Cutaneous leishmaniasis of the face treated with imiquimod 3.75%☆

Leishmaniasis cutánea facial tratada con imiquimod al 3,75%

Cutaneous leishmaniasis (CL) is an infection with a global distribution, considered a ñeglecteddisease by the World Health Organisation, and which affects up to one million people each year. Its management represents a therapeutic challenge due to the toxicity of the drugs used and the possible development of resistance to them. In this context, American infectious disease and tropical medicine guidelines[1] do not recommend any particular first-line treatment and advocate for a personalised choice depending on the characteristics of the lesion, the parasite and the host. We report the case of a patient with CL of the face treated with imiquimod 3.75%, a concentration not previously reported in the treatment of CL.

A 21-year-old Spanish female, with no disease history of note or recent travel, sought treatment for an asymptomatic, firm, erythematous–oedematous plaque on the tip of her nose, measuring 2 cm in diameter, which had developed two months earlier (Fig. 1a). Histology testing showed lymphohistiocytic dermal inflammatory infiltrate. Molecular testing (polymerase chain reaction) confirmed *Leishmania infantum* infection. Faced with the difficulty in infiltrating intralesional meglumine antimoniate, given the lesion's induration and location, a decision was made to start imiquimod 3.75% (Zyclara, Meda Pharma) on alternate days. The patient had an inflammatory reaction (Fig. 1b) that was well-tolerated, and so the treatment was continued for two months. After four months of follow-up, no relapse has been seen and the lingering aesthetic defect is minimal (Fig. 1c).

Imiquimod is a topical immunomodulator approved for the treatment of viral warts and premalignant cutaneous lesions. In CL, imiquimod stimulates secretion of interferon gamma by CD4 T helper-1 lymphocytes by activating macrophages to destroy amastigotes.[2] This mechanism of action would reduce the development of resistance, and we believe that it could be useful for treating areas of subclinical infection (i.e. apparently healthy areas surrounding the lesion that are actually infected), as in its use for the treatment of premalignant lesions. Indeed, in our patient, the inflammatory reaction in the area treated (Fig. 1b) was slightly greater than in the clinically affected area (Fig. 1a). Imiquimod 3.75% causes a more controlled inflammatory reaction than imiquimod at higher concentrations. It was formulated to improve problems of tolerability and adherence to the drug at a concentration of 5%. This reduced inflammatory reaction also leads to a better aesthetic outcome, making it particularly interesting as a treatment for facial lesions. There is no evidence on the use of imiquimod at low concentrations to treat CL.

Seeberger et al.[3] found that imiquimod 5% showed temporary effectiveness as a treatment for CL. Crawford et al.[4] concluded that imiquimod 5% was superior to intralesional pentavalent antimoniate, both in monotherapy and in combination with the latter. Other authors[5–7] have demonstrated its effectiveness at concentrations of 5% and 7.5%, as co-adjuvant treatment to pentavalent antimoniates. However, two other similar studies[8,9] did not succeed in yielding the same results. In addition, isolated cases of response to imiquimod in CL resistant to first-line treatments have been published, suggesting that it could be an alternative should the parasite develop resistance.[10]

Facial CL should always be treated with a view to minimising the aesthetic consequences.[1] In cases of localised CL in immunocompetent patients in the Old World, local options are the treatments of choice.[1] In our case, imiquimod 3.75% was chosen to limit the inflammatory reaction in an aesthetically significant area. Our patient showed highly satisfactory results and good drug tolerance.

Given the variety of scenarios possible in CL and the disadvantages associated with the treatments available, the outcome in this case suggests that imiquimod at low concentrations may be a good treatment option in cases of CL with no criteria for systemic treatment, in aesthetically compromised areas, especially where the infiltration of pentavalent antimoniates is problematic or there is resistance to them.

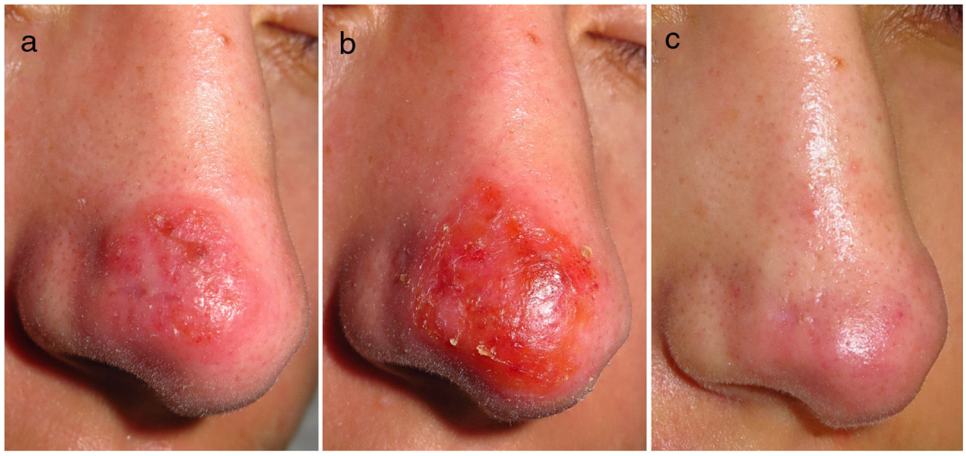

Figure 1. Course of cutaneous leishmaniasis: before, during and after imiquimod 3.75%. **(a)** Erythematous–oedematous plaque on the patient's nose prior to starting treatment. **(b)** Local inflammatory reaction three weeks after starting imiquimod. **(c)** The patient's nose with no leishmaniasis lesions four months after ending treatment.

DOI of original article: https://doi.org/10.1016/j.eimc.2020.04.005.

☆ Please cite this article as: Marti-Marti I, Alsina M, Giavedoni P, Fuertes I. Leishmaniasis cutánea facial tratada con imiquimod al 3,75%. Enferm Infecc Microbiol Clin. 2021;39:108–109.

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https://doi.org/10.1016/j.eimce.2020.11.012

Importance of prediction of bacteremia in the emergency departments: Six years later☆

Importancia de la predicción de bacteriemia en los servicios de urgencias: seis años después

Dear Editor,

Six years ago, we had the honour of publishing a review in Enfermedades Infecciosas y Microbiología Clínica under the title "Utilidad de los biomarcadores de inflamación e infección en los servicios de urgencias" [Usefulness of inflammation and infection biomarkers in the Emergency Department].[1] The goal of this review was to set out the published scientific evidence, clarify existing points of debate, compare the usefulness of the main inflammation and infection biomarkers (IIBMs) and, based on these, produce a number of recommendations for the use thereof in order to improve the diagnosis, prognostic assessment and management of patients with infection in the emergency department. The different models for predicting bacteraemia published up to then were also reviewed, from the most widely used and validated in emergency departments (EDs), such as that by Shapiro et al.,[2] to other simpler ones that have also been used and even validated following the publication of the review, such as that by Cuervo et al.[3] However, we then concluded that it was necessary to continue the search for a more useful bacteraemia model that was easier to obtain in patient care in EDs, so that it could be implemented in regular clinical practice.[1] In the same way, reference was made to different considerations in indicating and acquiring blood cultures in EDs. Although even today there are no definitive answers to all the questions that were raised back then, there has indeed been significant progress, just as we sought back then and continue to do so now,[4] through collaborative efforts from scientific associations in the fields of emergency medicine and infectious disease with shared problems, language and realities.[5]

The end of that review highlighted, in one of its concluding remarks, that, in the near future, other variables, including IIBMs,[6] would eventually be incorporated into the classic models used almost exclusively up to then, such as that by Shapiro et al.[2] In this vein, following six years of research, procalcitonin (PCT) can be said to have filled a significant gap in the latest predictive models published, which are better able to offer a prognosis as to the presence of bacteraemia[7]; this has been acknowledged by various authors who, in recent articles, have individually investigated predictive factors for bacteraemia. For these, the finding of a PCT level $\geq$0.51 ng/ml yielded the best prognostic performance among the different variables analysed, with an odds ratio of 4.52 (95% confidence interval [CI]: 4.20–4.84, $p < 0.001$).[8] Similarly, in articles comparing the results of several IIBMs for predicting sepsis and bacteraemia in patients diagnosed with serious infection in EDs,[9,10] PCT yielded a similar performance for the diagnosis of sepsis than, for example, presepsin. However, its power was significantly superior to presepsin for predicting bacteraemia in blood cultures obtained in the ED from patients with suspected serious infection.[4,9] All this has enabled the development and validation in a recently published study of a predictive model for bacteraemia with five variables ("5MPB-Toledo").[7] The model includes temperature >38.3 °C (1 point), Charlson Comorbidity Index $\geq$3 (1 point), respiratory rate $\geq$22 respirations per minute (1 point), leukocyte count >12,000/mm^3 (1 point) and PCT $\geq$0.51 ng/ml (4 points). Patients are categorised as low-risk (0–2 points), moderate-risk (3–5 points) or high-risk (6–8 points), with a likelihood of bacteraemia of 1.1%, 10.5% and 77%, respectively. The area under the curve of the receiver operating characteristic (AUC-ROC) for the model following re-sampling was excellent: 0.946 (95% CI: 0.922–0.969).

Therefore, as suspicion of bacteraemia from EDs is extremely important for patients and for the system (taking blood cultures, administering suitable antimicrobials early, deciding to admit or to

☆ Please cite this article as: Rubio Díaz R, Nieto Rojas I, Julián-Jiménez A. Importancia de la predicción de bacteriemia en los servicios de urgencias: seis años después. Enferm Infecc Microbiol Clin. 2021;39:108–109.