INTRODUCTION

Extramammary Paget’s disease is an uncommon cutaneous adenocarcinoma, characterized by glandular differentiation and an insidious course. The standard treatment, although possible loss of tissue function and disease recurrence are seen. The EMPD-V recurrence rates are high despite aggressive surgical intervention. The diagnosis is made histopathologically, and management is based on wide surgical excision. The histopathological features are similar in mammary and extramammary Paget’s disease. The Paget’s cells are present singly or in small clusters and characteristically stain with hematoxylin and eosin. Identification of new therapeutic strategies less mutilating/aggressive than reexcision, x-ray therapy, or chemotherapy is warranted.

We report a case where complete clinical and histological resolution of non-invasive EMP-V of the vulvar was achieved with minimal adverse effects after six weeks of imiquimod application. Imiquimod is an immunomodulator that stimulates the production of a range of cytokines including IL-1, IL-6, IL-8, and IL-12, and especially interferon IFN-a and TNF. Imiquimod is generally well tolerated, without any major side effects or tissue damage. Imiquimod may be a useful alternative or adjuvant in the treatment of EMPD.

CASE REPORT

Hear we present a case one patient with rEMPD-V, who responded to topical imiquimod therapy. A 72 year old female with a history of hypertension and diabetes underwent margins free vulvectomy due to EMPD-V (1995). She abandoned follow-up and returned 8 years later with a benign erythematous papule lesion near to the surgical scar. She returned with the same lesion two years later and then treated for 4 years with topical corticoid and new lesion appeared in vulvar (Figure 1a). On examination, bilateral well-defined hypo-pigmented lesion (Figure 1a).

We report the case of a 72-year-old woman with biopsy-proven EMPD-V of the thigh treated successfully with imiquimod application thrice weekly for 6 weeks.

Keywords: extramammary Paget’s disease of the vulva (EMPD-V), imiquimod

RESUMO

Apesar de rara, a doença de Paget extramamária recorrente da vulva (DPEMr-V) é uma condição grave porque, subjacente à malignidade interna, podem acompanhar lesões cutâneas superficiais. A doença de Paget extramamária é uma condição caracterizada por erupção cutânea crônica do tipo eczema de pele ao redor da região anogenital em homens e mulheres. Sob o microscópio, é muito parecida com o tipo mais comum da doença de Paget mamária, que ocorre na mama. A doença de Paget extramamária ocorre mais comumente em mulheres com idades entre 50 a 60 anos. Contudo, a excisão cirúrgica é o padrão geralmente aceito para a DPEMr-V. As taxas de recorrência da DPEMr-V são altas, apesar da intervenção cirúrgica agressiva. O tratamento tópico com imiquimod creme a 5% pode ser eficaz na remoção de lesões. Relatamos o caso de uma mulher de 72 anos com DPEMr-V comprovada por biópsia, tratada com sucesso com imiquimod, com aplicações três vezes por semana, durante 6 semanas.

Palavras-chave: doença de Paget extramamária recorrente da vulva (DPEMr-V), imiquimode

ABSTRACT

Although rare, extramammary Paget’s disease (EMPD) is a serious condition because underlying internal malignancy may accompany superficial cutaneous lesions. Extramammary Paget disease is characterised by a chronic eczema-like rash of the skin around the ano-genital regions of males and females. Under the microscope it looks very similar to the more common type of mammary Paget’s disease that occurs on the breast. Extramammary Paget disease most commonly occurs in women aged between 50-60 years. Although surgical excision is the generally accepted standard of care for EMPD. The EMPD-V recurrence rates are high, despite aggressive surgical intervention, treatment with topical imiquimod 5 percent cream has reportedly been efficacious in clearing lesions. We report the case of a 72-year-old woman with biopsy-proven EMPD-V of the thigh treated successfully with imiquimod application thrice weekly for 6 weeks.

Keywords: extramammary Paget’s disease of the vulva (EMPD-V), imiquimod

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ted leukoplakia-like lesion was observed on the vulvar and gluteus area. The biopsy specimen was positive for rEMPD-V and the differential diagnosis was confirmed by histopathology (HE – Figure 1b) and immunohistochemistry (Table 1). The immunohistochemistry was positive for CK 7 (Figure 1c), EMA (Figure 1d) and CEA (Figure 1e).

Due to chronic underline diseases a surgery was not advised to the 72 years old patient. Therapeutic options were discussed with the patient and she agreed to undergo and patient consent form signed to treatment with imiquimod 5% cream for 6 weeks.

The imiquimod treatment was started on 10.08.2005. One week after, she attended the emergency room with headache and influenza-like symptoms. She received medical attention and also a gynecological evaluation (Figure 2). Due to pain, burning and ulceration at the target site she returned on 24.08.2005 (Figure 3) and the topical application was discontinued for two weeks. On the next visit, she presented significant improvement with only a mild hyperemia (Figure 4) and the medication was restarted. After the complete treatment schedule, the patient evaluation and biopsy were negative (Figures 5a-d). The follow-up confirmed successful disease approach (Figure 6). The patient has remained clinically free of EMPD-V for approximately 1 year.

![Figure 1b](image1b.png)
**Figure 1b** – Representative biopsy specimen of rEMPD-V with Paget's cells (15.06.2005).

![Figure 1c](image1c.png)
**Figure 1c** – CK 7 (15.06.2005).

![Figure 1d](image1d.png)
**Figure 1d** – EMA (15.06.2005).

![Figure 1e](image1e.png)
**Figure 1e** – CEA (15.06.2005).

![Figure 2](image2.png)
**Figure 2** – rEMPD-V evaluation one week after topical treatment with imiquimod 5% (17.08.2005).
Figure 3 – Local adverse events associated with imiquimod use inducing treatment discontinuation (24.08.2005).

Figure 4 – Lesion improvement at treatment target site – 2 weeks of treatment followed by 2 weeks of topical imiquimod temporary discontinuation (08.09.2005).

Figure 5a – rEMPD-V remission after completion of imiquimod topical therapy. Clinical evaluation.

Figure 5b – To confirm freedom from disease seven sharp punch biopsies were done and showed none sign of recurrent disease (11.11.2005).

Figure 5c – Mild chronic inflammation in the absence of pagetoid cells (11.11.2005).

Table 1 – Immunohistochemical Staining.

<table>
<thead>
<tr>
<th>Immunohistochemistry</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>CK 7</td>
<td>Positive</td>
</tr>
<tr>
<td>EMA</td>
<td>Positive</td>
</tr>
<tr>
<td>CEA</td>
<td>Positive</td>
</tr>
<tr>
<td>GCDFP-15</td>
<td>Weakly positive</td>
</tr>
<tr>
<td>HMB-45</td>
<td>Negative</td>
</tr>
<tr>
<td>S-100 protein</td>
<td>Negative</td>
</tr>
<tr>
<td>Melan-A</td>
<td>Negative</td>
</tr>
<tr>
<td>c-erbB-2</td>
<td>Negative</td>
</tr>
<tr>
<td>p53</td>
<td>Negative</td>
</tr>
</tbody>
</table>
CONCLUSION

The management of EMPD-V can be challenging and occasionally frustrating. Several factors contribute to the disease recurrence and treatment failures. This report suggests that Imiquimod may be considered as an alternative treatment for patients with rEMPD-V avoiding suffering, permanent disfiguration and functional deficits. The immune response modifier, imiquimod cream, appears to be a promising additional therapy.

Conflict of interest

No conflict of interests to be declared.

REFERENCES


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