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Case Report

Extramammary Paget's disease: presenting in an unusual site

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Abstract Extramammary Paget's disease (EMPD) is a rare neoplasm with only a limited number of reported cases in literature. It is mainly composed of intraepidermal Paget cells and possesses variable clinical behaviour and histological appearance leading to difficulty in diagnosis. We here report a case of primary EMPD in a 71-year-old male who presented with gradually progressive, pruritic, eczematous lesion in suprapubic region, not responding to topical medications. Histological assessment showed Paget cells infiltration throughout the epidermis with dermal invasion. Using immunohistochemistry, the expression of CK7, carcinoembryonic antigen (CEA) was examined to elucidate cellular differentiation of the carcinoma.

Key words
Suprapubic region, Paget's cells, cytokeratin 7, carcinoembryonic antigen.

Introduction

Extramammary Paget's disease (EMPD) is a rare neoplasm of apocrine gland-bearing skin such as vulva, perianal region, scrotum and penis.[1] However, it has also been described in other apocrine gland-bearing areas including axillae, thigh, face, eyelids, face, abdomen, external auditory canal.[1,2] It is defined as marginated plaque resembling Paget's disease clinically and histologically. It occurs more frequently in women in their sixth to eighth decades of life.[3,4] Clinically it presents as itchy, scaly, erythematous and eczematous patch or plaque. The significance of this disease lies in the fact that the innocuous cutaneous lesion may be an ominous forerunner of underlying malignancy. Although the clinical and histological features of mammary Paget's disease are well established, the source of neoplastic cells in EMPD remains controversial. To the best of our knowledge, primary EMPD of suprapubic region has not been described previously. We, therefore, report this particular case here.

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Case report

A 71-year-old male presented to the dermatology OPD with an erythematous, eczematous plaque on the suprapubic region of 8 months duration. It initially started as a small, erythematous scaly patch that progressed slowly but relentlessly, despite various topical medications over 4-5 months. It was extremely pruritic. There was no history of bladder or bowel disturbances. His past history and family history were unremarkable.

Dermatological examination revealed a 12×10 cm well-marginated, polycyclic, eczematous plaque on the suprapubic region. The plaque

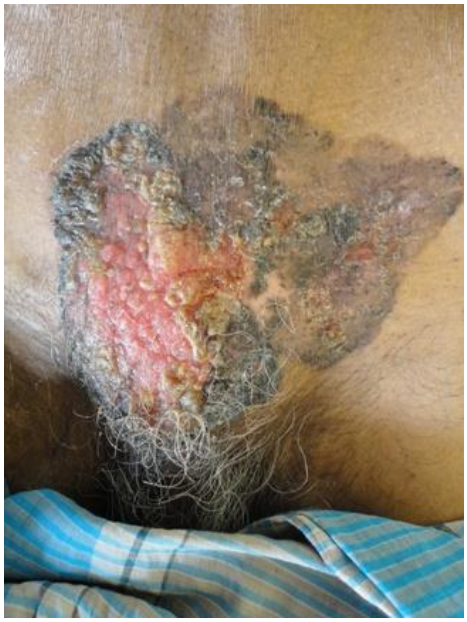

Figure 1 Polycyclic, well-demarcated, eroded, eczematous plaque on suprapubic region.

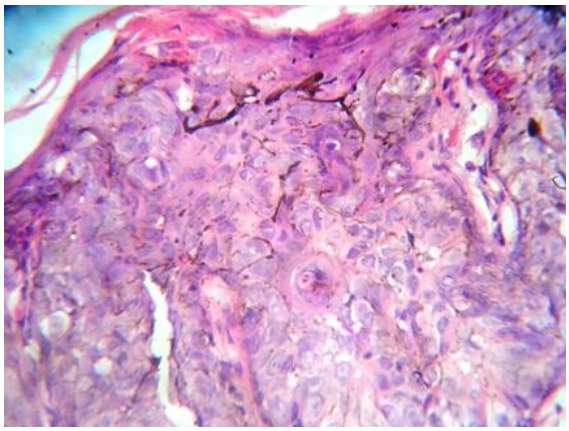

Figure 2 Hematoxylin and eosin staining showing Paget's cells with distinctive pale cytoplasm dispersed throughout the epidermis.

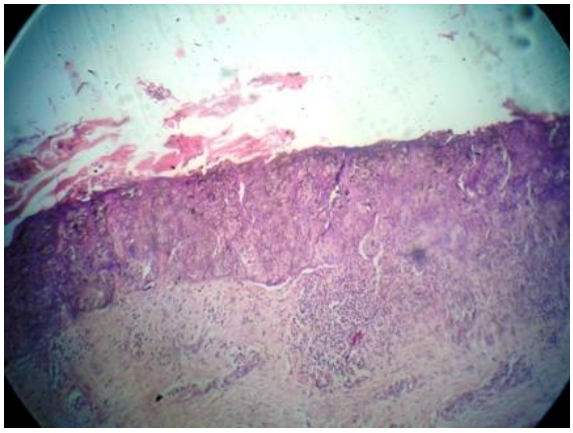

Figure 3 Paget's cells invading the dermis.

showed pigmentation at the periphery. It was covered with grayish yellow crusts, which on removal showed shallow ulcerations with some pinpoint bleeding points at places (**Figure 1)**. There was no regional lymphadenopathy and the skin elsewhere was normal. Proctoscopic examination revealed no significant abnormality.

Routine blood tests were normal, but serum CEA level was elevated. Ultrasonography and contrast enhanced computed tomography of the abdomen and pelvis did not reveal any mass or retroperitoneal lymph node. Colonoscopic finding was unremarkable. Skin biopsy from the lesion with hematoxylin and eosin staining showed presence of fair number of round to oval large cells having large, prominent nuclei and ample clear cytoplasm infiltrating throughout the epidermis, indicative of Paget's cells. The basal layer was flattened. Dermis showed chronic inflammatory cells with invasion of Paget's cells into the dermis at places (**Figure 2** and **3**). Immunohistochemical staining (using peroxidase-antiperoxidase technique) was positive for CK7 and CEA.

Discussion

EMPD is a rare disease. It was first described as a distinct clinical entity by Radcliffe Crocker in 1889. It occurs more frequently in women in their sixth decades of life.[2,3] Hatta *et al.*[4] reported that male patients outnumbered female patients in Japan, in contrast to the previous reports from Western countries. EMPD has a predilection for areas with high density of apocrine glands such as vulva, penis, scrotum, perianal region and axillae.

EMPD often presents as a well-defined, moist, erythematous, scaly, eczematous patch with hypo- or hyperpigmentation. Intense pruritus and burning sensation are commonly reported.[5]

Clinically the lesion of EMPD may resemble squamous cell carcinoma *in situ*, melanoma or benign dermatosis. The hallmark is relentless progression despite topical medications and sharp raised margin.

There are usually three patterns of EMPD: a) an *in situ* epithelial form without associated carcinoma, b) an epithelial form with associated adnexal carcinoma and c) associated with visceral malignancy of either genitourinary tract or gastrointestinal tract.[6] EMPD cells themselves have the potential to invade the dermis and metastasize.

There is a strong association between the presenting anatomical site and the underlying visceral carcinoma.[7] Helwig and Graham reported a frequency of visceral carcinoma associated with perianal EMPD in the range of almost 86%.[8] The frequency was much lower in vulval EMPD; the difference may be reflective of difference in the lymphatic drainage and indistinct boundaries in perianal region.

Perhaps the most controversial aspect of EMPD pertains to its pathogenesis. The current theories on the origin of Paget's cells are: a) an adenocarcinoma in pluripotent epidermal cells, b) an underlying adenocarcinoma of apocrine or eccrine glands or c) the multicentric effect of a carcinogenic stimulus in the epidermis. Paget's cells in mammary and extramammary Paget's disease seem to have different origins i.e. those of mammary Paget's disease ascend to the epidermis from lactiferous ducts, whereas those of EMPD originate in the epidermis itself.[8] The level of invasion of Paget's cells in EMPD can be classified into three grades: *in situ* in epidermis, microinvasion into the papillary dermis and deep invasion into the reticular dermis or subcutaneous tissue.[9] According to this classification our case can fall into the third grade.

Differential diagnosis of EMPD includes tinea corporis, erosive lichen planus, lupus vulgaris, Bowen's disease, mycosis fungoides, and squamous cell carcinoma. In our case, we confirmed our diagnosis by doing histopathological examination and immunohistochemical studies. The characteristic histopathology of EMPD is Paget's cells which are present in groups, clusters or as single cells within the epidermis and show nuclear enlargement with atypia, prominent nucleoli, and well-defined ample cytoplasms.[10] The basal layer is compressed but preserved. The cells can extend into the contiguous epithelium of dermal appendages. Sialomucin is found in the cytoplasm of Paget's cells. It usually stains with colloidal iron, alcian blue, PAS stain and mucicarmine. Immunohistochemistry is a useful adjunct in making correct diagnosis. Low-molecular-weight cytokeratin stains cytokeratin 7 (CK7) and anti-cytokeratin (CAM 5.2); carcinoembryonic antigen (CEA) are sensitive markers for EMPD.[11]

As the disease is rare, there is little knowledge of the most effective treatment. Primary treatment is surgical and involves wide local excision and frozen section evaluation of the margins. Depth of invasion and multiple lymph nodes metastasis are important prognostic factors of EMPD. Unfortunately, there is high rate of recurrence. Role of radiotherapy in the treatment of EMPD is conflicting.[12] Radiotherapy may be used as a supplement to aggressive surgery. Other treatment modalities that can be tried are topical 5-fluorouracil, imiquimod; cryosurgery; systemic chemotherapy and photodynamic therapy.

To conclude, the key to diagnosis of EMPD is high degree of suspicion. Any eczematous or thickened area where apocrine glands are normally located and which does not resolve with appropriate therapy should arouse the suspicion of EMPD.

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