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Clinical Science

Staged marginal contoured and central excision technique in the surgical management of perianal Paget's disease

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Clear margins

Abstract

BACKGROUND: Extramammary Paget's disease (EMPD) is an adenocarcinoma of the apocrine glands with unknown exact prevalence and obscure etiology. It has been divided into primary EMPD and secondary EMPD, in which an internal malignancy is usually associated. Treatment for primary EMPD usually consists of wide lesion excision with negative margins. Multiple methods have been proposed to obtain free-margin status of the disease. These include visible border lesion excision, punch biopsies, and micrographic and frozen-section surgery, with different results but still high recurrence rates.

METHODS: The investigators propose a method consisting of a staged contoured marginal excision using "en face" permanent pathologic analysis preceding the steps of central excision of the lesion and the final reconstruction of the surgical defect.

RESULTS: Advantages of this method include adequate margin control allowing final reconstruction and tissue preservation, while minimizing patient discomfort.

CONCLUSIONS: The staged contoured marginal and central excision technique offers a new alternative to the armamentarium for surgical oncologists for the management of EMPD in which margin control is imperative for control of recurrence rates.

Extramammary Paget's disease (EMPD) is a rare skin disease consisting of adenocarcinoma of the apocrine glands, with slow progression and obscure etiology. EMPD is considered a heterogeneous condition that comprises 2 different classifications. Primary EMPD is a neoplasm thought to originate in the Paget's cells of the epidermis in the sweat glands. Secondary EMPD originates from epidermotropic spread of malignant cells from an underlying carcinoma. The most frequent carcinomas include those of the adnexal organs, genitourinary area, and gastrointestinal tract. Still, associated neoplasms are found in only 25% of patients with EMPD.[1,2]

The precise etiology of EMPD has not been completely elucidated. Cell origin remains controversial. Although immunohistochemical staining shows the epithelial glandular nature of these cells, a precise origin remains unclear for

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primary EMPD. For EMPD associated with malignancy, an oncogenic stimulus has been suspected, but there is no conclusive evidence.

Epidemiology

Because EMPD is considered a rare condition, its incidence and prevalence are not known. The majority of papers published in the medical literature consist of retrospective studies or small case series. It has been reported that in breast cancer, the proportion of Paget's disease is 0.7% to 4.3%.[2]

EMPD accounts for 6.5% of all cutaneous Paget's disease and is more common among women. Generally, the tumor affects older patients, with an average age at diagnosis of 68 years.[3,4]

Because EMPD affects areas of the skin containing apocrine sweat glands, its location can vary widely. The most commonly affected site is the vulva. In one of the largest case series, the vulva was affected in 65% of cases, followed by the perianal region, penis, scrotum, or inguinal region.[5] Perianal EMPD is uncommon, either with or without association with carcinoma of the anus or rectum. Only 180 cases have been described in the medical literature.[6] The rate of concomitant malignancy in perianal EMPD ranges from 33% to 86%, the majority consisting of tubo-ovarian and colorectal cancers. When underlying invasive carcinoma is diagnosed, the prognosis is dismal.[7]

Histology and progression of disease

The most important aspect of the pathologic examination consists of the presence of Paget cells. These malignant cells are usually larger than keratinocytes, with enlarged, clear cytoplasm and large nuclei, located in the epidermis as solitary cells or in clusters (Pagetoid arrangement). These nests can displace basal keratinocytes. All layers of the epidermis can be affected.[1]

When the diagnosis is supported by immunohistochemical studies, attention must be paid to the presence of carcinoembryonic antigen and cytokeratins such as CK7, PKK1, GR 53, and 35βH11. These antigens are present in Paget cells as well as apocrine and exocrine glands, which favors the hypothesis of the origin of these tumors.[8] Recently, the presence of human epidermal growth factor receptor 2 was found in >30% of patients studied, with a possible implication on disease severity.[9]

Metastasis is usually characterized by contiguous spread followed by lymphatic drainage. The main sites of metastasis are ipsilateral or bilateral inguinal lymph nodes followed by para-aortic nodes and lungs. Secondary EMPD is an expression of intraepithelial metastasis of a primary tumor.[3]

Clinical presentation

Because EMPD consists of a slow-growing intraepidermal neoplasm, its clinical presentation is often insidious and nonspecific. For perianal EMPD, it presents as a rash in the affected region with itching and pain. Other more rare presentations include bleeding, presence of a lump, or alterations in defecation.

Because of the relatively benign appearance of the lesions, they tend to progress over decades before proper medical evaluation. Usually, this condition is approached as a nonspecific rash and treated initially with topical drugs, obtaining only partial relief of symptoms. Differential diagnoses are vast and include Bowen's disease, Langerhans cell histiocytosis, malignant melanoma, squamous cell carcinoma, condyloma acuminatum, spread of rectal carcinoma, Crohn's disease, hidradenitis suppurativa, mycosis fungoides, and Merkel cell carcinoma. It is usually after the persistence of symptoms that biopsy is solicited and diagnosis made.[1,10]

Lesions can vary in color from pink to dark red; larger lesions usually present with a variety of colors. Its surface may have a scale or oozing with crusts. There may also be patchy erosions or leukoplakia. More advanced lesions may be irregular with poorly defined borders. Given the centrifugal growth, there may be complete involvement of the anogenital region, leading to the formation of polygonal borders.[11] Once the diagnosis is obtained, workup seeking a primary neoplasm is mandatory.

Treatment

Myriad treatment options have been proposed for EMPD in the perianal region. The mainstay of therapy for noninvasive disease remains the surgical wide excision of the lesion. Surgeons may face multiple challenges in these patients, such as the extent of the lesion, damage to structures related in the anogenital region, the morbidity they constitute by themselves, diminished quality of life, and high recurrence rates.

A staging classification for perianal Paget's disease was proposed by Shutze and Gleysteen[12] in 1990 (Table 1) showing the description of each stage and the recommended therapy. This classification can be used as a guideline, but it has not been validated in further studies, and its recommendations should be taken with caution. We propose a new staging and treatment classification for EMPD that includes more updated data on this disease as an update for the previous system proposed by Shutze and Gleysteen (Table 2).

It is clear that local control of the disease is the mainstay of therapy for perianal EMPD. The main variables to be evaluated are the extent of the tissue to be removed and the potential curability of the disease with this method.

Current reports in the literature for surgical management of EMPD reveal that surgical excisions (with 1-cm to 3-cm margins and 0.5 cm deep into subcutaneous fat) have a recurrence rate of 33% to 60% for patients with perianal disease and 18% to 50% for those with vulvar EMPD.[13,14] Intraoperative biopsies are usually taken 1 cm from the visible lesion edges and are analyzed in the 4 quadrants, including