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Primary perianal extramammary Paget's disease: Case report with review

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Abstract

Extramammary Paget's disease (EMPD) is a rare cancer which involves the skin and apocrine glands. It involves the vulva, perianal region, scrotum, penis and axilla. Primary disease originates from intraepidermal cells and secondary originates from underlying neoplasm. The disease presents with thickened plaque like lesion with erythema or white scaly appearance. The cancers of urinary tract like the bladder, urethra and prostrate are associated with EPMD involving the genitalia and rectal tumours are associated with perianal disease. The disease affects females more than males with the median age being 72 years. Primary perianal EMPD is even rare in presentation. It is a slow growing tumour and the prognosis is usually favourable other than advanced stage and old age. The surgical resection with clear margins is considered to be the standard of care and provides good outcomes. However, if surgery is not feasible other treatment options like imiquimod 5% topical cream and radiation therapy may be offered. We present a young male with perianal EMPD who was managed with surgical resection with clear margins with split skin graft leading to a favourable outcome.

Keywords: Perianal Paget's disease; Surgical resection; Clear margins; Skin grafting

1. Case report

A 39 year old male was referred to us with a history of a perianal non healing lesion since 3 years. It started as a small patch and was managed by dermatologists and surgeon elsewhere as fissure in ano, eczema, fungal infection etc. It had increased in size and involved both sides of the perineal lesion. The patient had pruritus with mild pain in the perianal area with the skin having a leathery feel (Fig. 1). There was no discharge and there was no history of constipation, or any problems in continence. There was no bleeding per rectum. The patient consumed alcohol occasionally and he was not a smoker. General physical examination was normal without any peripheral lymphadenopathy. On perianal examination there was a thickened plaque like area in the perineal region which involved left side more than the right as like a butterfly sparing the external anal opening. On per rectal examination the resting anal tone, squeeze was normal. Colonoscopy was performed till ileocaecal junction and was normal. An ultrasound examination of abdomen was normal and it did not reveal any lymph nodes in the inguinal region.

There was a clinical suspicion of EMPD or a non healing ulcer. We performed a punch biopsy which was suggestive of primary perianal EMPD. The patient was counselled for a sphincter saving surgical resection with per operative frozen section for the margin status (Figs. 2 and 3). The frozen section revealed clear margins and intraepidermal disease. Split thickness skin graft was taken from the thigh and applied with pressure at the perianal area (Fig. 4). The post operative period was uneventful and the patient had around 40% graft uptake. The final histopathology confirmed primary perianal EMPD with

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negative margins confirmed on immunohistochemistry as CK 7 and GCCDFP-15 positive (Fig. 5).

The patient is doing well and is completely relieved of his symptoms. There is no evidence of any residual disease or recurrence on more than 2 years of follow up which includes clinical examination and short colonoscopy on an annual basis (Fig 6)

2. Discussion

EMPD was first described by Crocker as a rare disease of scrotum and penis (Crocker, 1889). Darier and Coulillaud first reported perianal Paget's disease (Darier and Coulillaud, 1893). Perianal EMPD is a rare disease as published in experience of high volume centres. Disease presents in elderly patients with a mean age of 60 years. In contrast our patient is a young male (Rajendran et al., 2014; Isik et al., 2016; Perez et al., 2014). Because of its rarity the disease is often misdiagnosed. The patients usually present late after multiple treatment protocols by various clinicians. Presentation includes single or multifocal lesions that are dry, erythematous area which gradually progress to eczematoid, crusted, ulcerated or papillary lesions. Pruritus may precede these skin lesions (Rao and Henry, 2004). It has to be differentiated from superficial spreading melanoma, Bowen's disease, neuroendocrine carcinoma, mycosis fungoides, psoriasis, leucoplakia, eczema and fungal infection (Jones et al., 1979). Another differential diagnosis is pagetoid effect which is intra epidermal spread of visceral carcinoma (Minicozzi et al., 2010). The disease which involves the vulva, perianal region, scrotum, penis and axilla may be primary if it arises from the skin or secondary in case arising from an underlying neoplasm, which is reported in 24% of patients with a worse prognosis (Chanda, 1985). Rectal adenocarcinoma involving the perianal area or the tumour of urinary tract involving the genitalia is usually associated.

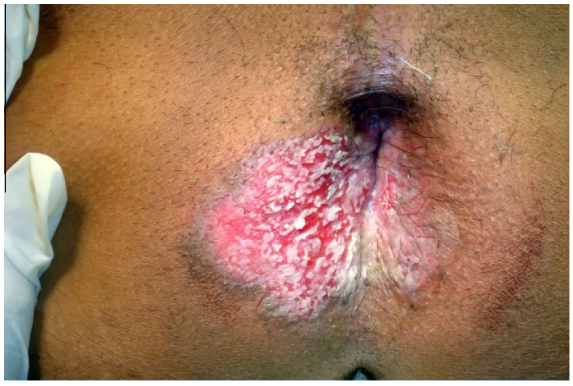

Figure 1. Perianal Paget's disease.

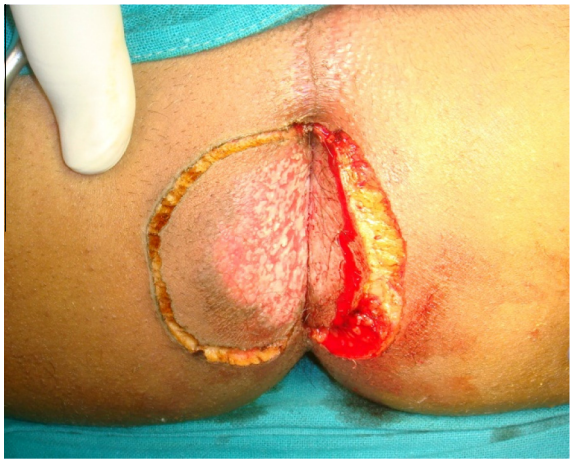

Figure 2. Excision of involved perianal skin.

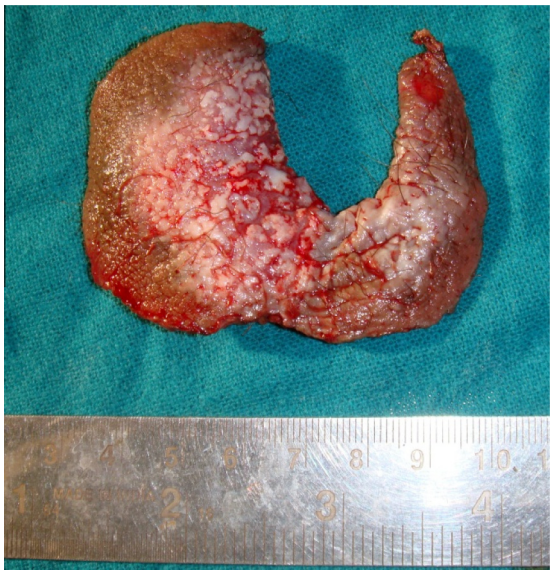

Figure 3. Excised Skin of paget's disease.

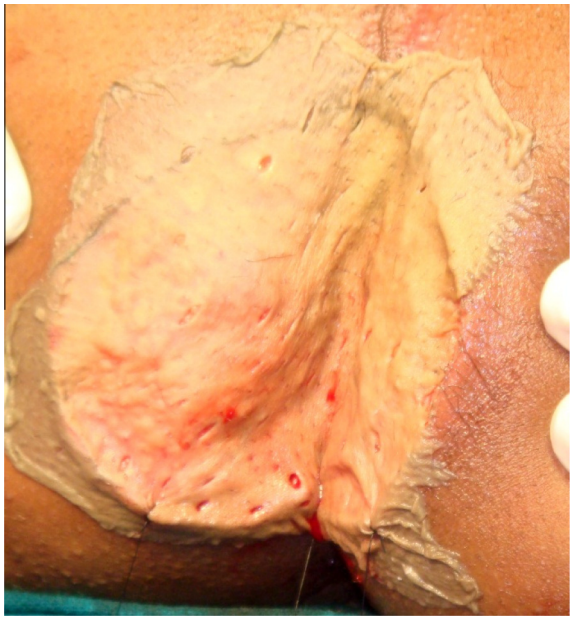

Figure 4. Skin grafting over raw wound.

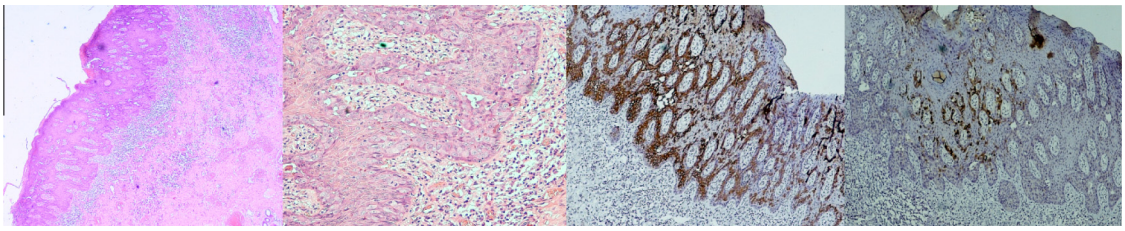

Figure 5. Histological features of excised specimen.

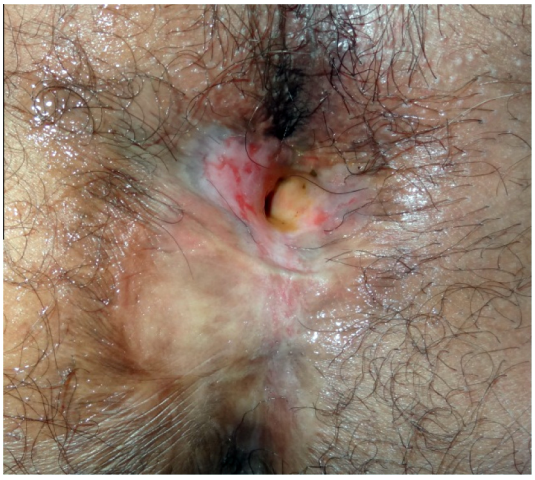

Figure 6. Healed scar after 2 years follow-up.

Surgical resection is the standard of care which involves wide local resection margins and reconstruction with skin or muscle flaps. But, the disease may extend to areas beyond the visible margins and are a common cause of recurrence. Moh's microscopic technique to evaluate the specimen margins has reduced the recurrence as compared to the wide surgical resection alone. This includes removal of tumour, review of margins under microscope by surgeon, tumour mapping and resection of positive margins, potentially sparing the normal tissue while achieving the complete tumour resection (Drake et al., 1995). This technique may be cumbersome and Yang et al. reported an intraoperative frozen section biopsy which reduces the positive margins and rate of recurrence (Yang et al., 2005). This surgical resection with intraoperative frozen section biopsy evaluating the margins and depth of the specimen histologically was followed in our case with good results. Other modalities like abdominoperineal resection with or without inguinal lymph node dissection, chemotherapy, radiotherapy and local palliative management have been described based on the stage of the disease (Shutze and Gleysteen, 1990).

Topical treatment with Imiquimod 5% applications has been used for the treatment of EMPD. This is supposed to be immune modulating in action affecting the T cell lymphocytes. The treatment involves thrice weekly application for 6–16 weeks. The results have been variable. Side effects like local irritation, erosions, ulcer, pain and general myalgia, fatigue and headache have been reported. The topical imiquimod treatment may be offered to patients not undergoing surgery due to various reasons (Dias et al., 2010).

Several investigators have made a strong case for the use of primary radiotherapy for curative intent in patients not considered suitable for surgery, and for the use of postoperative radiotherapy after resection (Brown et al., 2002). Photodynamic therapy, topical % fluorouracil, topical bleomycin, CO_2 laser, and docetaxel have been described as other treatment options but lack consistency.

Histologically, the Paget cells appear as large, pale, vacuolated cells with vesicular nuclei and prominent nucleoli. A cleft-like separation is often seen between the Paget cells and the adjacent non-neoplastic keratinocytes. The Paget cells may be single or arranged in rows or small nests, concentrated above the basal layer of the epidermis. They may also extend to the epithelium of adnexal structures. Dermal invasion is seen in small proportion of cases and implies a poor prognosis (Jones et al., 1979). In immunohistochemistry, the Paget cells frequently show positive reactivity to epithelial membrane antigen, CEA, gross cystic disease fluid protein, and low molecular weight cytokeratins. Primary disease is usually CK7 positive and CK20 negative whereas secondary associated with urothelial carcinoma is usually CK7 and CK20 positive (Brown et al., 2002). CK7 (cytokeratin 7) is a simple keratin that has a restricted distribution in many simple, pseudostratified, and ductal epithelia and mesothelia. The lack or extreme paucity of CK7 distribution in tissues such as colonic epithelium is used to diagnostic advantage. The restricted topography of CK7 makes it especially useful in evaluating the origin of adenocarcinomas because this keratin is present in most breast, lung, ovarian, pancreaticobiliary, and transitional cell carcinomas, but it is either absent or present in only rare cells in colorectal, renal, and prostatic carcinomas (Bhargava et al., 2010). GCDFP-15 (Gross cystic fluid protein 15) is recognized as a specific marker for breast carcinomas (primary and metastatic); thus, one should use good judgement in situations in which a carcinoma of breast origin is suspected (Chivukula, 2010).

Hence, EMPD is a rare disease where limited knowledge is available for diagnosis and management. Even rare are the primary perianal EMPD. The standard treatment remains surgical resection with negative margins. This offers best results although recurrence is common. Wide

local surgical resection was done in our case with intra-operative histological assessment of the margins by frozen section and reconstruction achieving good results. Other treatment modalities like topical creams, radiation and photodynamic therapy require more research to be used as primary modality for treatment and the results lack consistency.

Conflict of interest

None.

References

Bhargava, R., Dabbs, D.J., 2010. In chapter Immunohistology of metastatic carcinomas of unknown primary. In: Dabbs, David J. (Ed.), Diagnostic Immunohistochemistry: Theranostic and Genomic Applications, 3rd ed. Saunders, Elsevier Inc., p. 212.

Brown, R.S., Lankester, K.J., McCormack, M., Power, D.A., Spittle, M. F., 2002. Radiotherapy for perianal Paget's disease. Clin. Oncol. (R. Coll. Radiol.) 14, 272–284.

Chanda, J.J., 1985. Extramammary Paget's disease: prognosis and relationship to internal malignancy. J. Am. Acad. Dermatol. 13, 1009–1014.

Chivukula, M., 2010. In chapter Immunocytology. In: Dabbs, David J. (Ed.), Diagnostic Immunohistochemistry: Theranostic and Genomic Applications, 3rd ed. Saunders, Elsevier Inc., p. 902.

Crocker, H.R., 1889. Paget's disease affecting the scrotum and the penis. Trans. Pathol. Soc. Lond. 40, 187–191.

Darier, J., Coulillaud, P., 1893. Concerning a case of Paget disease of the perineal and scrotal area [French]. Ann. Dermatol. Syphiligr. (Paris) 4, 25–33.

Dias, C.J., Vale, E., Viana, I., Martins, O., 2010. Treatment of primary extramammary Paget's disease of perineum with topical imiquimod 5% cream. Eur. J. Dermatol. 20, 532–533.

Drake, L.A., Dinehart, S.M., Goltz, R.W., et al., 1995. Guidelines of care for Mohs micrographic surgery. Am. Acad. Dermatol. J. Am. Acad. Dermatol. 33, 271–278.

Isik, O., Aytac, E., Brainard, J., Valente, M.A., Abbas, M.A., Gorgun, E., 2016. Perianal Paget's disease: three decades experience of a single institution. Int. J. Colorectal Dis. 31 (1), 29–34.

Jones Jr., R.E., Austin, C., Ackerman, A.B., 1979. Extramammary Paget's disease. A critical reexamination. Am. J. Dermatopathol. 1, 101–132.

Minicozzi, A., Borzellino, G., Momo, R., Steccanella, F., Pitoni, F., de Manzoni, G., 2010. Perianal Paget's disease: presentation of six cases and literature review. Int. J. Colorectal Dis. 25, 1–7.

Perez, D.R., Trakarnsanga, A., Shia, J., Nash, G.M., Temple, L.K., Paty, P.B., Guillem, J.G., Garcia-Aguilar, J., Weiser, M.R., 2014. Management and outcome of perianal Paget's disease: a 6-decade institutional experience. Dis. Colon Rectum 57 (6), 747–751.

Rajendran, S., Koh, C.E., Solomon, M.J., 2014. Extramammary Paget's disease of the perianal region: a 20-year experience. ANZ J. Surg.

Rao, V.R., Henry, D.H., 2004. Extramammary Paget's disease. Commun. Oncol. 1, 109–115.

Shutze, W.P., Gleysteen, J.J., 1990. Perianal Paget's disease. Classification and review of management: report of two cases. Dis. Colon Rectum 33, 502–507.

Yang, W.J., Kim, D.S., Im, Y.J., Cho, K.S., Rha, K.H., Cho, N.H., et al., 2005. Extramammary Paget's disease of penis and scrotum. Urology 65, 972–975.