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CASE REPORT

Primary invasive triple extramammary Paget's disease with regional lymph node metastasis: A case report and review of the literature

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ABSTRACT

Extramammary Paget's disease (EMPD) is a rare intraepidermal carcinoma and predominantly involves apocrine gland-bearing areas, such as anogenital regions and axillae. EMPD usually involves a solitary area and, less often, two areas in the same patient (double EMPD). The simultaneous involvement of bilateral axillae and anogenital region, called triple extramammary Paget's disease (TEPD), is an extremely rare subgroup of diseases that has been reported mostly from studies conducted in Japan. Because of its rarity, the clinical course, pathology/immunohistochemical staining features, and prognosis of TEPD are still unclear. Herein, to our knowledge, we present the first case of primary invasive TEPD with regional lymph node metastasis in Taiwan, and review the literature.

Introduction

Extramammary Paget's disease (EMPD) is a rare intraepidermal carcinoma that predominantly involves apocrine gland-bearing areas such as vulva, scrotum, and perianal regions as well as axillae. It is subdivided into primary and secondary EMPD based on whether there is an underlying malignancy, such as adenocarcinoma of skin appendage or noncutaneous carcinoma. The majority of primary cases are confined to the epidermis, but the incidence of dermal invasion has been reported to be as high as 18.8%.[1] Dermal invasion is significantly associated with lymph node metastasis, distant metastasis, and poor prognosis.[1,2]

Primary triple extramammary Paget's disease (TEPD) represents a very rare condition where the simultaneous occurrence of EMPD is noticed over bilateral axillae and the genital region. To our knowledge, case series of TEPD have been mostly reported in Japan,[3,4] and TEPD in other races is extremely rare.[5] The clinical course and prognosis of this rare disease are still unclear owing to the small number of reported cases and heterogeneous entities.[3,5,6] Herein, we present a case with primary invasive TEPD and review the literature. To our knowledge, this is the first Taiwanese TEPD case to be presented.

Case report

A 70-year-old man attended our dermatology clinic with a 6-year history of an erythematous plaque on the left armpit and a 5-year history of reddish plaques on bilateral groins and scrotum. He had previously received topical antifungal agents and topical corticosteroid for these skin lesions for 3 years in a local hospital with poor response. Moreover, cryotherapy over whole skin lesions every 1–3 weeks has also been given for about 1 year. Initially, the cryotherapy showed some clinical improvement over focal skin lesions, which healed with scaring and pigmentary change clinically, but skin lesions recurred and progressed under treatment later. During the entire treatment course, this patient did not undergo any investigation for the histopathologic examination. Owing to the progression of the disease under the aforementioned treatment, he was referred to our clinic. Dermatology findings revealed an erythematous confluent erosive plaque over the base of the penis, the left side of the scrotum, and the left inguinal area. A residual shallow erosion was noticed over the left armpit, and an erythematous plaque was found on the right armpit. Hyper- and hypopigmented plaques with scarring change were noticed over the left armpit and the right inguinal area (Figure 1). Incisional biopsies were performed from the clinically involved areas of bilateral armpits and left scrotum. The pathology of the right

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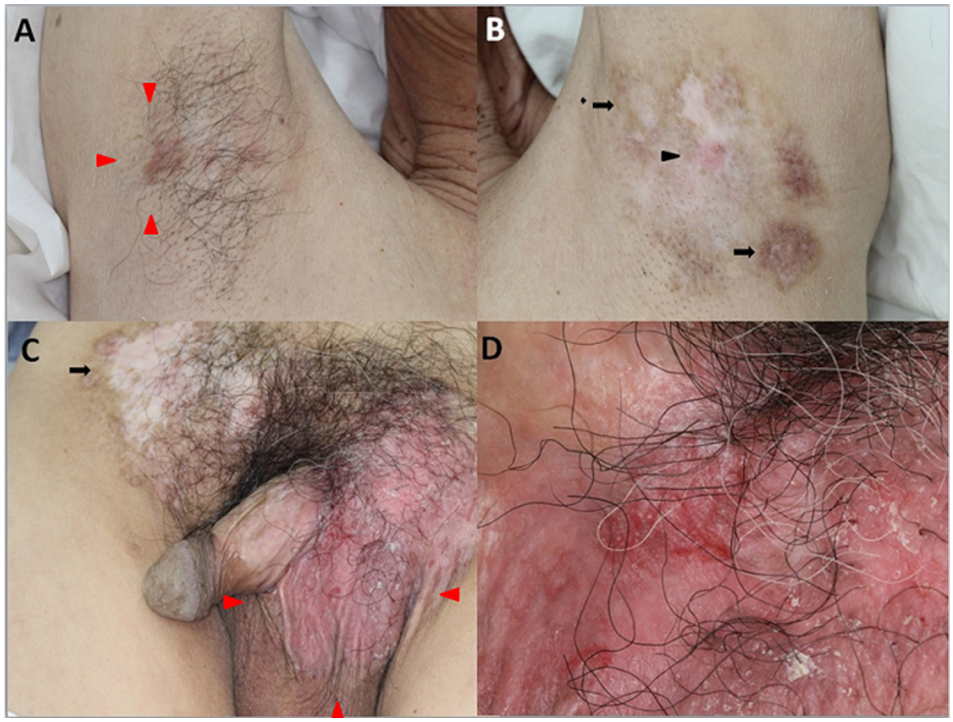

Figure 1 (A) The patient presented an asymptomatic, incidentally noticed erythematous plaque on right armpit; (B) a residual shallow erosion (arrowhead) with multiple hyperpigmentation and hypopigmentation (arrow) that was caused by repeat cryotherapy; (C) an extensive erosive plaque over pubic area was also noticed; and (D) closer view of the plaque. Pigmentary change caused by cryotherapy was also visible over right inguinal region (arrow). Extramammary Paget's disease was histologically confirmed over the three aforementioned areas. Positive surgical margin sites in first wide excision were demonstrated (red arrowhead) over (A) right armpit and (C) inguinal area.

armpit and the left scrotum showed clustered intraepidermal Paget's cells with pleomorphic and hyperchromatic nucleus and pale cytoplasm. Paget's cells were immunoreactive to cytokeratin 7 (CK7) (Figure 2). The biopsy from the left armpit showed no epidermal involvement, while displaying clustered atypical cells with abundant pale cytoplasm within the fibrotic dermis (Figure 3). The atypical cells were immunoreactive to CK7, gross cystic disease fluid protein-15 (GCDFP-15), and GATA3. There was neither palpable inguinal nor axillary lymphadenopathy. Sonography over the breast and the left axilla did not show any abnormality. Results of laboratory investigations were unremarkable, and tumor markers, including carcinoembryonic antigen (CEA), were within normal limits except for the mildly elevated prostate-specific antigen (4.67 ng/mL; (normal range, 0–3 ng/mL). Routine esophagogastroduodenoscopy, colonoscopy, and three sets of urine cytology did not show any evidence of malignancy. A whole-body positron emission tomography/computed tomography (PET/CT) revealed no fluorodeoxyglucose (FDG)-avid focus except for a small lymph node with mildly increased FDG uptake in Level II of the right neck, being considered with uncertain clinical significance.

After the full cancer workup, this patient underwent wide excision with a 3-cm margin over bilateral armpits and inguinal area, and skin defects were repaired by split thickness skin grafts harvested from inner thighs. Because hematoxylin and eosin pathologic examinations showed positive surgical margins over the lateral border of the right armpit and the lower border of the inguinal area accompanied with dermal invasion on the inguinal area, those two lesions were reexcised with frozen section examinations. All initial frozen section samples of margins from the right armpit were negative for tumor cells. Three frozen section samples

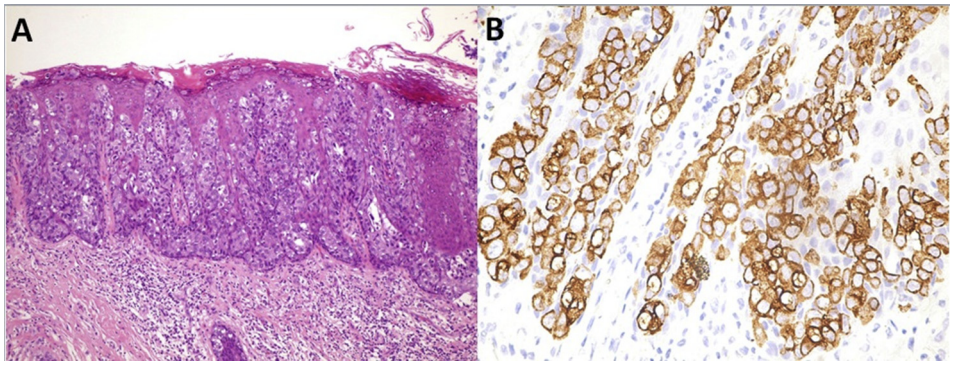

Figure 2 (A) Histopathologic examination showed typical clustered intraepidermal Paget's cells with pleomorphic and hyperchromatic nucleus and pale cytoplasm over all specimens except that from first incisional biopsy of left armpit (H&E; original magnification, × 100); and (B) Paget's cells were strongly immunoreactive to cytokeratin 7 (CK7; original magnification, × 400). H&E = hematoxylin and eosin.