



## Case Report

Perianal Paget's disease<sup>☆</sup>

Ornella Sari Cassol <sup>a,b,\*</sup>, Júlia Pastorello<sup>b,c</sup>, Bruna de Oliveira<sup>d</sup>,  
Lucas Henrique Lenhardt<sup>d</sup>, Suéllen Montagna<sup>d</sup>, Vanessa Locatelli Pietrobelli<sup>d</sup>

<sup>a</sup> Hospital da Cidade de Passo Fundo (HCPF), Departamento de Coloproctologia, Passo Fundo, RS, Brazil

<sup>b</sup> Instituto Meridional (IMED), Campus Passo Fundo, Passo Fundo, RS, Brazil

<sup>c</sup> Hospital da Cidade de Passo Fundo (HCPF), Departamento de Oncologia Clínica, Passo Fundo, RS, Brazil

<sup>d</sup> Universidade Federal da Fronteira Sul (UFFS), Faculdade de Medicina, Passo Fundo, RS, Brazil

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## ABSTRACT

Paget's disease most commonly affects the breast. Extramammary involvement is rare, and the most commonly affected sites are the vulva, anus, perianal region, and axilla. The disease may progress to invasive adenocarcinoma or synchronous cancers. Due to the lack of distinctive features and nonspecific presenting symptoms, Paget's disease may be misdiagnosed as other conditions, thus delaying the correct diagnosis. We report a case of extramammary Paget's disease in the perianal region that initially presented as an irregular, circumferential, scaling lesion with eczematous eruptions. Immunology and immunohistochemistry confirmed the diagnosis. Although surgery is the standard treatment, the patient opted for pelvic radiotherapy associated with radiosensitizing chemotherapy.

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## Doença de Paget perianal

## RESUMO

A doença de Paget acomete mais comumente a mama. Os focos extramamários são raros e os locais mais habitualmente acometidos são vulva, ânus, região perianal e axila. A patologia envolve a evolução da doença para adenocarcinoma invasivo ou neoplasias sincrônicas. Devido à singularidade e sua aparência inespecífica, a doença pode ser confundida com outras comorbidades, retardando o diagnóstico. O objetivo foi relatar um caso de doença de Paget extramamária na região perianal, a qual inicialmente apresentou lesão circunferencial com erupção eczematosa, descamativa e irregular. A confirmação diagnóstica foi por meio

<sup>☆</sup> Department and institution to which the paper should be attributed: Hospital da Cidade de Passo Fundo (HCPF), Passo Fundo, RS, Brazil.

\* Corresponding author.

E-mail: [cassol.ornella@gmail.com](mailto:cassol.ornella@gmail.com) (O.S. Cassol).

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de exames imuno-histoquímico e imunológico. O tratamento padrão da doença é cirúrgico, porém optou-se por radioterapia pélvica associada à quimioterapia radiosensibilizante.

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## Introduction

Paget's disease is a rare clinical entity. It most commonly affects the breast, accounting for 1%–3% of all cases of invasive cancer diagnosed annually. Extramammary presentation of Paget's disease is characterized by the presence of epithelial cells associated with intraepithelial adenocarcinoma. This disease was first described by Sir James Paget in 1874.<sup>1</sup> Extramammary disease most frequently occurs in apocrine gland-bearing sites, such as the vulva, anus, perianal region, and axilla.<sup>2</sup> Until 2016, approximately 200 cases of perianal Paget's disease were reported in the literature.<sup>3</sup>

This disease most commonly affects women and white people in general, with a peak incidence between 50 and 80 years of age, but some authors have reported a similar incidence in men and women.<sup>3</sup> Genetic alterations may play a role in the pathogenesis of primary Paget's disease, as activation of the RAS/RAF and PI3K/AKT pathways is involved in the mechanism of extramammary Paget's disease (EMPD).<sup>4</sup>

The clinical presentation is nonspecific. Pruritus (70%), burning, suppuration, and bleeding are common symptoms, but in about 10% of cases the disease is asymptomatic.<sup>1</sup> Chronic skin disorders and refractory fungal infections are the main differential diagnoses, and biopsy thus becomes essential to confirm the diagnosis. The prognosis is favorable, with depth of invasion as the most important prognostic indicator.<sup>5</sup>

Histologically, primary Paget's disease is characterized by large vacuolated cells containing mucin, the so-called Paget cells.<sup>6</sup> They may also contain cytokeratin and carcinoembryonic antigen, which can be detected by immunofluorescence. CK7, CK19, and C-erb B2 are immunohistochemical markers for the diagnosis of EMPD.<sup>4</sup>

Surgical excision is the gold standard treatment. The recommended approaches include wide surgical excision for noninvasive lesions and abdominoperineal excision or excision of the rectum according to the affected site for invasive disease or lesions associated with carcinoma. Radiotherapy is rarely used as a primary treatment, but older patients, often deemed medically unfit for surgery, are most likely to benefit from it. Typical side effects of perianal radiotherapy include acute dermatitis, moist desquamation, and skin atrophy.<sup>3</sup>

## Case report

A 79-year-old woman presented with a 1-year history of an anal lesion that became pruritic. The patient failed to respond to standard topical therapy, and biopsy was indicated. She had a history of prior non-Hodgkin's lymphoma in remission (chemotherapy ended in 2012). The physical examination revealed an irregular, circumferential, scaling,



**Fig. 1 – Lesion before treatment: irregular, circumferential, scaling, pale-pink anal lesion of 3 cm long with eczematous eruptions.**

pale-pink lesion of 3 cm long, with eczematous eruptions and indefinite borders (Fig. 1). Immunology and immunohistochemistry confirmed the diagnosis of EMPD. The cells stained positive for CK7 and BRST-2, suggesting an adnexal gland origin from the pilosebaceous infundibulum. Systemic staging and investigation of synchronous cancers in the genitourinary, gastrointestinal, and mammary tracts were performed, with all of them yielding negative results. Surgical abdominoperineal resection was indicated. However, the patient refused surgical treatment and opted for pelvic radiotherapy associated with radiosensitizing chemotherapy, according to the protocol for anal canal tumors (Fig. 2). The patient received the proposed treatment and is currently being followed in the outpatient clinic, with significant regression of the perianal lesion.

## Discussion

Clinical cases of EMPD are unusual, which explains the lack of accurate epidemiological data on this disease and the importance of this report.<sup>5</sup>



**Fig. 2 – Outcome after treatment with pelvic radiotherapy associated with radiosensitizing chemotherapy.**

The disease has a predilection for postmenopausal white women, and clinical signs include eczematous eruptions in glandular tissue and associated pruritus.<sup>7</sup> The presence of Paget's cells is considered a premalignant condition, progressing to invasive adenocarcinoma within or below the superficial lesion in 4%–17% of cases. As for synchronous cancers, approximately 20%–30% of patients have non-contiguous carcinomas involving the breast, rectum, bladder, urethra, vagina, or ovary.<sup>3</sup>

The histological hallmark of EMPD is the presence of malignant intraepithelial adenocarcinoma cells occurring singly or in small groups within the epidermis. The immunohistochemical profile shows positive staining for low molecular weight cytokeratins, contributing to differentiate it from other skin tumors.<sup>3</sup>

The differential diagnosis includes benign conditions, such as eczema and contact dermatitis, and malignant conditions, such as Bowen's disease, melanoma, and basal cell carcinoma. Histopathology defines the diagnosis, staging, and follow-up of EMPD.<sup>8</sup>

Surgery is the initial treatment of choice for perianal disease. For premalignant lesions, wide local excision with or without flaps is indicated, while abdominoperineal resection

is indicated for invasive disease. Other options include pelvic radiotherapy, systemic chemotherapy or topical chemotherapy with 5-fluorouracil, photodynamic therapy, and laser therapy.<sup>4</sup>

## Conclusion

Paget's disease is an uncommon entity whose diagnosis is often delayed due to nonspecific presenting symptoms. Extramammary involvement is rare, and the most commonly affected sites are the vulva, anus, perianal region, and axilla. The gold standard for treatment is surgery, but other options include the use of radiotherapy and chemotherapy.

## Conflicts of interest

The authors declare no conflicts of interest.

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