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LETTERS TO THE EDITOR

Genital Warts, Lymphangioma, and Treatment with Imiquimod[☆]



Verrugas genitales, linfangioma y tratamiento con imiquimod

Dear Editor:

After carefully reading the letter to the editor, “Genital Warts, Lymphangioma, and Treatment with Imiquimod”, by Monteagudo et al.¹ concerning our recently published case report, we would like to respond with several clarifications.

The patient was an adult woman who presented with multiple papular lesions, some pedunculated, in the vulvar region, which had first appeared some years earlier. She reported that she had been assessed 5 years earlier for similar lesions, which were diagnosed as genital warts (*condyloma acuminata*) and treated with imiquimod cream 5% applied 3 times a week for less than 16 weeks, with apparent complete resolution of the lesions and no local side effects of note. However, since this information was reported to us by the patient when we first recorded her medical history, we do not have the results of any histologic study or molecular diagnostic tests with genotyping of the human papillomavirus that would allow us to confirm the diagnosis definitively.

On physical examination, the lesions, which were located on the anterior vulvar fourchette and the labia majora, were observed to be highly monomorphic and composed of multiple papular elements forming a cobblestone pattern. We also observed an increase in the volume of the mons pubis and slight edema of the soft tissue. The patient reported that the edema had been present for a long time and was not related to the application of the imiquimod cream.

Given the complexity of the differential diagnosis, one of the wart-like lesions was biopsied and imaging studies were carried out; the results facilitated a diagnosis of acquired circumscribed vulvar lymphangioma.¹

In this case, the treatment option chosen was surgical excision of the larger lesions and curettage and electrodesiccation of the smaller lesions, with a good clinical

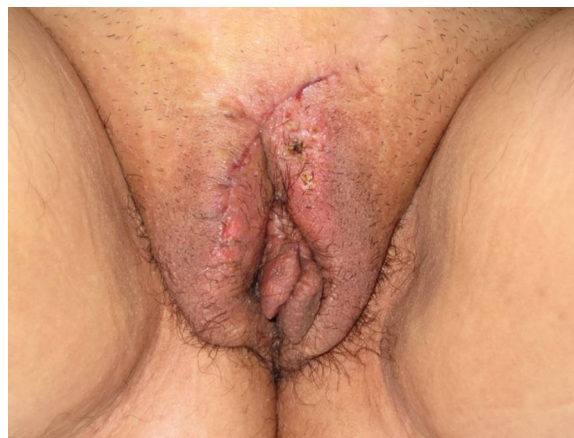


Figure 1 Clinical appearance of vulvar lesions following surgery and electrocoagulation.

and cosmetic outcome (Fig. 1). The patient has remained asymptomatic, but is being followed up regularly with cycles of cryotherapy to treat small papular elements that continue to appear.

With respect to the hypothesis suggested by Monteagudo et al. regarding the possible etiologic and pathogenic role of imiquimod in lymphedema, and consequently in the appearance of vulvar lymphangiomas, we consider that it is more likely that the lesions presented by this patient 5 years earlier were also vulvar lymphangiomas and that they responded partially to imiquimod, as described in other cases reported in the literature.²

As has been reported previously, imiquimod can act as an angiogenesis inhibitor through the induction of endothelial cell apoptosis and the inhibition of interleukins and other proangiogenic factors.³ There have been reports of its usefulness, with variable response, in the management of vascular lesions of different types: infantile hemangiomas,⁴ lymphoendotheliomas,⁵ lymphangioma circumscriptum,⁶ and Kaposi sarcoma⁷ affecting both genital⁸ and nongenital areas.

In conclusion, we reported on a case of acquired vulvar lymphangioma circumscriptum, a condition that can, given the site affected, present a diagnostic challenge because of the similarities with genital warts as well as a therapeutic challenge because it tends to recur. With respect to treatment, some authors have reported the usefulness of ablative approaches, including surgical excision, laser therapy, and

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cryotherapy and of topical antiangiogenic treatments, particularly imiquimod and rapamycin.⁹

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L. Padilla-España,* J.B. Repiso-Jiménez,
J.F. Millán-Cayetano

*Servicio de Dermatología, Hospital Costa del Sol,
Marbella, Spain*

*Corresponding author.

E-mail address: laura.padilla.espana@gmail.com

(L. Padilla-España).

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Dear Editor:

We have read with interest the article “Pseudoverrucous Lesions of Recent Appearance on the Vulva” in which the authors report the case of an adult woman with acquired vulvar lymphangioma.¹ In their article they stress the need to correctly diagnose the condition and to avoid confusion with other disorders, such as genital warts, in order to identify the appropriate treatment and the underlying cause (lymphadenectomy, radiation therapy for pelvic carcinoma, Crohn disease, or tuberculosis).^{1,2}

In the clinical history, the authors note as an interesting fact that the patient had been diagnosed 5 years earlier with genital warts, which were treated successfully with imiquimod 5% cream. In our opinion, the value of the article would have been even greater if the authors had analyzed the possible role of imiquimod therapy in the pathogenesis of the lymphangioma.

It is possible that the imiquimod therapy may, while resolving the infectious process, have given rise to

lymphedema and that this condition then favored the development of the lymphangioma. Edema and lymphedema are adverse effects reported to be associated with imiquimod treatment. These conditions may resolve rapidly (for example, in the genital area),³ or persist for months or even years (reported in 1 case on the cheek following prolonged use of imiquimod to treat lentigo maligno melanoma).⁴ The influence of lymphedema on the development of lymphangiomas is also well known.^{2,5}

We do not know whether the initial diagnosis of genital warts was confirmed by histopathology. If that diagnosis was not confirmed, it is possible that the earlier lesions were, in fact, lymphangioma. In that event, the interest of the case would be in the partial response to treatment with imiquimod. Imiquimod has been shown to be an effective therapy in some cases of lymphangioma circumscriptum. Occasionally, as occurred in this case, the lesion recurs months later.⁶ It is thought that imiquimod has an antiangiogenic effect and induces apoptosis of the tumor cells.^{6,7}

In conclusion, we found this recent report of a cases of acquired lymphangioma circumscriptum very interesting. It would be important to know what imiquimod regimen was used and the duration of treatment, as this information could be used to hypothesize about the possible role of imiquimod in the development of the lymphangioma.

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