CASE REPORT

A Rare Case of Extramammary Paget's Disease Mimicking Chronic Dermatitis

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ABSTRACT

Extramammary Paget`s disease (EMPD) is a rare malignant dermatological condition that usually occurs in regions with high concentrations of apocrine sweat glands. The vulva is the most commonly affected region, but it can also involve the skin of the penis, perianal area, scrotum, and perineum. This is a case of a 77-year-old postmenopausal lady who presented with a non-resolving and persistent itchy skin lesion on her genital area that had been spreading over three years and had not responded to topical and systemic steroids or antifungals. This case highlights the diagnosis challenges due to its almost similar features to genital dermatitis and fungal infection. Early recognition of this disease at the primary care level is important due to the high incidence of associated invasive disease with this rare condition.

INTRODUCTION

Extramammary Paget's disease (EMPD) is a rare form of intraepithelial adenocarcinoma.[1] It often affects the vulva in women and the perianal region in men, though it can also affect other cutaneous sites of the body that are rich in apocrine glands.[1] Only a few hundred cases of EMPD have been documented globally in the literature, making it a very rare condition.[2] Primarily, the disease manifests in the epidermis or cutaneous adnexa in its original form. Secondary EMPD, which is less common, is when EMPD is linked to an underlying cancer, usually affecting the urinary tract or lower gastrointestinal system.[3] The diagnosis of EMPD should be considered in all patients with chronic pruritic skin lesions in regions of the body with high concentrations of apocrine sweat glands, especially if the conditions do not respond to the usual antifungal and anti-inflammatory treatment. This is so that an early referral for skin biopsy can be made and the diagnosis is not further delayed. In the present case, the clinical manifestations, biopsy findings, and the management strategies of this rare dermatologic condition are discussed in detail. The importance of early diagnosis is essential to optimize the treatment outcomes.

CASE PRESENTATION

A 77-year-old postmenopausal woman with underlying hypertension and dyslipidaemia experienced pruritus over her vulva region for over three years. She first noticed a small red patch in the bilateral vulval region, which eventually spread over time. The lesion was itchy and became easily inflamed. Constitutional symptoms or any symptoms suggestive of underlying visceral malignancy were also absent. The lesion was initially managed as tinea cruris by several general practitioners. She had been treated with four courses of oral antifungal, topical antifungal, topical steroids, and oral antihistamine for over three years, however, with no improvement.

Local examination revealed a well-demarcated erythematous plaque over her bilateral labia majora, extending to her bilateral inguinal region. (Figure 1). No similar lesions were seen in the nipple area or other parts of the body. Inguinal lymph and axillary nodes were not palpable bilaterally. Per speculum examination was normal. Other systemic examinations were unremarkable.

Baseline investigations, including full blood count, fasting blood glucose, liver function test, and renal function test, were normal. Urine analysis showed microscopic haematuria. High vaginal swab test revealed normal genital flora. Liquid-based cytology for the Human Papilloma Virus (HPV) DNA PCR test was negative for both high-risk and low-risk groups of HPV DNA viruses. Her pap smear was normal, with no evidence of malignancy or infection.

A skin biopsy of the labia majora was done, and the histopathology findings confirmed the diagnosis of EMPD (Figure 2). Paget`s cells were observed within the epidermis, where the tumour cells exhibit vesicular, round to oval nuclei, prominent nucleoli, and mitotic activity. The underlying dermis showed mild infiltration by chronic mononuclear inflammatory cells, with focal pigmentary incontinence seen. The tumour cells were positive for CK7, CEA, and PAS with diastase and mucicarmine, and negative for CK20. She was subsequently referred to the gynae-oncology team for further occult malignancy screening and further management.

DISCUSSION

Extramammary Paget's disease (EMPD) is a rare form of intraepithelial adenocarcinoma which affects anatomic regions with a high concentration of apocrine sweat glands.[3] Up to 65% of EMPD cases involve the vulva, although other frequently affected areas include the perianal area (20%) and male genitalia (14%), such as the scrotum or penis.[4] It most commonly affects individuals between the ages of 50 and 80, with a peak occurrence at 65 years old.[2] The higher occurrence in this age group is likely due to age-related factors, such as cumulative genetic mutations, hormonal changes, and prolonged exposure to potential carcinogens, all of which increase the risk of developing these malignancies in older adults.[4] To the best of our knowledge, the prevalence of EMPD in Malaysia has not been formally documented, likely due to its rarity, although several individual cases have been reported. The most recent data on EMPD comes from mainland China, where its prevalence was approximately 0.04 per 100,000 people in 2016, with a higher incidence in males.[5] However,our case highlights that females can also be affected.

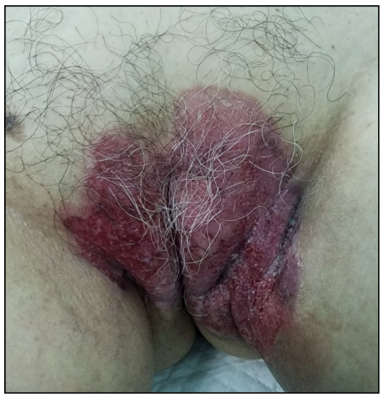

Figure 1: Well-demarcated erythematous plaque is seen over the vulvar region, extending into the bilateral inguinal region, with the left side being more prominent.

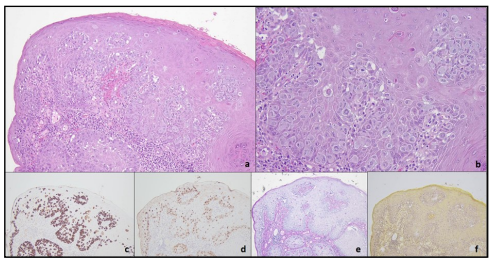

Figure 2: a) Section from the labia majora skin tissue exhibit epidermal infiltration by clusters and singly dispersed tumour cells (H&E, 100x), b) The tumour cells are polygonal epithelial cells with pale-staining, finely granular to vacuolated cytoplasm (Paget's cells), exhibiting vesicular, round to oval nuclei, prominent nucleoli and mitotic activity (H&E, 200x). The tumour cells demonstrate positive staining towards c) CK7, d) CEA, e) PAS with diastase and f) mucicarmine.

The disease most frequently manifests as a primary form that starts in the cutaneous adnexa or epidermis. Although invasive disease may be associated with a worse prognosis, primary EMPD is not life-threatening when it is restricted to the epidermis.[3] As seen in our patient's histopathology report, the Paget's cells are confined to the epidermal region, thus confirming the diagnosis of

primary EMPD. Meanwhile, the secondary form of EMPD is caused by the epidermal invasion of malignant adenocarcinoma cells and is linked to an underlying remote adenocarcinoma.[4] The occurrence of concurrent adnexal and other visceral cancers is highly correlated with EMPD.[7] Between 11 to 20% of cases of vulvar EMPD are linked to a distant carcinoma of the breast, cervix, vagina, bladder, colon, rectum, ovary, liver, gallbladder, or skin (melanomas, basal cell carcinomas), whereas 4 to 17% of cases of vulvar EMPD are linked to an underlying adnexal carcinoma, arising from apocrine sweat glands or Bartholin's glands.[4]

In addition to melanoma, lichen sclerosis, psoriasis, mycosis fungoides, and fungal infections, contact dermatitis is among the differential diagnoses for EMPD.[6] A strong clinical suspicion of EMPD should be considered when a skin lesion in the vulvar, perianal, genital, or axillary regions fails to respond to conventional topical treatments.[3] This is consistent with our patient–who developed a chronic, itchy skin lesion on her genital area for three years and did not show any improvement with topical, systemic steroids and antifungals. Misdiagnosis resulting from non-specific clinical symptoms frequently delays diagnosis and proper treatment.[7] In the case of our patient, it took three years to establish the correct diagnosis. Individuals diagnosed with EMPD usually exhibit distinct, long-lasting, and non-healing erythematous or eczematous plaques, which may be accompanied by crusting, scaling, papillomatous lesions, lichenification, ulceration, or bleeding features.[6]

Diagnosis of EMPD is done histopathologically. The diagnosis is typically obtained following a histological examination conducted in the presence of a chronic dermatosis that is not responding to local therapies (such as corticosteroids and antifungals) and is frequently made after the disease has progressed by an average of two years.[5] The presence of Paget cells is a key diagnostic feature. Paget cells are characterized by polygonal epithelial cells with pale-staining, vacuolated cytoplasm, vesicular nuclei, prominent nucleoli, and mitotic activity, infiltrating the epidermis. These cells are absent in both dermatitis and fungal infections on histopathological examination (HPE).

Furthermore, the tumour cells obtained from our patient were positive for CK7, CEA, PAS with diastase, and mucicarmine, which are characteristic of EMPD. Special stains play a crucial role in supporting the diagnosis. The CK7 and CEA immunostains specifically highlight Paget cells, while PAS with diastase confirms the presence of cytoplasmic mucin within these cells, further distinguishing EMPD from other dermatological conditions. In contrast, fungal infections typically exhibit fungal hyphae or spores on histopathological examination, whereas dermatitis presents with non-specific inflammatory changes without Paget cells or positive immunohistochemical markers. The main challenge lies in distinguishing these conditions clinically.

For every patient with biopsy-proven EMPD, a comprehensive work-up for occult malignancy should be conducted.[7] The recommended approach is to start with a review of systems of the patient, particularly with emphasis on genitourinary and gastrointestinal symptoms, and should be followed by a physical examination that includes breast examination and a screening for lymphadenopathy and multifocal diseases.[8] Further investigations for all patients should include urine cytology, cystoscopy, chest X-rays, imaging of the abdomen and pelvis, colonoscopy, and other tests such as serum prostate-specific antigen for male patients, as well as Pap smear and mammography for female patients.[6]

Surgical excision continues to be the cornerstone of care for EMPD. Mohs Micrographic Surgery (MMS), which offers accurate margin control and lower recurrence rates, is regarded as the preferred method.[2] MMS has shown significant promise, particularly in its capability to precisely excise and manage the margins of both deep and peripheral resections within a single plane. This technique improves accurate orientation, mapping, and targeted re-excision of microscopic tumour extensions, leading to better surgical outcomes.[7] Relapses are common due to the subclinical nature of the disease, even after surgical excision with wide margins and micrographic surgery.[9]

Alternative treatment modalities, including topical chemotherapy, photodynamic therapy, and radiation therapy, may be advantageous for patients who are reluctant to pursue surgical options or who do not qualify for surgical intervention.[1] In addition, nonsurgical treatment may be appropriate in situations when surgery is not feasible or as an adjuvant or salvage therapy to surgery.[10] Since relapses are common with all known therapy methods, prolonged periods of close observation is required for every patient.[9] Surgical excision with negative margins remains the most effective method to reduce the risk of local recurrence and enhance long-term recovery in non-invasive diseases.[10] In our case, after a thorough evaluation, no occult malignancy was detected. Given the patient's advanced age, a nonsurgical approach was chosen, with topical chemotherapy using imiquimod cream as the preferred treatment.

As EMPD is frequently associated with underlying malignancies, it is crucial for primary care providers to recognize this condition early. Timely identification allows for appropriate referrals and interventions, potentially enhancing patient outcomes through the prompt management of any related by malignancies.

CONCLUSION

EMPD should be considered in older patients with chronic, non-resolving skin lesions in apocrine-rich areas, particularly when standard treatments fail. While this is not the first case of EMPD in Malaysia, previously published cases demonstrate variability in the anatomical sites affected and the extent of skin involvement. Notably, a common feature across these cases is a prolonged delay in diagnosis, often spanning several years which highlights the ongoing challenge if limited awareness of this rare dermatological condition among primary healthcare providers. It is imperative that primary care physicians possess a comprehensive understanding of the clinical manifestations of EMPD and conduct thorough physical and systemic examinations to identify potential underlying malignancies. Early detection is essential for facilitating timely referrals and optimizing patient outcomes.

CONSENT

Written informed consent was obtained from the patient for the publication of this case report and the accompanying clinical images.

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