Concurrent manifestations of primary extramammary Paget's disease involving the left axilla and the left groin with nodal and bone metastasis

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ABSTRACT:
Primary extramammary Paget's disease (EMPD) is a rare type of skin cancer, as a less aggressive intraepithelial adenocarcinoma. Patients usually present with skin lesions at apocrine gland sites such as the vulva, penoscrotal area, perianal area, umbilical area, and, less commonly, the axilla. EMPD is primarily an intraepidermal neoplasm but has the potential to invade deeper structures and metastasis. This case report presented a patient diagnosed with concurrent sites of primary EMPD, with one site showing nodal and bone metastasis. Making an accurate diagnosis of EMPD can be challenging as case occurrences are rare.
Key words: Apocrine, intertrigo, metastasis, skin cancer, Toker cell

Introduction

Extramammary Paget's disease (EMPD) is a rare type of cancer that is common in Caucasians and tends to occur in individuals aged 45 to 75, although it can affect people of any race and age[1].

EMPD can be categorized into primary and secondary forms. Primary EMPD originates as an intraepidermal neoplasm while secondary EMPD develops from an underlying neoplasm[2].

EMPD usually manifests in a single anatomical region such as the genital or perianal area but multiple regions can be affected simultaneously[3]. The most common locations for EMPD are the vulva in women, and the penoscrotal area and trunk in men. Primary EMPD arising in regions lacking apocrine glands is termed ectopic EMPD[4].

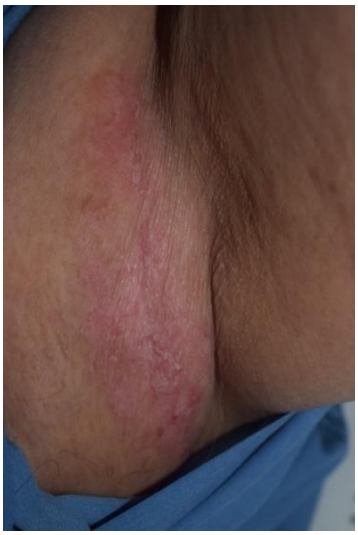

Figure 1 Chronic erythematous plaque on left axilla

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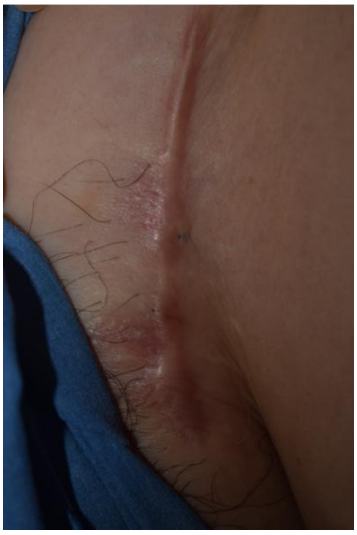

Figure 2 Old surgical scar on left groin

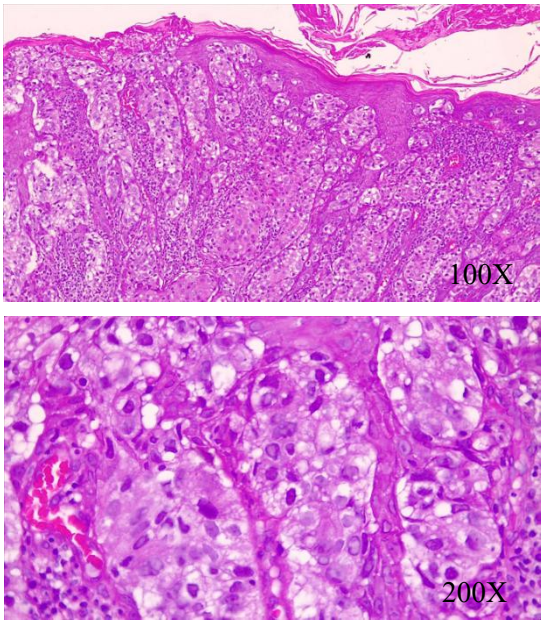

Figure 3 Histopathological findings of the left groin revealed atypical pagetoid cells with dermal invasion

Making an accurate diagnosis of EMPD can be challenging, with a reported median delay of 2 years from the onset of symptoms to conclusive diagnosis. In some cases, EMPD may exist for 10 to 15 years before signs of cancer or metastases become apparent[5]. Poor prognosis is associated with factors including dermal invasion, the presence of cutaneous nodules, and lymph node metastasis[6].

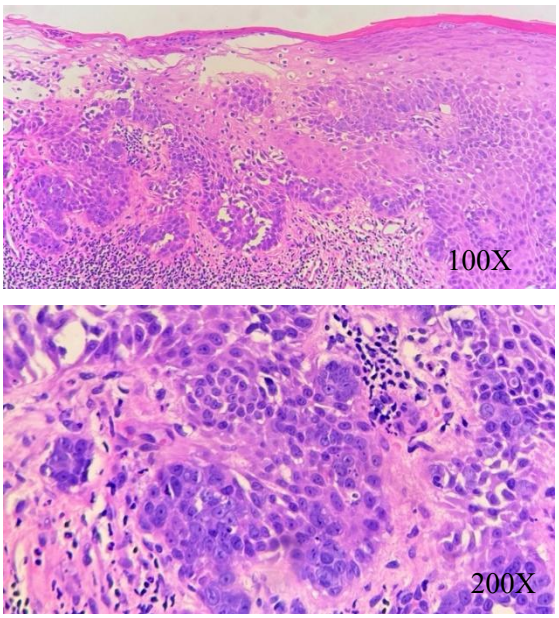

Figure 4 Histopathological findings of the left axilla revealed atypical pagetoid cells in epidermis without dermal invasion

This report highlights a rare presentation of a patient with multiple concurrent primary EMPD affecting the left groin and left axilla with nodal and bone metastasis.

Case report

A 61-year-old Thai female presented with pruritic erythematous plaque with scale on the left axilla [Figure 1], which exhibited a wax-and-wane behavior and had been ongoing for 15 years. The patient was initially diagnosed with psoriasis and received topical corticosteroids. Four years before presenting to Hospital A, the patient developed similar lesions in the left groin [Figure 2] and initially applied topical corticosteroids. Two years later, she visited a private hospital, where a skin biopsy from the left groin revealed an irregular epidermal hyperplasia composed of large atypical cells.

These cells had abundant cytoplasm and large pleomorphic and hyperchromatic nuclei, arranged in nests and as single cells along the dermoepidermal junction and in the reticular dermis [Figure 3]. The biopsy of the lesion from the left groin was positive for anti-cytokeratin AE1/AE3 and CK7 but negative for Melan-A, HMB45, and CK20. No additional immunohistochemical staining was performed and the patient was diagnosed with EMPD. A wide excision was performed to remove the lesion at the left groin but the surgical margin was not documented. After undergoing surgery, the patient was lost to follow up.

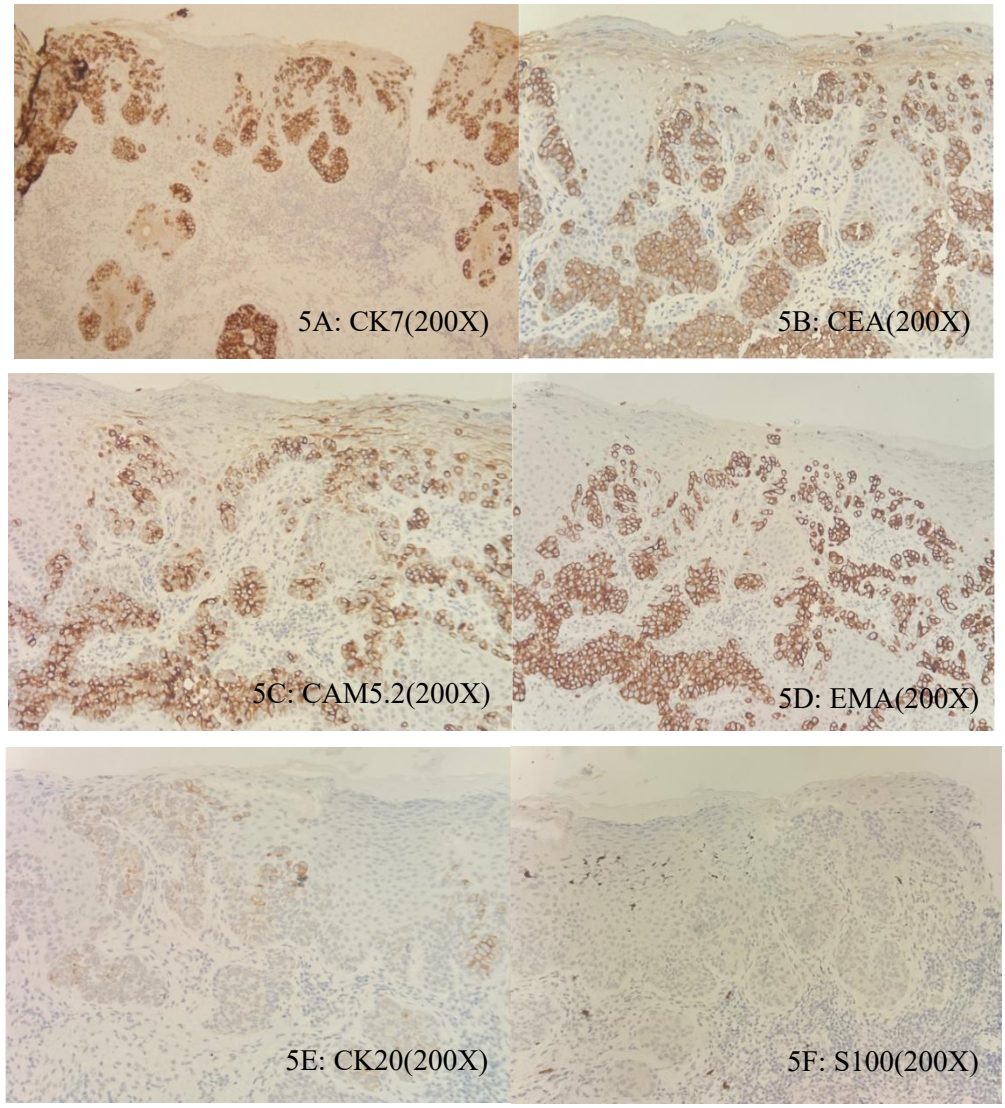

Figure 5 Immunohistochemical staining of the lesion on the left axilla showed positive for CK7, CEA, CAM5.2, and EMA (Figure 5A-D: 200X CK7, CEA, CAM5.2, and EMA, respectively). Immunohistochemical staining showed negative for CK 20 and S100 (Figure 5E-F:200X CK20 and S100, respectively)

The patient experienced worsening of the lesion in the left axilla and sought care at Hospital B. A skin biopsy from her left axilla revealed atypical pagetoid cells in the epidermis, without dermal invasion [Figure 4]. Immunohistochemical staining results of the lesion on the left axilla were positive for CK7, CEA, CAM5.2, and EMA [Figure 5A-D, respectively; 200X], while CK20 and S100 were negative [Figure 5E-F; 200X].

The patient's medical record revealed a mammogram categorized as BI-RADS 2, indicating benign findings. CT scan of the chest and whole abdomen showed multiple groin lymph nodes (up to 1.4 cm), small axillary lymph nodes (2–4 mm), and no intraabdominal lymph node enlargement. A transvaginal ultrasound identified a uterus with multiple intramural masses (up to 3.8 cm), likely consistent with myoma uteri. A ThinPrep Pap test was negative for intraepithelial lesions or malignancy. Esophagogastroduodenoscopy (EGD) and colonoscopy detected gastritis and polyps in the descending and ascending colon.

Histopathological examinations of the biopsies from the stomach and sigmoid colon were negative for malignancy. PET/CT identified a hypermetabolic node in the bilateral inguinal region (1.5 cm), a left axillary node (0.7 cm) suspected as nodal metastasis, and hypermetabolic foci in the left C3 and T12 vertebrae suggestive of bone metastasis. The patient subsequently underwent wide local excision of the left groin with bilateral groin node dissection, wide local excision of the left axilla with axillary lymph node dissection, and flap reconstruction.

The surgical pathology report revealed that all lymph nodes from bilateral groin tested positive for metastatic carcinoma. Immunohistochemical staining demonstrated positivity for EMA, GCDFP-15, CAM 5.2, GATA3, and CK7 with focal positivity for CEA and CK20. By contrast, the lymph nodes from the axilla were negative for malignancy.

The patient was diagnosed with primary EMPD of the left groin and left axilla, with bone and nodal metastasis. She received three cycles of cisplatin and paclitaxel and underwent a follow up CT scan of the chest with contrast. The CT scan showed two new left supraclavicular and paraesophageal regions measuring 0.7 cm and 0.8 x 1.2 cm, a few osteolytic lesions at the T7 body, an osteoblastic lesion at T12, and one at the fifth rib. An MRI of the spine showed suspected metastases at C3, T2, T7, T12, L3, and S3. The patient was treated with cisplatin and 5-fluorouracil for 2 cycles and advised to continue the treatment with chemotherapy.

Discussion

EMPD is an uncommon intraepidermal adenocarcinoma primarily found in the genital and perianal regions, with occasional involvement of the axilla. Clinical presentations vary but erythematous plaques and pruritus are frequently observed. EMPD diagnosis typically follows consideration of other possibilities and unsuccessful treatments[7,8]. EMPD is associated with concurrent malignancies in 5 to 42% of cases, irrespective of the timing of its development, and can manifest at multiple sites[3]. A literature review identified 20 reported cases with multiple lesion sites involving 19 males including 17 Asian males. Only one female patient presented with bilateral axillary lesions. In our case study, a female patient presented with multiple lesions located in the left inguinal region and the left axilla, differing from previously reported sites. This case was notable for the presence of metastasis, which was not reported in earlier cases[3].

EMPD can become invasive, extending into the dermis and metastasizing to regional lymph nodes or distant sites. Therefore, a comprehensive diagnostic evaluation is necessary including an assessment for underlying internal malignancies, a skin biopsy, and immunohistochemical staining to confirm

the diagnosis and evaluate the extent of the disease.

Immunohistochemistry is a critical tool for confirming the diagnosis of EMPD. Cytokeratin stains such as CK7 and CAM 5.2, serve as sensitive markers to both EMPD and mammary Paget's disease (MPD)[9] and all patients should be examined for secondary malignancy. Patients with EMPD have an increased risk of developing secondary primary malignancies independent of EMPD[10]. In this case, the immunohistochemistry test to exclude the gastrointestinal or genitourinary tract was not performed, while the patient proved negative for primary internal malignancy.

The differential diagnoses included multiple sites of invasive EMPD, primary adenocarcinoma with Pagetoid spreading, and metastatic carcinoma. For the groin lesion, no additional immunohistochemical analysis was performed.

The primary treatment for EMPD is typically surgery, with Mohs micrographic surgery showing promising clinical outcomes and lower recurrence rates based on the available data. Alternatives such as photodynamic therapy and topical treatments like 5-fluorouracil and imiquimod have also been investigated and may be suitable in certain cases. Therapeutic intervention may be considered based on the patient's clinical condition[11]. In this case, the patient presented with multiple lesions involving the left axilla and left groin, accompanied by nodal and bone metastasis. The patient had undergone surgical treatment and received three cycles of cisplatin and paclitaxel. Patients with EMPD typically have a favorable prognosis, with a 5-year overall survival rate between 75% and 95%[11]. In this case, the patient had multiple sites of involvement with nodal and bone metastasis. This portends a poor prognosis with less than 10% five-year survival rate[12].

Conclusions

The patient was diagnosed with primary EMPD of the left groin and left axilla, with bone and nodal metastasis. The coexistence of concurrent EMPD and metastatic primary EMPD is exceptionally rare. A standardized treatment protocol for metastatic EMPD has not yet been established and chemotherapy remains the cornerstone of disease management[12].

This diagnosis should be considered in patients with eczematous cutaneous lesions in intertriginous areas, particularly in elderly individuals unresponsive to treatment. Early diagnosis, work up for secondary or concurrent malignancy, and long term follow up are important in EMPD.

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