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Review

Extra-mammary Paget's disease of the perianal region: A review of the literature emphasizing the operative management technique

Ioannis D. Kyriazanos, Nikolaos P. Stamos, Lazaros Miliadis, Grigorios Noussis, Christos N. Stoidis*

Department of Surgery, Naval and Veterans Hospital of Athens, Athens, Greece

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ABSTRACT

The perianal skin is a common area for extra-mammary Paget's disease development. The unique clinical, histopathological, and immunohistochemical features which this medical phenomenon demonstrates, along with its rarity and frequent association with synchronous or metachronous carcinomas, present us with a treatment challenge. In order to organize the surgical treatment, it is important to determine whether the disease is localized exclusively to the perianal skin or associated with metastasis or ano-rectal carcinomas.

Despite several controversies concerning its optimal therapeutic management, wide local excision of the skin and subcutaneous tissue in the perianal region is generally recommended for the treatment of the non-invasive form of the disease. Such an aggressive operative management usually results in a large perianal tissue defect, which can not be primarily suppressed without resultant tension and possible complications, requiring a special technique for its coverage. Various techniques have been described in the literature for the treatment of these defects, often associated with unfavourable long term results, i.e. split-thickness skin grafts and vacuum-assisted closure devices. More recently several authors have reported favourable results using various transposition or rotation local skin flaps, myocutaneous flaps of the gluteal and thigh muscles, and V-Y island flaps to cover these areas of tissue loss.

In this article we present a short review of the literature concerning perianal Paget's disease with special attention to its management and a demonstration of the operative technique we prefer on patients with perianal non-invasive Paget's disease, i.e. wide local excision with a 2 cm margin in the anal mucosa and use of U and V-Y shaped perianal fatty-cutaneous island flaps for reconstruction by covering the bilateral anal skin defects.

Contents

* Corresponding author. Tel.: +30 210 9235157; fax: +30 2310 643149.
E-mail address: aris.80@hotmail.com (C.N. Stoidis).

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Introduction

Originally reported in 1893 by Darier and Coulillaud, perianal Paget's disease (PPD) is a rare intraepithelial adenocarcinoma, arising from dermal apocrine sweat glands [1]. The background experience recorded on this disease is limited as most publications are case reports of which only a small number of about 200 has previously been reported [1–3].

The true incidence of the disease is difficult to be estimated due to its rarity [4,5]. According to the latest international literature it represents the 20% of cases of extra-mammary Paget's disease (EMPD), less than the 1% of anal disease, and 6.5% of all cases of Paget's disease [3].

Despite the similar clinical and histopathologic appearances of Paget's disease of the nipple and the anus, mammary Paget's disease is invariably associated with underlying ductal carcinoma whereas perianal Paget's disease may or may not be associated with underlying malignancy [6–10]. Furthermore, the underlying carcinoma associated with perianal Paget's disease has a wide spectrum of presentation including apocrine or eccrine. The rate of malignancy associated with perianal Paget's disease ranges from 33% to 86% [11]. The majority is colorectal and tubo-ovarian cancers [12].

The lesion occurs most commonly in the sixth and seventh decades of a human life span with an average age of 63 years. It can be found in both men and women; however, it is most commonly detected in postmenopausal Caucasian females [13,14].

As PPD represents an uncommon form of a cutaneous malignant neoplasm, several oncologic factors can affect therapeutic decision making, involving accurate diagnosis, preoperative staging and assessment of the patient's general condition.

Localization-spread

There is consistent evidence for considering EMPD a heterologous entity with regard to histological and clinical features and potential for metastatic spread. The most commonly affected areas are the vulva, perineum, perianal region, scrotum, penis, or pubic area [15]. Especially, for the perianal region its incidence percentage rises to 20% of the cases, as has been previously referred to [3].

The patient may relapse many times even to the extent of developing invasive features, metastasis, or association with anorectal adenocarcinomas [16]. Lymph node metastasis of EMPD in most cases involves inguinal, perirectal, retroperitoneal, iliac, and paraaortic lymph nodes [17]. Distant metastasis involves predominantly the liver, bone, lung, and suprarenal glands [18]. Cutaneous metastasis has also been reported in a patient with perianal EMPD with dermal extent treated 14 years before for rectal adenocarcinoma [19]. Even intraepithelial Paget's disease can metastasize. In two cases, after surgical treatment, metastases are reported as synchronous to that of the iliac and inguinal lymph nodes in one case and subsequent to the liver's one in the other [20,21].

Classification-staging

Concerning the depth of invasion Paget cells can be found at all levels of the epidermis. They can migrate with in the epidermis in a horizontal as well as vertical direction. Therefore, PPD can be categorized as either non-invasive (tumour confined onto epidermis) or as invasive disease (tumour penetrating the basement membrane and entering into underlying stroma) [22,23].

A new clinical entity, the minimally invasive Paget's disease has drawn specific attention for its definition and management. Minimally invasive Paget's disease is defined as at least one group of Paget's cells protruding no more than 1 mm below the basement membrane and entering into underlying stroma [24,25].

A staging classification of perianal Paget's disease and appropriate treatment of each stage have been proposed [22,23]. Prognosis remains good for Stage I (Paget's cells found in perianal epidermis and adnexa without primary carcinoma), while it worsens for Stage II (invasive cutaneous disease penetrating the basement membrane and entering into underlying stroma and/or synchronous localized malignancies, i.e. IIa adnexal malignancy, IIb visceral malignancy), and for Stages III and IV, where regional and distant metastatic disease are attested, respectively (Table 1).

Etiology-pathogenesis

Although seven cases of familiar EMPD have been reported, the oncogenetic basis of the disease is still unknown [14]. Two major theories of PPD's pathogenesis have been proposed, postulated as being at least two different pathologic processes that have common clinical and histological features [26]. In the first theory accounting for the majority of the cases, perianal Paget's is characterized as primary (of cutaneous origin) arising as a primary adenocarcinoma in epidermis in the form of abnormal differentiation of epidermal

Table 1
Perianal Paget's disease classification and accompanying suggested therapy [23].

Stage	Description	Management
I	Paget's cells in the perianal epidermis and adnexa without primary carcinoma	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	Paget's disease in which associated carcinoma has spread to regional nodes	Inguinal lymph nodes dissection and abdominoperineal resection/wide local excision
IV	Paget's disease with distant metastases of associated carcinoma	Chemotherapy, radiotherapy, local palliative management