CASE REPORT

Perianal Paget's disease: a diagnostic dilemma

Shehab Jabir,¹ Manaf Khatib,¹ Sa'd Ali,² Niri Niranjani¹

¹St. Andrews Centre for Plastic Surgery and Burns, Broomfield Hospital, Chelmsford, Essex, UK

²Department of Pathology, Broomfield Hospital, Chelmsford, Essex, UK

Correspondence to

Dr Shehab Jabir,
shihab.jabir@googlemail.com

SUMMARY

Perianal Paget's disease (PPD) is part of the spectrum of pagetoid skin lesions occurring outside the region of the nipple/areolar complex that are collectively referred to as extramammary Paget's disease (EMPD). However, unlike Paget's disease of the breast, which in the vast majority of cases is invariably associated with an underlying ductal carcinoma, most cases of EMPD occur as either insitu or invasive adenocarcinomas with visceral malignancy being a rare entity. We present a case of a 50-year-old man who was referred to us with PPD. This case highlights the difficulties associated with making a clinical diagnosis of this condition. Furthermore, investigative workup to exclude possible malignancy with associated metastatic spread as well as the treatment options available are also discussed. In addition, this case highlights the need for a multidisciplinary team approach when dealing with this difficult problem.

BACKGROUND

The term extramammary Paget's disease (EMPD) is used to describe pagetoid skin lesions affecting areas other than the nipples and rich in apocrine glands such as the axilla and anogenital region. The vulva is by far the commonest anogenital site affected by EMPD with perianal involvement being a distinct rarity.¹ Perianal Paget's disease (PPD) was initially described by Darier and Coullaud in 1893, about 19 years after Sir James Paget described the characteristic breast lesion in 1874.² Unlike Paget's disease of the breast, which involves the nipple and points to an underlying associated ductal carcinoma, PPD is described as a cutaneous adenocarcinoma usually of either dermal apocrine or eccrine gland origin with glandular differentiation.³ It commonly occurs as an invasive adenocarcinoma or an insitu adenocarcinoma although cases of underlying visceral malignancy have also been reported.¹

Histologically, PPD is similar to Paget's disease of the breast comprising of large pale cells, referred to as Paget's cells, with abundant basophilic or amphophilic finely granulated cytoplasm which infiltrate the epidermis and are scattered between compressed squamous epithelial cells.⁴

Owing to its rarity, the true incidence of PPD is not known. However, estimates suggest that around 20% of all cases of EMPD involve the perianal region. It occurs in men and women, but appears to have the highest incidence in the vulva of postmenopausal Caucasian women in either the sixth or seventh decade of life.³

We report a case of a 50-year-old man who presented to us 6 months after noticing a raised, red and itchy lesion around his perianal region which was initially thought to be dermatitis. Following

the diagnosis of PPD the lesion was excised surgically and reconstructed through a gluteal fold flap. The importance of appropriate diagnostic workup, a multidisciplinary approach to the treatment of such patients, and regular follow-up for possible recurrence was emphasised.

CASE PRESENTATION

A 50-year builder was referred urgently by his general practitioner for suspected lower gastrointestinal cancer to the colorectal unit. The history revealed that he had noted a raised, red, itchy lesion around his anus over the past 10–12 months (see figure 1). It occasionally bled on scratching and at times felt sore to touch. There was no change in bowel habit, no weight loss and no family history of colorectal cancer. He was otherwise medically fit and was not on any regular medication. Examination revealed an erythematous, inflamed, keratotic lesion around his perianal region with occasional white spots and raised edges. Digital rectal examination was normal. Rigid sigmoidoscopy was also normal with no involvement of the anal canal or mucosa. In addition,

Figure 1 Note the red, raised plaque-like lesion extending concentrically outwards from the perianal region.

To cite: Jabir S, Khatib M, Ali S, et al. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2013-200504

Figure 2 Note infiltration of the epidermis by medium-sized to large-sized cells with round to ovoid nuclei and pale amphophilic cytoplasm; $\times 5$ magnification (A); $\times 10$ magnification (B) and $\times 20$ magnification (C).

there was no inguinal lymphadenopathy. The lack of sinister features and the appearance of the lesion suggested probable dermatitis and hence he was referred to dermatology. The dermatology department concurred with this diagnosis and treated him with trimovate cream and Dermal wash and emollient. However, the lesion failed to resolve on this treatment prompting a punch biopsy for histological diagnosis. Microscopic examination of the histological specimen revealed irregular acanthosis with infiltration of the epidermis by medium-sized to large-sized cells with round to ovoid nuclei and pale amphophilic cytoplasm (see figure 2A–C). These appearances were consistent with PPD.

The case was discussed in a multidisciplinary meeting involving colorectal, plastic and oncology teams. As the lesion involved a large area surgical excision was considered the treatment of choice. However, prior to excision it was decided that the patient required imaging investigations including colonoscopy, MRI and CT. Once all of these investigations confirmed that the disease was confined to his perianal region a laparoscopic defunctioning ileostomy was performed. The patient then underwent wide local excision of the PPD with reconstruction through a gluteal fold flap. He was then discharged home 10 days later with weekly review at our plastics dressing clinic. Twelve months since the procedure his wounds had healed and there was no evidence of recurrence. However, review at 18 months revealed a small area of recurrence close to the anus (see figures 3 and 4). He is currently awaiting further surgical excision of this small area of recurrence.

INVESTIGATIONS

Although most cases in the literature describe PPD confined to the epidermis with only local involvement, the potential for PPD to metastasise has also been documented. Furthermore, cases have been described where PPD has been associated with anorectal adenocarcinomas. Hence, it is crucial that metastatic disease including association with other bowel malignancies is excluded prior to surgical excision. Imaging investigations

Figure 3 A small area of recurrence measuring approximately 2 cm in diameter within the natal cleft after 18 months postexcision.

Figure 4 Remnant of scar pattern left behind by the gluteal fold flap which was used to fill the defect immediately postexcision.

including colonoscopy, CT and MRI are important in excluding metastases as well as helping with planning of the operation.

DIFFERENTIAL DIAGNOSIS

The lesions produced by PPD are similar in appearance to a number of other skin lesions including dermatitis, lichen simplex, psoriasis, eczema, leukoplakia, Bowen's disease, pagetoid melanoma, basal and squamous cell carcinoma, condylomata acuminata, mycosis fungoides and the epidermal phase of neuroendocrine carcinoma.^{3 5 6} Owing to its rarity it is only seldom considered a possibility and treatment is usually directed at more common entities such as dermatitis as was the case in this patient. The history and examination are usually inconclusive and may not cause one to suspect PPD initially. However, unresponsiveness to treatment should prompt an urgent biopsy. PPD is a histopathological entity and hence the primary mode of diagnosis is through full-thickness samples of affected perianal skin. It is also important to stress that PPD may also be secondary to an underlying visceral malignancy and appropriate diagnostic workup should be considered when this is clinically suspected.

DISCUSSION

The exact pathological mechanisms underlying PPD are yet to be demystified, however, there are currently two theories to explain its pathogenesis. The first theory, which accounts for a majority of cases, suggests that EMPD is a primary cutaneous adenocarcinoma arising in the epidermis.³ According to this theory, epidermal stem cells undergo aberrant differentiation extending into the contiguous epithelium of hair follicles and eccrine sweat glands. This primary Paget's disease may then spread from its in-situ location in the epidermis into the underlying dermis and may even metastasise to local lymph nodes and distant sites. The second theory on the other hand, which accounts for only a limited number of cases, holds that PPD is secondary to an underlying neoplastic process such as an adnexal carcinoma or an internal malignancy (commonly a gastrointestinal or genitourinary carcinoma) which has subsequently spread into the contiguous epidermis of the skin.⁷ These two theories have been supported by histological and immunohistochemical studies which have identified a number of differences between the primary intraepithelial variant and Paget's disease which has spread from an internal malignancy.

Treatment of PPD is determined by depth of invasion, involvement of surrounding lymph nodes and any metastatic spread. Kyriazanos *et al*³ have attempted to devise a staging system for PPD taking into account the aforementioned factors and tailoring treatment in accordance to stage (see table 1). Although this staging system does not encompass all variant

Table 1 Staging system for perianal Paget's disease taking into account the clinical and histological aspects and tailoring treatment in accordance to stage

Stage	Clinical/histological description	Treatment
I	Pagetoid cells in the perianal epidermal epidermis with no adnexal involvement	Wide local excision
IIA	Cutaneous Paget's disease with associated adnexal carcinoma	Wide local excision
IIB	Cutaneous Paget's disease with associated anorectal carcinoma	Abdominoperineal resection
III	Secondary Paget's disease where the associated carcinoma has spread to regional lymph nodes	Inguinal lymph node dissection and abdominoperineal resection/ wide local excision
IV	Secondary Paget's disease with distant metastases of associated carcinoma	Chemotherapy, radiotherapy, local palliative management

situations where PPD may be involved with other associated malignancies (up to 42% of patients with PPD may have concurrent malignancies of renal, hepatocellular, colorectal, vulva and bladder origin) it does provide the clinician with a framework to organise his or her thoughts on a management plan. Surgical excision with a margin of 1–3 cm is the treatment of choice.⁸ In most cases, the resultant defect would preclude direct closure necessitating reconstruction through local or regional flaps. A number of flaps have been utilised to close defects in this region including transposition or rotation skin flaps, bilateral myocutaneous flaps of the gluteal and thigh muscles and V-Y island flaps. Apart from wide local excision, Moh's micrographic surgery (MMS) is another potential option.⁹ MMS involves intraoperative microscopic evaluation of 100% of the tissue margin through horizontal frozen sections by the operating surgeon himself. In contrast, the conventional bread-loaf technique for checking tissue margins using vertical sections examines only around 0.1–1% of the margin making the likelihood of missed tumour very likely. In addition to superior rates of tumour removal, the MMS technique of microscopically guided excision of tumours also leads to maximal tissue conservation and is usually performed under local anaesthetic. Hendi *et al*⁹ report a recurrence rate of 16% for primary EMPD treated with MMS while the recurrence rate for conventional excision is variably reported to be between 31% and 61%.

A number of non-surgical modalities are also available to treat PPD and include topical and systemic chemotherapy, radiotherapy and photodynamic therapy (PTD).³ Indications for these non-surgical modalities include elderly patients who are not fit to undergo a procedure under general anaesthetic, significant metastatic disease burden, unwillingness of patients to undergo mutilating surgery and those with occult and multifocal disease.

Topical chemotherapeutic agents such as imiquimod, topical 5 fluorouracil and bleomycin may be employed for symptomatic relief and in certain cases have been reported to reduce tumour burden prior to surgical excision.³ Systemic chemotherapy with paclitaxel and trastuzumab has been shown to be effective in metastatic EMPD where an over expression of human epidermal growth factor receptor 2 protein (which occurs in 20–60% of cases) results in deep dermal invasion and metastatic spread of the tumour.³ Radiotherapy has been successfully used in cases of postoperative local recurrence, as an adjunct to surgical

excision and in selected cases as the primary therapeutic intervention. The standard dose employed in most cases is between 40 and 50 Gy.^{2–10} Disadvantages with radiotherapy include radiation reaction which may be associated with proctitis, enteritis and cystitis. Li *et al*¹¹ have used PTD to treat one case of PPD. The lesion and its margins were visualised by application of a fluorescent agent, aminolevulinic acid/protoporphyrin IX (PpIX), prior to application of PTD. Once its margins were delineated, the lesion was treated with a 630 nm laser at 120 J/cm². The treatment was repeated at 40 days and the authors reported no recurrence at 7 months with minimal scarring and functional loss. However, long-term follow-up and successful application to a greater number of patients is necessary before PTD could be considered part of the standard armoury for treatment of PPD.

Learning points

- ▶ Extramammary Paget's disease poses a diagnostic challenge. One should approach these lesions with a high index of suspicion.
- ▶ Thorough investigation is essential to exclude metastatic disease especially given the fact that a significant percentage of these patients may have other concurrent neoplastic conditions.
- ▶ Perianal Paget's disease requires a multidisciplinary team approach to manage these patients due to the multiple comorbidities these patients are likely to experience.
- ▶ Recurrence is possible even after wide local excision and an apparently successful outcome. Hence these patients require long-term outpatient follow-up.

Contributors SJ was responsible for inception of the report and writing of the manuscript. MK edited the manuscript. SA provided the pathology slides and figure captions. NN was the operating surgeon and was responsible for final approval of the manuscript.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- 1 Le Fur R, Mears L, Dannawi Z. A peri-anal extramammary Paget's disease associated with two well-differentiated invasive intramucosal sigmoid carcinomas, a very rare case: an immunohistochemical and clinical review of extramammary Paget's disease. *Ann R Coll Surg Engl* 2004;86:W26–31.
- 2 Amin R. Perianal Paget's disease. *Br J Radiol* 1999;72:610–12.
- 3 Kyriazanos ID, Stamos NP, Miliadis L, *et al*. Extra-mammary Paget's disease of the perianal region: a review of the literature emphasizing the operative management technique. *Surg Oncol* 2011;20:e61–71.
- 4 Lloyd J, Flanagan AM. Mammary and extramammary Paget's disease. *J Clin Pathol* 2000;53:742–9.
- 5 Honda Y, Egawa K. Extramammary Paget's disease not only mimicking but also accompanying condyloma acuminatum. A case report. *Dermatology* 2005;210:315–18.
- 6 Chung J, Kim JY, Gye J, *et al*. Extramammary Paget's disease of external genitalia with bowenoid features. *Ann Dermatol* 2013;25:88–91.
- 7 Sarmiento JM, Wolff BG, Burgart LJ, *et al*. Paget's disease of the perianal region—an aggressive disease? *Dis Colon Rectum* 1997;40:1187–94.
- 8 Chan JY, Li GK, Chung JH, *et al*. Extramammary Paget's disease: 20 years of experience in Chinese population. *Int J Surg Oncol* 2012;2012:416–18.
- 9 Hendi A, Brodland DG, Zitelli JA. Extramammary Paget's disease: surgical treatment with Mohs micrographic surgery. *J Am Acad Dermatol* 2004;51:767–73.
- 10 Mann J, Lavaf A, Tejjwani A, *et al*. Perianal Paget disease treated definitively with radiotherapy. *Curr Oncol* 2012;19:e496–500.
- 11 Li L, Deng Y, Zhang L, *et al*. Treatment of perianal Paget's disease using photodynamic therapy with assistance of fluorescence examination: case report. *Lasers Med Sci* 2009;24:981–4.

Copyright 2013 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- ▶ Submit as many cases as you like
- ▶ Enjoy fast sympathetic peer review and rapid publication of accepted articles
- ▶ Access all the published articles
- ▶ Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow