CASE REPORT

Extramammary Paget's Disease of the Perianal Region

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Abstract Extramammary Paget's disease (EMPD) is uncommon and only a few cases have been reported in the literature. They are identical to the Mammary Paget's disease. This can occur where the apocrine glands are in abundance, more commonly in the genitalia and perianal area. We report here a case of Extramammary Paget's disease in the perianal region. The colourful background of this ulcer is analysed and the literature reviewed.

Keywords Ulcer · Extramammary · Paget's disease · Perianal

Case Report

An 86-year-old man presented with a non-healing itchy ulcer in the perianal region for 8 months, which was treated as a fungal ulcer without improvement. He gave history of tuberculous fistulae in ano treated successfully about 40 years ago. On examination, he had a large irregular ulcer in the perianal region measuring about 5 × 4 cm, on the right side extending from 6 to 11 o'clock positions (Fig. 1a), with indurated edges. The wedge biopsy of the ulcer edge showed Paget's tumour cells in the basal layer of the epidermis with clear eosinophilic cytoplasm, large pleomorphic nuclei and mitosis and was re-

ported as Extramammary Paget's disease (EMPD) (Fig. 2). A complete excision was done with clinical free margins, and the defect was closed using local skin flaps by multiple Z plasties (Fig. 1b). The final histopathology confirmed the diagnosis with lesion at its edges. During the preoperative workup, he was found to have raised prostate-specific antigen (PSA) levels (26 ng/ml), and his ultrasound revealed a nodule in the right lobe of the prostate. Since he was complaining of severe backache radiating down his lower limbs, X-rays were taken which showed diffuse sclerosis with coarse trabeculations of L5 vertebral body and posterior elements, sacrum, ischium, pubis and iliac bones suggesting osteoblastic metastases. A 68Ga prostate-specific membrane antigen (PSMA) PET CT scan was performed which revealed a normal-sized prostate with focal T2 hypodense lesion in the right lobe with increased uptake. It also showed multiple discrete and diffuse sclerotic lesions in all vertebrae, pelvic bones, femora, sternum, few ribs on both sides and right scapula with increased uptake, which were highly suggestive of prostatic carcinoma with multiple skeletal metastases. A transrectal biopsy of prostatic nodule revealed it to be an adenocarcinoma. With the diagnosis of metastatic prostatic carcinoma, he was advised bicalutamide, denosumab and goserelin acetate, and three courses were administered at monthly intervals. After the first course, he improved dramatically from the backache, and after three courses, his PSA dropped (0.44 ng/ml). Since he could not afford, he was advised bicalutamide, zoledronic acid and goserelin acetate, and two further courses were administered. At the end of four courses, the PSA has further dropped (0.19 ng/ml). After the third course, small ulcers were found in the perianal region near the operative scar (Fig. 1c). Imiquimod ointment was applied thrice a week, and subsequently, the ulcers started healing well (Fig. 1d). The chemotherapy is still on at monthly intervals, and the patient is keeping good health.

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Fig. 1 Extramammary Paget's disease. **a** Preoperative appearance. **b** Excision and reconstruction. **c** Recurrence of ulcer (*red arrow*). **d** Improvement after imiquimod therapy (*yellow arrow*)

Fig. 2 Histopathology (HP) and immunohistochemistry (IHC). Paget's cells (*yellow arrows*); abnormal mitosis (*red arrows*)

Discussion

Mammary Paget's disease (MPD) of the nipple was first described by Sir James Paget in 1874 [1] and the Extramammary Paget's disease (EMPD) was described on the penis and scrotum by Radcliffe Crocker in 1889. Morphologically and histologically, they are identical, but only the site of occurrence differs.

EMPD is a rare malignancy of unknown aetiology. It commonly appears in middle-aged women, thrice predominant over men. Its course may extend over 10–15 years without evidence of any malignancy or its spread. Dermal invasion and lymph nodal involvement are poor indicators.

EMPD targets the genital and perianal skin and other sites in the skin rich in apocrine glands. EMPD arises as a primary cutaneous adenocarcinoma in most cases, where the epidermis gets infiltrated with neoplastic cells with glandular differentiation. In a quarter of cases, it is associated with an underlying in situ or invasive apocrine carcinoma, probably due to infiltration of the deeper adnexa by epidermal Paget cells. EMPD is associated with other malignancies like those of urethra, urinary bladder, vagina, cervix, endometrium and prostate, very rarely the axilla, buttocks, thighs, eyelids and external auditory canal [2], and perianal EMPD is associated with colorectal carcinoma in 25–35% patients. There is no evidence to support the link between the distant tumours and the cutaneous EMPD.

Clinically, it appears like an eczematous lesion, starting with erythema, crusting and increased maceration, with pruritus, leading to excoriations and lichenification. Pain and bleeding also occur.

Skin lesions like basal cell carcinoma, Bowen's disease, cutaneous candidiasis, intertrigo, irritant contact dermatitis, lichen simplex, psoriasis and tinea cruris are differential diagnosis.

The diagnosis of EMPD requires a high degree of clinical suspicion and histopathological and immunohistochemical diagnosis. The marker BerEp4 has been proposed as a useful marker, which is positive in 100% of cases of EMPD. GCDFP15 (BRST2) and CK20 differentiate secondary from primary Paget's disease. Cytokeratins CK7, CK20 and Ki67 are positive in urothelial malignancies.

Though optimal treatment of EMPD is controversial, wide surgical excision of all the involved epidermis using

transverse and vertical frozen sections, with 2-cm clear margins and reconstruction with local skin flaps is considered effective. Recurrence varies between 30 and 60% and Mohs micrographic surgery offers lower recurrence rates to 25% [3]. Some describe successful treatment with topical 5-fluorouracil [4], 5% imiquimod cream applied thrice a week for 16 weeks [5] and a combination of paclitaxel and trastuzumab [6]. Radiotherapy is indicated in unfit patients and for recurrent or residual disease. Systemic chemotherapy (mitomycin and 5-fluorouracil (5-FU) and carboplatin and 5-FU) and photodynamic therapy using tumour-localizing photoreactive drug-like aminolevulinic acid with appropriate wavelength light to destroy the cells [7] are useful.

Once the diagnosis of EMPD is made, an extensive workup is essential to rule out an underlying or associated malignancy, before therapy is started.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

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