Extramammary Paget disease: five perianal case report and treatment options

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INTRODUCTION

Extramammary Paget disease (EMPD) is a rare tumor [1]. PPD is one of the rarer subset of EMPD [2, 3], and classified into two categories according to its source, respectively derives from the perianal intraepidermal stem cells and potential malignancies outside the perianal region [4]. The most frequent manifestations are similar to chronic perianal eczema, which can lead to misdiagnosis and worsen the prognosis of patients [5].

Histopathology is the gold standard to confirm correct diagnosis of PPD with the findings of Paget cells containing pale clear cytoplasm, large circles of hyperchromatic nuclei and clusters in the tissue [5].

CASE REPORT

Case 1

A 61 years old female underwent Milligant-Morgant hemorrhoidectomy due to anal itching and stinging sensation, which did not disappear after applying budesonide cream for 3 months. Postoperative pathology coincidentally found Paget cells (Fig. 1B). A 3 × 4 cm oval erythematous perianal skin lesion with pale secretions and surgical wound was noted (Fig. 1A).

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Figure 1: (A) Case 1: (a) oval erythematous perianal skin lesion with pale secretions, brownish pigmentation and surgical wound; (b) scout line determined by negative macroscopic margins > 1 cm (black); (c) wide excision with sphincter preservation; (d) surgical specimen; (e) skin flap transfer surgery; (f) Type S sutures the skin wound between the flaps after completion of surgery; (g) the incision was basically healed and the mucosa was slightly everted on postoperative Day 60. (B) HE stain and IHC in case 1. (a) Low and Higher power view show clusters of Paget cells with pleomorphic nuclei and pale cytoplasm in the epidermis (Inset HE × 200). (b) Paget cells showing strong immunoreactivity for CK7.

Figure 2: (A) Case 2: (a) well-defined pink butterfly-like patches interspersed with white secretions above the surrounding skin, and its size was 4 × 5 cm; (b) surgical specimen; (c) mapping of the incision for skin flap; (d) after completion of the wide local excision of PPD plus skin flap transfer surgery; (e) the incision was basically healed, nevertheless the reconstructed anal is relatively narrow on postoperative Day 60. (B) HE stain and IHC in Case 2; (a) clusters of cells with pleomorphic nuclei and pale cytoplasm in the epidermis (inset HE × 200); (b) Paget cells showing strong immunoreactivity for CK5/6.

4 × 5 cm (Fig. 2A). PPD was diagnosed with to use of phosphorus epithelial cell carcinoma antigen (Fig. 2B).

WLE was performed with negative macroscopic margins of 2 cm to ensure no residual tumor. Mapping the incision of the skin flap was performed, and each flap like a triangle and radially distributed around the defect, which was 1-2 cm thick. Full-thickness suture among the flaps for anal reconstruction were performed. The pathology reported an affected area of 3.5 cm × 4.3 cm and negative resection margins. On postoperative Day 60, the reconstructed anus was found to be relatively stenosed, therefore digital dilatation of the anus was performed once a day until defeation was more easily possible. There has been no evidence of recurrence for 2 years.

Case 3

A 68 years old man was aware of perianal skin induration without pain for 3 years. A reddish oval skin lesion 4 cm in diameter was removed with WLE of PPD plus skin flap transfer (Fig. 3A). PPD was diagnosed with a biopsy, although the margins of the perianal skin incisions at 3, 6, 9 and 12 points at lithotomy were negative in the intraoperative frozen specimens. However postoperative pathological diagnosis found mucinous adenocarcinoma cells in the center of specimens and the anal canal incision edge, furthermore, Paget cells were found in the epidermis of perianal skin (Fig. 3B). Miles surgery was performed under general anesthesia. Negative margins were achieved and no tumor recurrence or metastasis was found after one and a half years of follow-up.
Figure 3: (A) Case 3: (a and b) skin induration around the anus, and scout line determined by negative macroscopic margins > 1 cm; (c) wide excision with sphincter preservation; (d) surgical specimen; (e) after completion of Miles surgery; (f and g) the incision was basically healed on postoperative Day 60. (B) Pathological findings of PPD and mucinous adenocarcinoma: mucinous adenocarcinoma cells with a lot of mucus and pleomorphic nuclei in the center of picture, Paget cell with pleomorphic nuclei and pale cytoplasm.

Figure 4: (A) Case 4: (a) clinical findings: a bleeding lump prolapsed out of anus, abnormal skin lesions around it; (b) after completion of the wide local excision of PPD plus skin flap transfer surgery; (c) the incision was basically healed on postoperative Day 60. (B) Pathological findings of PPD and tubular adenocarcinoma: Paget cell with pleomorphic nuclei and pale cytoplasm, and tubular adenocarcinoma with branched conduits.

Figure 5: (A) Case 5: (a) examination of perineal regions with well-defined irregular infiltrating erythema easy to notice; (b) perianal local skin lesions were improved after 30 radiotherapy sessions. (B) Pathological findings of PPD in left inguinal lymph node: Paget cell with pleomorphic nuclei and pale cytoplasm.

Case 4
A 78 years old man had a 6 months history of painless and bleeding lump prolapsing on defecation, along with pruritus of some abnormal skin lesions (Fig. 4A). Like Case 1, the patient underwent a hemorrhoidectomy. However, two kinds of tumor cells were found like Case 3, tubular adenocarcinoma of rectum and PPD (Fig. 4B). The patient refused Miles operation and accepted WLE of PPD plus skin flap transfer. The incision of the flap transfer was basically healed at 2 months after the second operation. Unfortunately, the patient died of recurrent tubular adenocarcinoma with metastasis 1 year after the surgery.

Case 5
A 67 years old woman with perianal mass for 8 years and perianal skin ulcer with pain for 6 months came to our hospital. Condyloma acuminata was excluded previously, and Paget disease was diagnosed by biopsy. The well-defined erythema surrounding the anus was \(7 \times 8\) cm in size with surface erosion, scab and impaired the last third of the labia majora (Fig. 5A). Serum tumor markers CEA and CA-199 were elevated. CT found bilateral inguinal lymph node enlargement. Positron emission tomography with computed tomography showed abnormal focal hypermetabolism of perianal skin and bilateral inguinal lymph nodes. A biopsy of left inguinal lymph node revealed metastatic adenocarcinoma (Fig. 5B). The patient refused surgery and decided to seek radiotherapy. After 30 radiotherapy sessions lasting 6 months and a total radiation dose 60 Gy, perianal local symptoms and skin lesions improved significantly. However the patient died of metastasis a year later.

DISCUSSION
WLE of PPD is a feasible option [6]. But, the circumferential skin defect leads to anal stricture and esthetic dissatisfaction [7]. Therefore, WLE plus skin flap transfer may be a better choice [8]. In our five cases followed up by telephone, three patients accepted WLE plus skin flap transfer without recurrence, and two patients eventually died after they did not completely accept our treatment.

Paget cells can metastasize horizontally or vertically [9]. Negative macroscopic margins > 1 cm with sphincter retention are
associated with a higher survival rate than local excision [10].
The extent of anal resection contains dentine line [11]. The
absent anorectal transitional epithelium is replaced by rectum
mucosa. Wide perianal soft tissue defect requires bilateral skin
flap transfer surgery and anal reconstruction. Patients with PPD
combined with other adjacent intestinal malignant tumors may
require Miles surgery.

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CONFLICT OF INTEREST STATEMENT
Heng Deng and Xiaoli Fang equally contributed to this work.
There is no conflict of interest between the authors.

ETHICS APPROVAL STATEMENT
Ethical approval to report this case was obtained from The Ethics
Committee of the Second Affiliated Hospital of Anhui University
of Chinese Medicine (APPROVAL NUMBER 20080885QH388-01.

PATIENT CONSENT FOR PUBLICATION
STATEMENT
For their anonymized information to be published in this article,
written informed consent was obtained retrospectively from the
patients and legally authorized representatives when the patient
has died.

REFERENCES
1. Konstantinova AM, Kazakov DV. Extramammary Paget dis-
ease of the vulva. Semin Diagn Pathol 2020;38:50687.
2. Nasioudis D, Bhadra M, Ko EM. Extramammary Paget dis-
ease of the vulva: Management and prognosis. Gynecol Oncol
2020;157:146–50.
3. Knight SR, Proby C, Ziyaie D, Carey F, Koch S. Extramammary
Paget disease of the perianal region: the potential role of
imiquimod in achieving disease control. J Surg Case Rep
2016;8:trjw110.
4. Fusumae T, Fukuda K, Hirai I, Nakamura Y, Tanese K, Iwata
T, et al. Outcomes in patients with extramammary Paget
disease with brain metastasis: A retrospective analysis. J Am
Acad Dermatol 2020;83:1832–4.
5. Garganese G, Inzani F, Mantovani G, Santoro A, Valente M,
Babini G, et al. The vulvar immunohistochemical panel (VIP)
project: molecular profiles of vulvar Paget's disease. J Cancer
Res Clin Oncol 2019;145:2211–25.
6. Pittman ME, Milsom J, Yantiss RK. Treatment effects can
mimic recurrent extramammary Paget disease in perianal
skin. Am J Surg Pathol 2018;42:1472–9.
7. Sapci I, Tiernan J, Gurunian R, Gorgun E. Wide local excision
of perianal Paget disease with split-thickness skin grafting.
Dis Colon Rectum 2020;63:406–7.
8. Park YY, Kim M, Cheong C, Kim SK, Song SY, Chung KY, et al.
Perianal Paget disease: a report of 2 cases. Ann Surg Treat Res
2017;93:336–41.
9. Morris CR, Hurst EA. Extramammary Paget disease: a review
of the literature-part I: history, epidemiology, pathogenesis,
presentation, histopathology, and diagnostic work-up. Der-
motol Surg 2020;46:151–8.
10. Kakinuma H, Iwasawa U, Kurakata N, Suzuki H. A case of
extramammary Paget's disease with depigmented macules
as the sole manifestation. Br J Dermatol 1994;130:102–5.
11. Tsuji T. Mammary and extramammary Paget's disease:
expression of Ca 15-3, Ka-93, Ca 19-9 and CD44 in Paget cells
and adjacent normal skin. Br J Dermatol 1995;132:7–13.