Laparoscopic extralevator abdominoperineal excision for the treatment of perianal Paget’s disease
A case report

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Abstract

Rationale: Perianal Paget’s disease (PPD) is a very rare intraepithelial adenocarcinoma. Very few cases of PPD have been reported till date, so the treatment remains controversial and more experience is needed.

Patient concerns: A 73-year-old female was admitted to several hospitals with diagnosed as “perianal eczema” in perianal lesion. After a variety of treatments, the patient’s condition did not improve.

Diagnoses: Abdominopelvic computed tomography and rectal magnetic resonance imaging showed thickening of the soft tissue around the anus, with significant enhancement. Histologic examination revealed the state of Paget’s cells.

Interventions: Laparoscopic Extralevator Abdominoperineal Excision (ELAPE) surgery was performed at our department.

Outcomes: The patient recovered well. After 10 months, a check-up revealed that her perianal area was disease-free.

Lessons: The aim of this report was to present the characteristics of PPD in order to improve its diagnosis and treatment. Laparoscopic ELAPE is a successful therapy.

Abbreviations: ELAPE = extralevator abdominoperineal excision, EMPD = extramammary Paget’s disease, LN = lymph node, MMS = Mohs micrographic surgery, MPD = mammary Paget’s disease, PDT = photodynamic therapy, PPD = perianal Paget’s disease.

Keywords: diagnosis, laparoscopic extralevator abdominoperineal excision, perianal Paget’s disease, surgery, treatment

1. Introduction

Paget’s diseases are divided into mammary Paget’s disease (MPD) and extramammary Paget’s disease (EMPD).[1] In 1874, Sir James Paget first reported Paget’s disease.[2] After 19 years, Darier and Couillaud reported about perianal Paget’s disease (PPD).[3] PPD is a subgroup of EMPD, which is an intraepithelial adenocarcinoma.[4] EMPD is rare,[5] and the incidence of PPD is even lower than EMPD.[6] The clinicopathological mechanism of the disease remains unclear. It is difficult to diagnose this disease, and the final diagnosis is based on biopsy and immunohistochemistry. Very few cases of PPD have been reported till date, so the treatment remains controversial and more experience is needed. Herein, we reported a case at our hospital, which will help to accurately diagnose and treat PPD.

2. Case report

2.1. Patient

A 73-year-old female Chinese patient had onset of a pruritic perianal lesion, without pain or bleeding. Due to its mild symptoms and similarity to hemorrhoids, it was left untreated. In the past 2 years, the perianal itch had exacerbated, accompanied by mild pain. The disease was treated as perianal eczema, but the clinical symptoms did not disappear. In October 2017, the patient visited our department for further treatment. Local examination revealed an erythematous skin lesion in the perianal area with surrounding lichenification, measuring about 6 cm × 8 cm. There were few 2 cm × 1 cm external hemorrhoids protruding from the anus (Fig. 1). There were no positive characteristics on abdominopelvic ultrasound, except for a gall bladder polyp. Abdominopelvic computed tomography and rectal magnetic resonance imaging showed thickening of the soft tissue around the anus with significant enhancement, which measured about 3.05 cm. Intraluminal normality was inspected by colonoscopy. Histology examination revealed the state of Paget’s cells (Fig. 2A). The immunohistochemistry was CK7+, CK20+,...
KI67+, CEA+, EMA+, HER-2(0), S100-, and HMB-. According to the results of abdominopelvic computed tomography and rectal magnetic resonance imaging, the patient was in stage II. She was diagnosed with hypertension, multiple lacunar infarction, carotid atherosclerosis, cerebral insufficiency, brain atrophy, mild fatty liver, hypertriglyceridemia, gallbladder polyps, severe osteoporosis, etc at our cardiology department 3 months ago.

2.2. Surgery

Given the patient’s condition, laparoscopic ELAPE surgery was conducted. The patient was treated with routine bowel preparation for 3 days and polyethylene glycol clysis for 1 day. The patient was placed in a jack-knife position (Fig. 3A). The anus was closed, then a spindle incision was made 1.5 cm outside the lesion area. The diseased tissue was separated upward along the gap between the external anal sphincter, the lateral levator ani muscle and the surrounding fat until it reached the starting point of the obturator fascia anal muscle, then the levator ani muscle was completely removed. In this process, it needed to be separated to the posterior rectal space at the rear (Fig. 3B), separated to the starting point of levator ani muscle and the pelvic floor peritoneum at the lateral side (Fig. 3C), and separated to the lower part of the cervix in front (Fig. 3D). Then we wrapped the anal canal and inserted it into the pelvis with latex glove. Next, a drainage tube was placed and the incision was sutured (Fig. 3E).

The rectal blood vessels were dissected and the local lymph nodes were removed under laparoscopy, and the rectum was separated in the direction of the pelvic floor, then we cut the peritoneum of the pelvic floor to meet the perineal operation plane, so that the rectum was completely dissociated (Fig. 3F).
Finally, the rectum was removed and the abdominal wall ostomy was completed with a circular stapler (Fig. 3G).

The total operation duration was 4 h and the estimated blood loss was 20 mL. No special complications occurred in the recovery room.

**2.3. Postoperative course**

The patient recovered well post-operation. She was given nutrition via an internal jugular vein injection, and received anti-infection treatment. There was a little exhaust in fistula on the third day post-surgery, and the patient drank a small volume
of water without further discomfort. On the fourth day, she drank a modicum of soup without adverse reaction. The drain was removed on the seventh day. The wound healed well, and excretory function was normal on the eighth day. She was discharged on the tenth day.

3. Discussion

3.1. Incidence

The true incidence of EMPD remains unknown, although it is believed to be relatively rare. The incidence of PPD is only 4.3% of that of EMPD. The Chinese are rarely affected by PPD.

3.2. Clinicopathological mechanism

The clinicopathological mechanism of the disease has not been clearly demonstrated. According to Helwing and Graham's follow-up study, 20 out of 38 patients had primary tumor, which indicates the relevance between PPD and regional cancer, or subjacent underlying glandular adnexal carcinomas. Hence, PPD was considered to be a manifestation of an unknown carcinogenic stimulus on apocrine structures, epidermis and glandular elements of the rectum and urethra. Commonly used immune markers include CK7, CK20, GCDFP-15, HMB45, CAM5.2, S100, immunohistochemistry. Commonly used immune markers include CK7, CK20, GCDFP-15, HMB45, CAM5.2, S100, EMAL, etc.

3.3. Clinical symptoms and immunohistochemistry

Clinical symptoms of PPD mainly include erythematous, whitish gray, dry and raised lesions, but may also develop into eczematoid, ulcerated, nodular, or papillary forms. The differential diagnosis of these lesions includes eczema, contactable or irritant dermatitis, seborrheic dermatitis, or Bowen’s disease. The diagnosis of the disease requires biopsy and immunohistochemistry. Commonly used immune markers include CK7, CK20, GCDFP-15, HMB45, CAM5.2, S100, EMAL, etc.

3.4. Stage system

Shutze has proposed a four stage classification for PPD. Stage I means Paget’s cells are only found in the epidermis and adnexa. Stage II implies cutaneous Paget’s disease with associated adnexal or anorectal carcinoma. Stage III denotes Paget’s disease with metastasis to regional nodes. Stage IV means Paget’s disease with distant metastasis of associated carcinoma. Recently, Ohara et al group retrospective analysis of 301 patients with invasive primary tumors and propose the TNM (T = tumor, N = regional lymph node, M = metastasis) staging system: stage I, T1N0M0; stage II, T2N0M0; stage III, any T1N1M0; stage IIIb, any TN2M0; stage IV, any TanyN1M1. T1 means: Tumor thickness 24 mm and no lymphovascular invasion; T2 means: Tumor thickness > 4 mm OR lymphovascular invasion; N1 means that only one lymph node (LN) metastasis, and N2 means 2 or more LN metastasis; M1 means that distant organ metastasis or LN metastasis beyond regional LN basin. While this staging system is still controversial.

3.5. Treatment

There is no standard treatment plan for Paget’s disease, because very few cases have been reported till date. Currently, radiotherapy, imiquimod, photodynamic therapy, surgical method, chemotherapy, and targeted therapy are available. First, Hata et al have a retrospective analysis of 41 patients between April 1993 and February 2012. At a median follow-up period of 41 months, 16 patients had developed recurrences, and the overall and cause-specific survival rates were 93% and 96% at 3 years, and 68% and 84% at 5 years. Radiotherapy is administered when the patient’s physical condition cannot withstand the surgery, or patients do not want to lose the integrity of structural function, or postoperative recurrence, or as an adjuvant to surgery.

Secondly, imiquimod can also be prescribed. Machida et al had a systematic review of literature, and a total of 63 cases were analyzed. They suggested this therapy can be used those who have experienced recurrence after multiple surgical resections or who are with poor surgical candidates. Thirdly, Shieh used photodynamic therapy to treat EMPD with an objective resolution rate of 60%. Fontanelli et al treated 32 patients with aminolevulinic-acid methyl-ester PDT, 9.4% had a complete resolution of the symptoms, 78.1% patients had a partial resolution, and 12.5% had a stable disease. If the patient cannot undergo surgery or the disease appears in cosmetically and functionally important areas, this method can be useful.

Fourthly, however, surgery remains the main treatment. The key to surgical resection is to ensure the negative margins. Some studies indicated that a margin of 1 cm could be sufficient for lesions with clinically clear margins, but the removal of the edge of 2 cm is also often recommended. According to Hatta et al study in 76 patients, they did not find the examined factors significantly correlated with local recurrence in surgical margin, recommended that a 2 cm is effective. Long et al had compared the recurrence between wide local excision and Mohs micrographic surgery (MMS), and recommended the MMS should be explored to improve outcomes. According to a systematic review and meta-analysis, they found the recurrence of MMS significant lower than that treatment of EMPD with wide local excision in the meta-analysis of the three observational studies describing treatment with this modality. Besides, mapping biopsy is also used in clinic. A retrospective study was performed to compare the prognosis between mapping biopsy and no mapping biopsy, the recurrence rate of mapping biopsy was much lower than those who did not have mapping biopsy (50% vs 11.5%). According to KATO et al report, they evaluated the accuracy of the Japanese guideline of mapping biopsy with MMS. There was only 5.9% patient recurrence using preoperative mapping biopsy, which is lower than the recurrence rated for MMS. So they hold the opinions that mapping biopsy is not inferior to MMS, while there are only 17 patients in the study.

In this case, wide local excision, abdominoperineal resection and MMS were three alternative methods according to the disease stage. However, we chose Laparoscopic ELAPE surgery, for it can ensure negative resection as much as possible and reduce the incidence of intraoperative perforation. Besides, patients will suffer less from complications of postoperative wound and have faster recovery of gastrointestinal function. Meanwhile, this method is much more convenient. First, we can obtain a better visual field and distinguish the surgical anatomy, which is the significant advantage of this procedure. Secondly, we can fully utilize the tactile function of the hand, which can accurately distinguish tumor and normal tissue. Sometimes tumors and normal tissues differ only in texture. Apart from those, it can reduce the difficulty of surgery. In ostomy, circular
fistula can be chosen to reduce edema. So we performed this type of surgery for the patient. Fifth, when the lesion has a distant metastasis, we can choose chemotherapy and targeted therapy. Tokuda et al reported 200 cases treated with the 5-fluorouracil and cisplatin, the overall response rate in the 22 cases was 59.0%.[25] Chemotherapy can also be administered when surgery and radiation are contra-indicated.[26]

Besides, targeted therapy is also used. Barth et al reported a patient who was with end stage renal disease on hemodialysis with EMPD of the scrotum metastatic to the lymph was treated with trastuzumab monotherapy and achieved a completed response.[27] A Chinese group reported a case that they use apatinib to treat a patient who is ineffective to chemotherapy with oral apatinib. Antiangiogenic target therapy may be an option for EMPD treatment.[28]

3.6. Prognosis

The prognosis of the disease depends on whether it extends to adnexal or anorectal carcinoma. The prognosis is poor when it is associated with regional visceral carcinoma. Besides, according to a follow-up analysis involving 495 EMPD patients, those patients with a primary in the truncal or penoscrotal disease had a much better overall survival than PPD.[29] As for our patient, she recovered well, with no bleeding or infection or other complications. After 14 months, a follow-up revealed that her perianal area was disease-free.

4. Summary

Only 200 cases of PPD have been reported till date,[30] so clinicians find it difficult to diagnose and treat this disease, while many patients are unaware of it. If the patient is diagnosed with “dermatitis” and conventional treatment is ineffective, biopsy must be promptly conducted to check for PPD. Laparoscopic ELAPE is a successful therapy.

Author contributions

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References

[1] Zhou X, Zhang W, Mai H, et al. Mammary and extramammary Paget’s disease presented different expression pattern of steroid hormone receptors. BioMed Res Int 2017;2017:71–5.
[2] Paget J. On disease of the mammary areola preceding cancer of the mammary gland. St Bartholomew’s Hosp Rep 1874;10:87–9.
[3] D’Ardier J, Collioulauf P. Sur un cas de maladie de Paget de la region perineonale et-crotale. Ann Dermatol Syph 1893;4:25–30.
[4] Tulchinsky H, Zmora O, Brzozowski E, et al. Extramammary Paget’s disease of the perianal region. Colorectal Dis 2004;6:206–9.
[5] Heymann WR. Extramammary Paget’s disease. Clin Dermatol 1993; 11:83–7.
[6] Dorigo O. Treatment outcomes in a large cohort of patients with invasive Extramammary Paget’s disease. Gynecol Oncol 2012;125:346–51.
[7] Helwig EB, Graham JH. Angenital (extramammary) Paget’s disease: a clinicopathological study. Cancer 1963;16:387–403.
[8] Jankulovski N, Spasevski L, Janevska V, et al. A true epidermotropic spicule neoplasm in the form of perianal Paget’s disease: a case report. J Med Case Rep 2013;7:162–6.
[9] Jahbar AS, Perianal extramammary Paget’s disease. Eur J Surg Oncol 2000;26:612–4.
[10] Vergari M, Filingeri V, Palmieri G, et al. Perianal Paget’s disease: a case report and literature review. Anticancer Res 2012;32:4461–4.
[11] Shutte WP, Gleysteen JJ. Perianal Paget’s disease: Classification and review of management: report of two cases. Dis Colon Rectum 1990; 33:302–7.
[12] Ohara K, Fujisawa Y, Yoshino K, et al. A proposal for a TNM staging system for extramammary Paget disease: retrospective analysis of 301 patients with invasive primary tumors. J Dermatol Sci 2016;83:234–9.
[13] Hata M, Koike I, Wada H, et al. Radiation therapy for lymph node metastasis from extramammary Paget’s disease. J Eur Acad Dermatol Venereol 2014;28:873–7.
[14] Machida H, Moini A, Roman LD, et al. Effects of imiquimod on vulvar Paget’s disease: a systematic review of literature. Gynecol Oncol 2015;139:165–71.
[15] Shieh S, Dee AS, Cheney RT, et al. Photodynamic therapy for the treatment of extramammary Paget’s disease. Brit J Dermatol 2002; 146:1000–5.
[16] Fontanelli R, Papadia A, Martineelli F, et al. Photodynamic therapy with MALA as non-surgical treatment option in patients with primary extramammary Paget’s disease. Gynecol Oncol 2013;130:90–4.
[17] Murata Y, Kuman K. Extramammary Paget’s disease of the genitalia with clinically clear margins can be adequately resected with 1cm margin. Eur J Dermatol 2005;15:168–70.
[18] Kanatukis J. Mammary and extramammary Paget’s disease. J Eur Acad Dermatol Venereol 2007;21:581–90.
[19] Hatta N, Yamada M, Hirano T, et al. Extramammary Paget’s disease: treatment, prognostic factors and outcome in 76 patients. Br J Dermatol 2008;158:313–8.
[20] Long B, Schmitt AR, Weaver AL, et al. A matter of margins: surgical and pathologic risk factors for recurrence in extramammary Paget’s disease. Gynecol Oncol 2017;147:358–63.
[21] Bae JM, Choi YY, Kim H, et al. Mohs micrographic surgery for extramammary Paget disease: a pooled analysis of individual patient data. J Am Acad Dermatol 2013;68:632–7.
[22] Park SO, Ha JH, Hong KY, et al. Usefulness of mapping biopsy in the treatment of penoscrotal extramammary Paget’s disease. Ann Surg Oncol 2017;24:3229–36.
[23] Kato T, Fujimoto N, Fuji N, et al. Mapping biopsy with punch biopsies to determine surgical margin in extramammary Paget’s disease. J Dermatol 2013;40:968–72.
[24] Martijnse IS, Dudink RL, West NP, et al. Focus on extralayer perineal dissection in supine position for low rectal cancer has led to better quality of surgery and oncologic outcome. Ann Surg Oncol 2012; 19:786–93.
[25] Tokuda Y, Arakura F, Uhara H. Combination chemotherapy of low dose 5-fluorouracil and cisplatin for advanced extramammary Paget’s disease. Int J Clin Oncol 2015;20:194–7.
[26] Zollo JD, Zentouni NC. The Roswell Park Cancer Institute experience with extra-mammary Paget’s disease. Brit J Dermatol 2000;142:59–65.
[27] Barth P, Dulaimi Al-Saleem E, et al. Metastatic extramammary Paget’s disease of scrotum responds completely to single agent trastuzumab in a hemodialysis patient: case report, molecular profiling and brief review of the literature. Case Rep Oncol Med 2013;2013:895151.
[28] Zhang YN, Chen Y, Gao F, et al. Advanced scrotal extramammary Paget’s disease treated with apatinib: a case report. Clin Genitourin Cancer 2017;15:30308–17.
[29] Herrel IA, Weiss AD, Goodman M, et al. Extramammary Paget’s disease in males: survival outcomes in 495 patients. Ann Surg Oncol 2015; 22:1625–30.
[30] Carbotta G, Sallusto P, Prestera A, et al. Perineal Paget’s disease: a rare disorder and review of literature. Ann Med Surg 2016;9:50–2.