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CASE REPORT

Extramammary Paget's Disease of the Penis and Scrotum

Vijay Sainath Reddy[1] · Shivam Gaba[1] · Mallika Tewari[1] · Gautam Prakash[2] · Sarita Mittal[3]

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Abstract
Extramammary Paget's disease (EMPD) is an adenocarcinoma arising from the skin or skin appendages which is sometimes associated with an underlying malignancy. EMPD is most commonly seen in the vulva, followed by perianal region, and the male genitalia. In most cases, patient presents with eczematous lesion persisting for long duration. A 77-year-old gentleman had a history of chronic eczematous lesion over penis and scrotum for the last 10 years. Examination revealed an erythematous plaque like eczematous lesion over the penis and scrotum. Biopsy with IHC of lesion is suggestive of EMPD. Wide local excision of lesion and left inguinal lymph node dissection with pedicled left superficial circumflex iliac perforator flap cover was done. The final histopathology with IHC confirmed the diagnosis of EMPD. The postoperative period was uneventful, and patient was discharged. EMPD of the penis and scrotum is a rare presentation, and it is ideally treated with wide excision.

Keywords Extramammary Paget's (EMPD) · Eczematous lesion · Cancer

Introduction

Paget's disease was first described by Sir James Paget in 1874. He had classified it into two types: mammary and extramammary. Extramammary Paget's disease (EMPD) is an adenocarcinoma arising from the skin or skin appendages in areas with apocrine glands sometimes associated with an underlying malignancy. EMPD is most commonly seen in the vulva (65%), followed by perianal region (20%), and the male genitalia (scrotum and penis) accounting for 14% of all cases. In 1889, Radcliffe Crocker first described EMPD in a patient with urinary bladder carcinoma, who presented an eczematous lesion on the penis and scrotum [1]. In most cases, it is an intraepithelial lesion not associated with any underlying or distant cancer. EMPD constitutes about 6.5% of overall cutaneous Paget's disease.

✉ Mallika Tewari
drmtewari@gmail.com

[1] Departments of Surgical Oncology, Institute of Medical Sciences, Banaras Hindu University, Varanasi 221005, U.P., India

[2] Departments of Plastic Surgery, Institute of Medical Sciences, Banaras Hindu University, Varanasi 221005, U.P., India

[3] Pathology, PathKind Diagnostics, New Delhi, India

Case

A 77-year-old gentleman presented in our out patient's department with an eczematous lesion involving the skin of the groin, penis, and scrotum.

The patient had a long history of a painless but gradually progressive reddish discoloration at base of the penis and scrotum for 10 years, without any other complaints. The patient had no history of cancer either current or treated in the past. He had Type 2 diabetes mellitus and was on oral hypoglycaemic medication with good blood sugar control and no other comorbidities or addictions.

Examination revealed an erythematous plaque like lesion over pubic area involving the base of the penis extending to its shaft and adjacent scrotal skin of around 7 cm × 5 cm with an induration of surrounding skin all around for about 0.5 cm. There was no associated inguinal lymphadenopathy. Rest of external genitalia was normal (Fig. 1). Systemic examination was also normal.

The patient underwent a positron emission tomography (PET) scan and an incisional biopsy of the lesion. The biopsy revealed possibility of EMPD and immunohistochemistry (IHC) evaluation was positive for GCDFP 15, p16, CK-7, GATA 3, and Her 2 favoring the diagnosis of EMPD. PET CT was done to exclude any underlying malignancy. A low grade metabolically (SUV max-3.18, max thickness of 7 mm) inactive mild to minimal skin and subcutaneous thickening at

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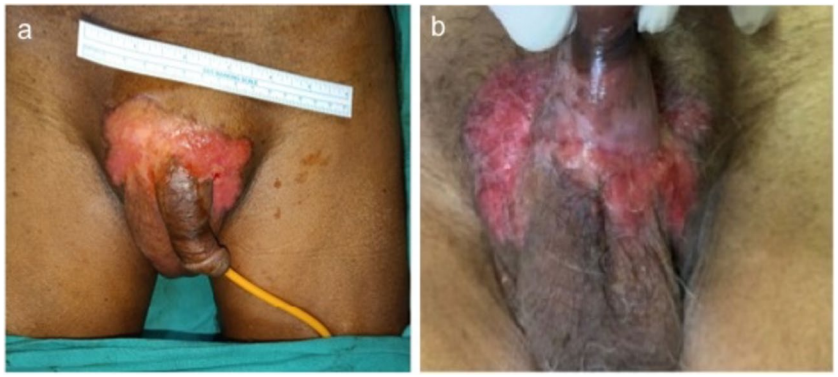

Fig. 1 Clinical photographs of the patient showing the affected region **a** Clinical picture showing the involvement of the scrotum by the disease **b** Clinical picture of the same patient showing circumferential involvement of the root of the penis and scrotum by the disease

pubic area and scrotal wall adjacent to the penis was reported on PET-CT. Low metabolically active (SUV max-4.38) subcentrimetric lymph nodes were seen at bilateral external illac and inguinal region. The rest of the body had normal uptake with no evidence of malignancy elsewhere. To further rule out an underlying malignancy, cystoscopy was performed which did not reveal any abnormality.

Patient was planned for a wide local excision of lesion and left inguinal lymph node dissection. After an en bloc wide excision of the lesion, a pedicled left superficial circumflex iliac perforator flap cover was done with the help of a plastic surgeon to cover the extensive defect after resection (Fig. 2). Intraoperative and postoperative period was uneventful. The final histopathological report with IHC markers

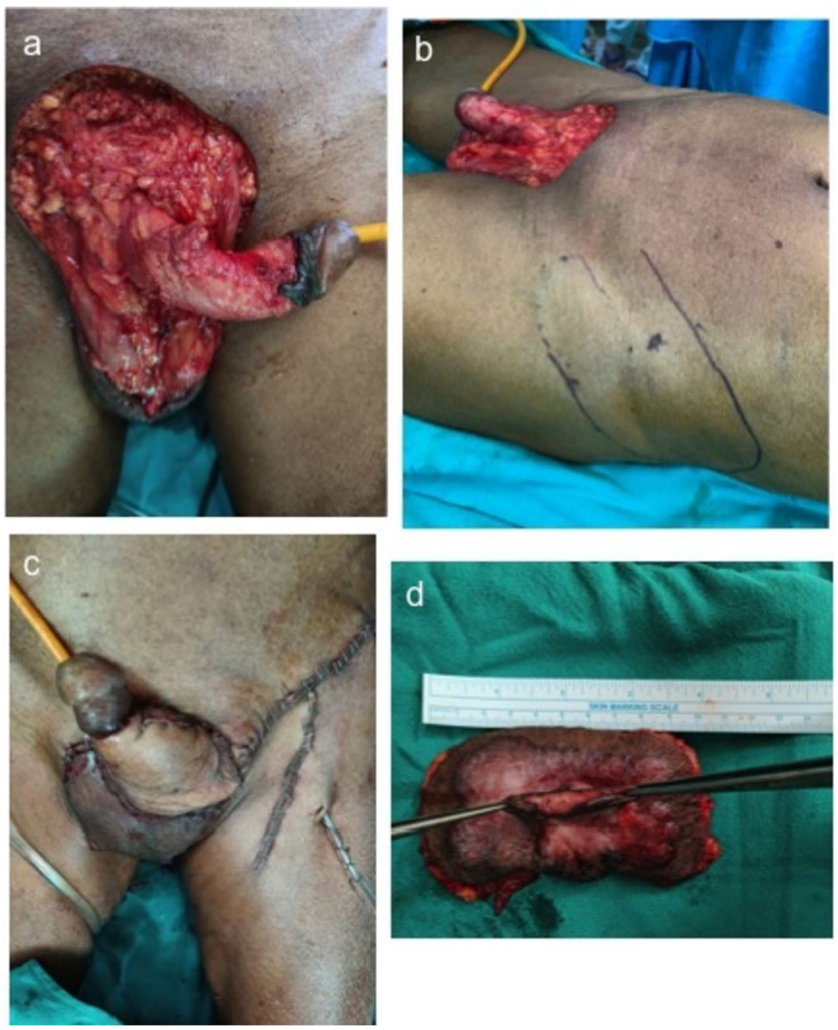

Fig. 2 **a** Enbloc wide local excision of the lesion. **b** A pedicled left superficial circumflex iliac perforator flap cover planned. **c** The surgical defect covered with flap and left inguinal lymph node dissection completed and wound closed over a drain. **d** The excised enbloc specimen

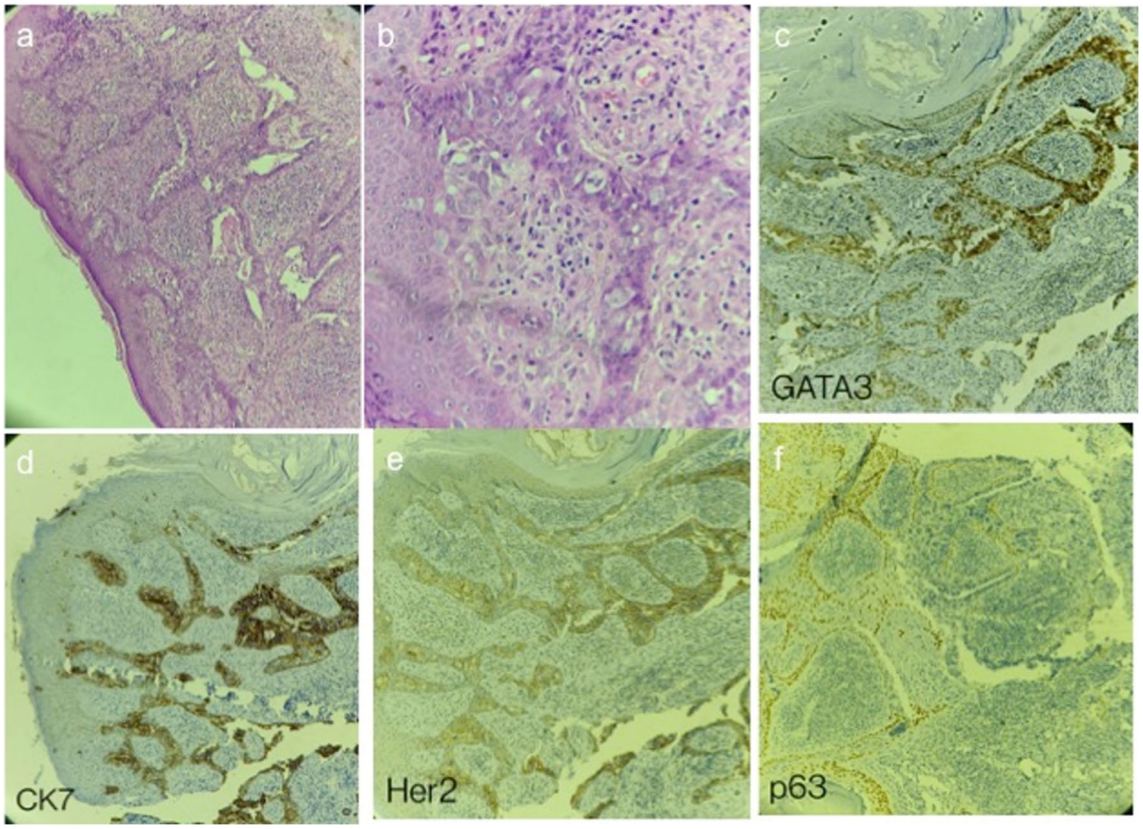

Fig. 3 Hematoxyline and eosin (HE) and immunohistochemistry (IHC) stained photomicrographs of the specimen. **a** HE10x, low power view showing epidermal layer with Paget cells in the basal region. **b** HE40x, high power view shows epidermis permeated by malignant cells arranged singly and in groups. **c** IHC GATA3, low power view shows strong nuclear positivity of GATA3 in Paget cells. **d** IHC CK7, low power view shows diffuse CK7 membranous positivity in the Paget cells. **e** IHC Her2, low power view shows Her2 membranous positivity in the Paget cells. **f** IHC p63, low power view shows nuclear p63 highlighting the squamous epithelial lining. Paget cells are negative for p63

(GCDFP 15 was positive in addition to p16, CK-7, GATA 3, and Her 2, and it is P63 and P40 negative) was suggestive of EMPD with invasion (Fig. 3). The depth of invasion was reported as 0.6 cm without lymphovascular invasion, and all margins were negative. The left inguinal lymph nodes were also uninvolved by the tumor (0/7).

Discussion

EMPD typically presents as non-specific erythematous, erosive, eczematous, or circinate lesions of the skin, and often multiple topical therapies are tried before a diagnosis is made. A median delay of 2 years has been reported since symptoms first appear to the definite diagnosis of the disease.

The precise pathogenesis of EMPD is not yet identified. Current evidence suggests that EMPD is encompassing at least two different forms: primary and secondary EMPD. The origin of primary EMPD is in skin, specifically the epidermis or the underlying apocrine sweat gland. This form, not associated with distant adenocarcinoma, is initially limited to the epithelium, but rarely progress to an invasive tumor, spreading to the dermis, blood, and lymphatic vessels and in advanced stages; it may produce lymph node or visceral, potentially lethal metastases. The secondary form of EMPD is associated with epidermotropic spread of malignant cells from an underlying adenocarcinoma from dermal adnexal glands or within contiguous epithelium, usually of genitourinary or gastrointestinal tract. Published reports suggest that up to 42% of patients have associated underlying malignancy; however, there is a low incidence of internal malignancy with penoscrotal EMPD [2]. Prognosis is good if disease is confined to epidermis and poor with involvement of dermis [3]. A staging system has also been proposed for invasive EMPD and the role of lymph node dissection in clinically node negative (N0) cases is debated. Sentinel lymph node biopsy in invasive EMPD and therapeutic lymph node dissection with adjuvant radiotherapy in node positive cases is being

studied though no consensus has been achieved due to rarity of the disease [4].

A biopsy is essential for diagnosis. Paget cells are recognized by the characteristic round, pale, vacuolated cytoplasm that stains strongly for mucin, with a large reticular nucleus located within the epidermis. The epidermis can be hyperplastic with overlying hyperkeratosis and parakeratosis. IHC examination is very important to the differential diagnoses with Bowen's disease, amelanotic superficial spreading melanoma and to determine whether it is a primary or secondary disease. Cutaneous melanoma expresses Melan A, S100 and HMB45 but not the other antibodies, while Bowen's disease expresses AE1AE3, p63, and eventually CK7. The IHC marker GCDFP-15 (or BRST2) is expressed in 50% of cases of primary EMPD, and it is negative in secondary types [5]; CK7 and Her-2 are considered specific and sensitive for Paget's disease [6] (Fig. 3).

Conclusion

EMPD of the penis and scrotum is a rare presentation mostly seen in elderly and can be treated by wide excision and flap coverage if defect is large and inguinal lymph node dissection if nodes are involved. Prognosis is good if it only involves epidermis.

Data Availability Data is regarding our patient and is available with us.

Declarations

Competing Interests The authors declare no competing interests.

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