Successful treatment of recurrent extramammary Paget’s disease of the penis and scrotum with imiquimod 5% cream

Efficacité d’un traitement par imiquimod 5 % pour une maladie de Paget extramammaire du pénis et du scrotum

Extramammary Paget’s disease (EMPD) is rare intra-epithelial adenocarcinoma involving primarily the epidermis. Cases affecting the penis and scrotum are rare [1], as involvement of male genitalia is found in less than 14% of the cases [2]. Surgery with a 2 to 3 cm margin followed by reconstruction remains the mainstay of treatment [3]. However, recurrence rate remains high and surgery has often significant consequences for the functional anatomy with irreparable tissue damage. Efficacy of imiquimod 5% cream has been assessed in different locations of female and male genitalia EMPD [2,4–9]. We report here a successful treatment with imiquimod for relapsing peno-scrotal EMPD after multiple relapse after surgery.

Case report

A 69-year-old caucasian male was referred for the management of recurrent EMPD of the scrotum during autumn 2009. His past medical history was notable for benign prostatic hypertrophy, dyslipidemia and EMPD of the scrotum in 1998. Since its diagnosis, he had had excisional local surgeries performed on four occasions, the last one having been performed nine years ago. He had had pruritic erythematous lesions of the scrotal area for the past several months prior to consultation. Examination revealed large erythematous, well-demarcated, slightly infiltrated, eczematous-like lesions of the scrotum. Besides, an erythematous telangiectatic patch extending slowly on the base of the penile shaft was noted (figure 1A). No regional lymph node enlargement was palpated and there was no other skin lesion elsewhere. Physical examination was unremarkable except prostate hypertrophy suggestive of prostate adenoma. Two punch skin biopsies were performed, one on the penis and one on the scrotum. Examination confirmed in both cases recurrence of EMPD without dermis invasion with large intraepidermal Paget cells revealed immunohistochemically with alcian blue and keratin seven stainings (figure 1B). Laboratory investigations including prostate specific antigen and pelvic imaging including rectosigmoidoscopy, urinary tract and inguinal lymph node ultrasonographies proved either negative or within normal ranges.

Because of this new recurrence after surgery, we decided to initiate local treatment with a daily application of imiquimod 5% cream (Aldara®, Meda Pharma, Paris, France) during six weeks. However, after one month, marked erythema and tenderness on the affected area where the topical treatment was applied, prompted us to reduce the frequency of its application to three-times per week for six weeks. One month after the completion of treatment, no residual or recurrent sign of EMPD was noted clinically (figure 1C). Post-treatment biopsy on the scrotum confirmed the disappearance of Paget cells (figure 1D). After 12 months of follow-up, no clinical recurrence was noted.

Discussion

Surgical excision with large margins (2 to 3 cm) remains the gold standard treatment of EMPD. However, extensive resections are often followed by a high local rate of recurrence as invasion of the epidermis by Paget’s cells often exceeds largely the visible limits of the lesions [1,3]. Thus, 32% to 50% of cases of male genital EMPD will recur after local resection [2]. Our patients underwent four excisions over a two year-period without achieving full eradication of the disease. Various treatments have been proposed in the literature such as local treatments (5-Fluorouracil, bleomycine), Mohs micrographic surgery, radiotherapy and dynamic phototherapy [1].

![Figure 1](image)

Figure 1

A. Extramammary paget’s disease of the scrotum and the base of the penile shaft. B. Biopsy of the scrotum displaying large epithelioid round cells with pale staining cytoplasms and hypertrophic nuclei (Hematoxylin & Eosin, × 400). C. Scrotum and penis one month following completion of imiquimod 5% cream application. D. Biopsy of the scrotum one month following completion of imiquimod 5% cream application: no evidence of Paget’s cells (Hematoxylin & Eosin, × 200)
traitement should offer a minimal amount of tissue destruction and low rates of recurrence. Several case reports have shown that topical imiquimod 5% cream could be of great value in the management of perineal EMPD. Efficacy has been reported on vulvar [4,5], perianal [4,6] and pennis-crotal forms of EMPD [2,7–9]. Unfortunately, the different treatment protocols chosen in these publications prevent from defining a clear protocol. Nevertheless, in our case, as in others [2], daily application was not well tolerated. Protocol based on a thrice a week basis seems reasonable as adhesion to the treatment is mandatory to have it performed till the end.

Imiquimod is an immune-response modifying agent that stimulates the production of several cytokines (IFN-α, TNF-α, IL-1, IL-6, IL-8, IL-10, IL-12). It leads to the combined activation of the innate local immunity and the TH1 immune pathways, in addition to the inhibition of TH-2 cytokines which are overexpressed in skin cancer [10]. Topical application of imiquimod cream has been shown to be effective in the treatment of other cutaneous malignant and premalignant conditions such as actinic keratoses, basal cell carcinoma and Bowen’s disease. Imiquimod seems to be effective in the EMPD of the scrotum and enables the preservation of the anatomical and functional structures. In the literature, this treatment has been offered to patients who have refused surgery. In our case, imiquimod has been proposed as an alternative because of multiple relapses despite the surgery. Some authors have even suggested that imiquimod could defer surgery [6]. Imiquimod is well tolerated when applied every two or three other day.

Our case confirms the short-term efficacy of imiquimod in peno-scrotal EMPD. Imiquimod could be proposed as first line treatment in replacement of surgery, especially if the patient refuses surgery or if surgical intervention has been already attempted without complete success. Imiquimod could also be given as neoadjuvant therapy to reduce the size of the lesion before surgery. However, it must be noted that imiquimod has been reported in only epidermal forms and without underlying neoplasia. Randomized controlled studies are necessary to define a standard treatment protocol. Medium and long-term follow up is essential to evaluate the rate of recurrence.

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References


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Tamponnade compliquant une maladie de Behçet

Tamponnade complicating a Behçet’s disease

La maladie de Behçet (MB) est une vascularite systémique caractérisée par une aphthose buccogénitale associée à des manifestations systémiques diverses dont les plus importantes sont les atteintes oculaires, cutanées, articulaires, neurologiques et vasculaires [1,2].