BRIEF ARTICLES

Sixteen Years of a Pruritic Unilateral Axillary Eruption: A Rare Presentation of Extramammary Paget's Disease

Amy Weiss BA[a], Robbie Drossner MD[b], Mark Jacobson, MD[c]

[a]Rutgers New Jersey Medical School, Newark, NJ
[b]Division of Dermatology, Overlook Hospital, Summit, NJ
[c]Departments of Medicine, Pathology, Montefiore Medical Center/Albert Einstein College of Medicine, Bronx, NY

ABSTRACT

Extramammary Paget's Disease (EMPD) is a rare intraepithelial adenocarcinoma of apocrine gland-bearing skin. The most common sites affected are the vulva in women and the perinanal, scrotal, and penile regions in men. One quarter of cases are extensions of an underlying visceral malignancy, usually colorectal or urothelial carcinoma. The typical presentation is an expanding erythematous plaque that shows large cells with vacuolated cytoplasm and centrally located nuclei on histology. Here we present a case of axillary EMPD that was incorrectly diagnosed and treated as various forms of dermatitis for over fifteen years. Fewer than fifteen cases of axillary EMPD have been reported in the literature in the past ten years.

CASE REPORT

An 81 year-old Caucasian female presented with a 16 year history of a pruritic rash in the left axilla (Figure 1). She reported that it started as a dime-sized red spot and gradually expanded to cover her entire axillary vault. She had been treated with a variety of topical medications, including steroids, pimecrolimus, antifungals, and anti-yeast creams. The rash improved but never cleared, despite multiple visits to various internists and dermatologists over the years. Patient denied fever, weight loss, malaise and had a negative review of systems.

On exam, there was an erythematous erosive plaque with white scale in the left axilla. The lesion measured 7x9 cm. There were no palpable lymph nodes. The right axilla and anogenital regions were clear. A 3.5 mm punch biopsy was performed and sent to the dermatopathologist.

Skin biopsy revealed a proliferation of large atypical epithelial cells with abundant mucin-containing cytoplasm within the epidermis, both at the dermo-epidermal junction and above it. Immunohistochemical staining was positive for CAM5.2 and CK7 (Figures 2-3) and negative for S100 protein and CK20,

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consistent with a diagnosis of Extramammary Paget's Disease.

The patient was referred to an oncologic surgeon for wide local excision of the lesion and primary closure. A CT scan of the chest prior to surgery was negative. Surgical margins were clear. At a six month follow up visit, the surgical scar was clear with no evidence of recurrent disease.

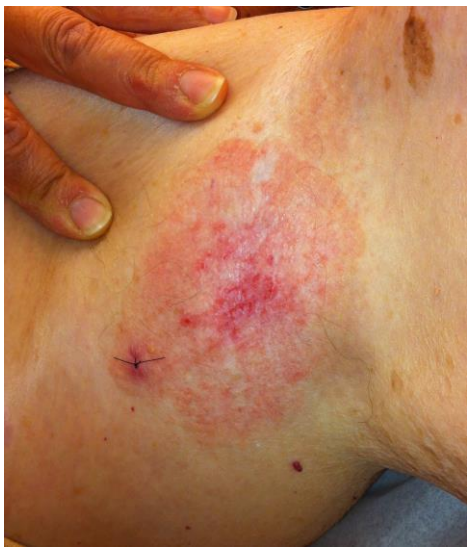

Figure 1: Erythematous, scaly, erosive plaque in the left axilla, measuring 7X9 cm

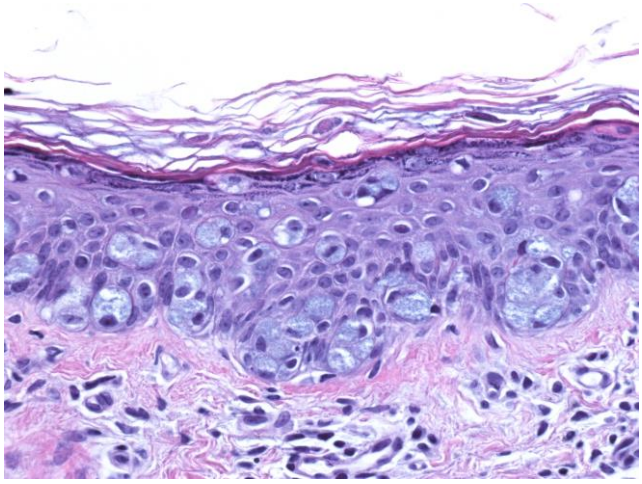

Figure 2: 40X H&E. Intraepithelial proliferation of large atypical cells with large nuclei, prominent nucleoli and abundant pale blue cytoplasm

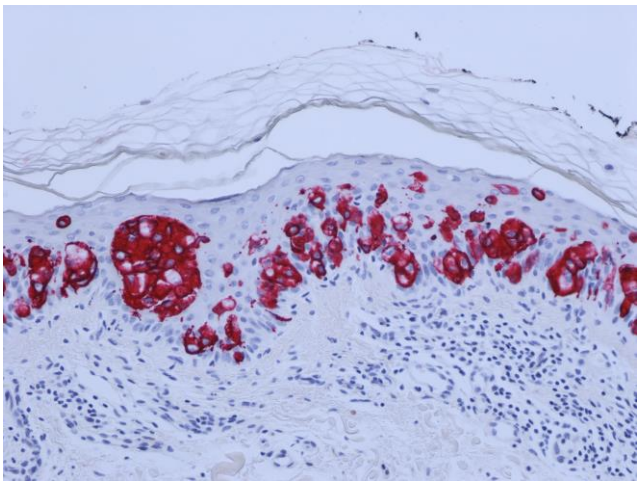

Figure 3: Biopsy with CK7 stain: highlighting low molecular weight cytokeratins of the tumor cells, not expressed by the surrounding epidermal cells

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DISCUSSION

Extramammary Paget's Disease (EMPD) is a rare intraepithelial adenocarcinoma of apocrine gland-bearing skin. The vulva in women and the perianal, scrotal and penile regions in men are the most commonly affected sites.[1] EMPD can be categorized as primary or secondary to an underlying malignancy. In approximately 25% of cases, EMPD represents extension of an underlying colorectal or urothelial carcinoma, or rarely an adnexal carcinoma. The remainder are primary intraepithelial adenocarcinomas.[2] EMPD of the axilla is rare, comprising less than 1% of cases.[1] A review of the literature shows fewer than 15 reported cases in the past ten years.

A slowly expanding erythematous plaque is a typical clinical presentation. The diagnosis must be confirmed by histological examination. Large cells with vacuolated cytoplasm and centrally located nuclei, so-called Paget cells, are distinctive, but immunohistochemical staining is important to exclude Pagetoid melanoma and squamous cell carcinoma, as well as differentiate between primary and secondary disease.[2]

EMPD rarely metastasizes. However, since it may be associated with an underlying visceral malignancy, most commonly apocrine carcinomas of the bladder, colon, rectum and reproductive organs, a workup for internal malignancies is important.[2] A CT scan of the chest, abdomen, and pelvis, as well as possible pelvic ultrasound, colonoscopy and mammogram, may be indicated, depending on the location of the cutaneous disease.[3] The location of the EMPD is useful in predicting the risk of an associated cancer. For example, 25-35% of

EMPD in the perianal area is associated with an underlying colorectal cancer. Positive staining for cytokeratin 20 and carcinoembryonic antigen in the tissue also raises the suspicion of underlying malignancy.[3]

Because EMPD of the axilla is so rare, there are no specific guidelines for visceral malignancy screening. Most patients with axillary EMPD have simultaneous EMPD in the anogenital region and the other axilla, the so-called "triple Paget's Disease."[1,2] Accordingly, Ohno, *et al.* has even recommended skin biopsy from the contralateral axilla and anogenital region, even if they appear clinically normal.[4] Treatment options for axillary EMPD are the same as those used for non-axillary EMPD, and they include Mohs micrographic surgery, wide local excision, radiotherapy, photodynamic therapy, CO2 laser ablation as well as the use of topical therapies such as imiquimod 5% cream, topical 5-fluorouracil, and retinoic acid.[1-4] The prognosis is good for primary EMPD confined to the epidermis, and the recurrence rate is low.[1,2] Monitoring for early detection of local recurrence is recommended at 6 months and long term, given the multifocal pattern often present in EMPD. In cases of secondary EMPD, the prognosis is related to the underlying malignancy.[1-4]

In this case, the only workup performed was a chest CT scan based on the location of the cutaneous disease. Biopsies of the anogenital region and contralateral axillae were not performed due to patient preference. This case is unusual because of its location and typical in its delay in

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diagnosis. It illustrates the need for any chronic, eczematous lesion of the axilla to be biopsied. It is impossible to clinically distinguish EMPD of the axilla from other chronic skin conditions such as eczema, intertrigo, psoriasis, lichen simplex chronicus and candidiasis, making the histopathology critical for diagnosis. Additionally, axillary EMPD may possibly be associated with a higher risk of underlying carcinoma than EMPD found in other regions, making early detection of this disease even more important.[1]

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Corresponding Author:
Amy Weiss, BA
37 Normandy Drive
Westfield, NH 07090
(908) 884-6121
Arw114@njms.rutgers.edu

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