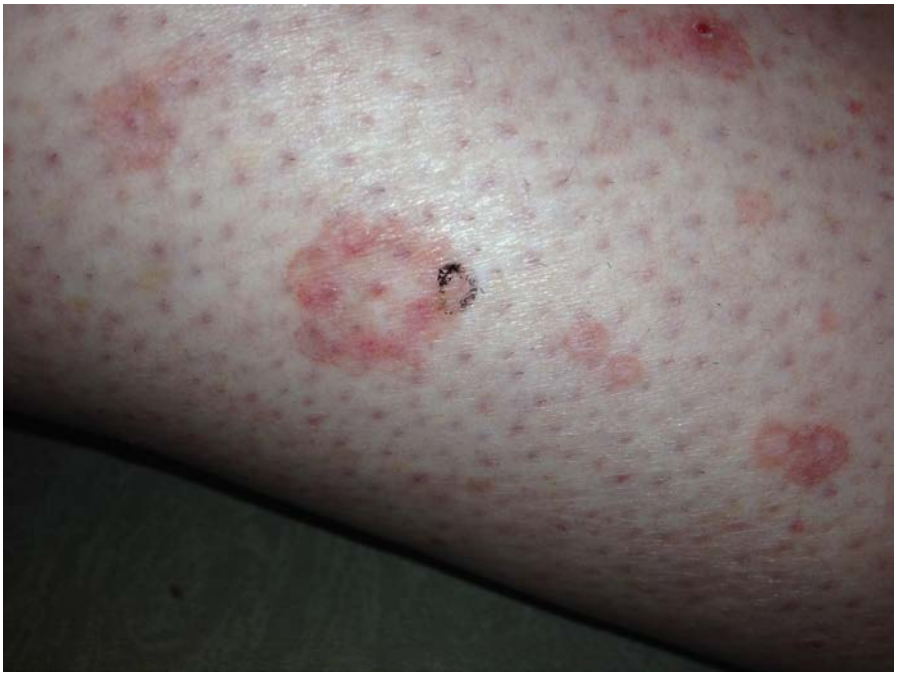
Figure 1



Eruptive disseminated actinic porokeratosis clinically manifesting as multiple erythematous, blanchable (illustrated above), well-defined papules and plaques with peripheral keratotic borders and atrophic centers on the lower extremities.

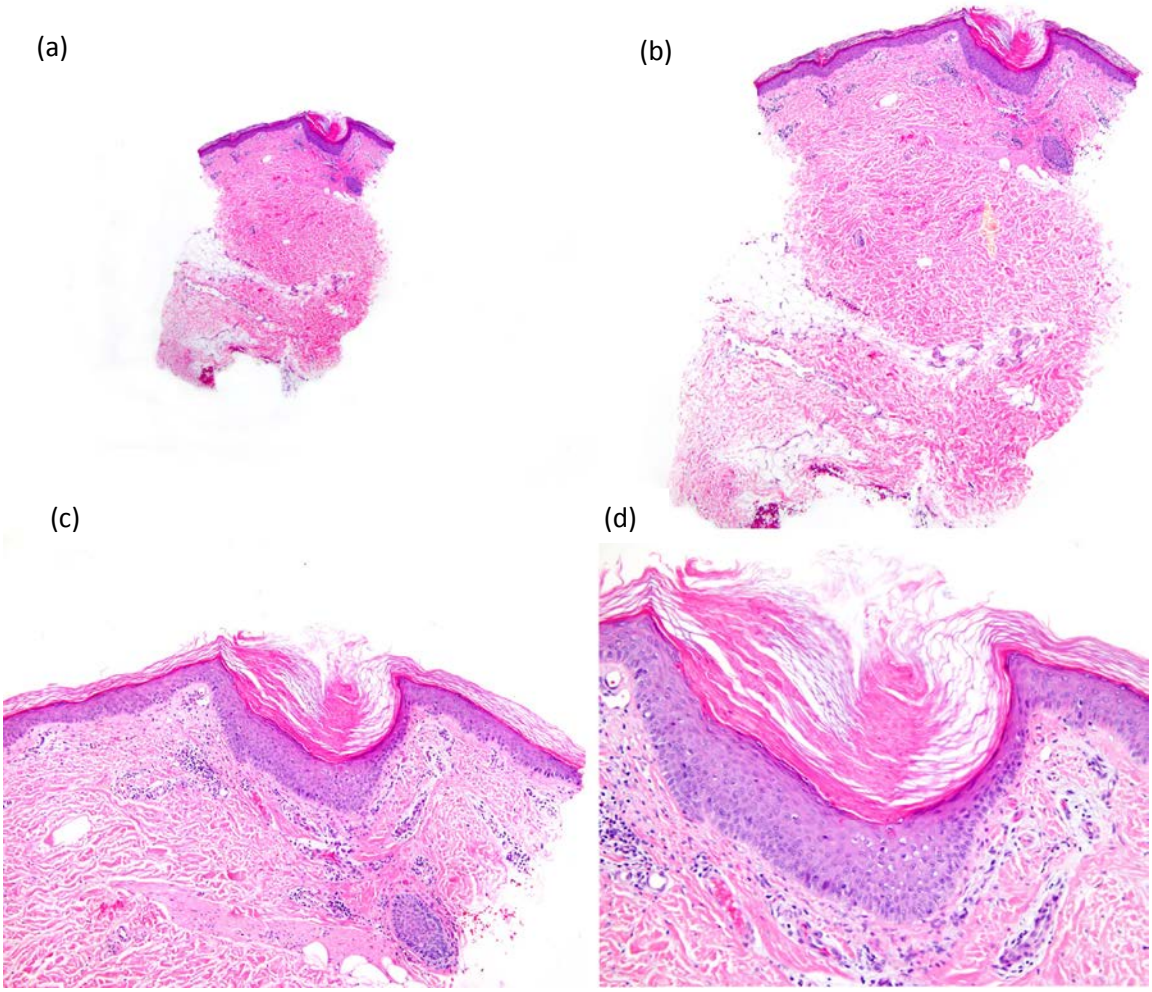
Eruptive Disseminated Porokeratosis

Figure 2



Biopsy site on the left leg of a representative plaque illustrating the ridge-like border typical of porokeratosis lesions.

Figure 3



a,b) Low and medium power showing follicular based angulated parakeratosis (cornoid lamella) with adjacent relatively atrophic epithelium (H&E 20X and 40X). c,d) Higher magnification showing dyskeratotic cells centered within follicles, angulated parakeratosis (cornoid lamella) and focal absence of granular cell layer diagnostic of porokeratosis (H&E 100X and 200X).

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