ORIGINAL REPORT

Cutaneous Leishmaniasis in Patients under Biologic Therapies: A Spanish CLINI-AEDV Multicentre Study

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Anti-TNFα agents have been associated with the reactivation of granulomatous infections, including leishmaniasis. Cases of atypical or recurrent cutaneous (CL) or mucocutaneous leishmaniasis (MCL) have been reported in patients on biologics. We conducted a retrospective analysis of a multicenter database to describe the clinical characteristics and management of CL and MCL in patients receiving biological therapy in an endemic area. Clinical features, diagnostics, therapies, and outcomes were analyzed. Seventy-one patients were included (63 CL and 8 MCL). The most common underlying condition was inflammatory bowel disease (33.8%). Lesions were multifocal in 40% and larger than 1 cm in 94.4%. Treatment failures were more frequent in MCL (50%) than CL (8.1%). Biologic therapy was discontinued in 53.5%, leading to worsening of the underlying disease in 44.7%. No significant difference in cure rates was observed between patients who continued vs. discontinued biologics (p=0.868). These findings highlight the clinical burden of CL and MCL in patients undergoing anti-TNFα therapy and suggest that discontinuation of biologic therapy did not significantly impact cure rates, emphasizing the need for standardized strategies balancing infection control and underlying inflammatory disease management.

Key words: leishmaniasis; parasitic; biological therapies; immunosuppression; TNFα antagonist; opportunistic infection.

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Leishmaniasis is a chronic protozoan infection of the mononuclear phagocyte system caused by various species of *Leishmania* and transmitted by female sandflies of the genera *Phlebotomus* (Old World) and *Lutzomyia* (New World). An estimated 700,000 to 1 million new cases occur annually worldwide. It is endemic in more than 90 countries, predominantly affecting regions of the Mediterranean basin, the Middle East, South America and parts of Asia and Africa. The clinical manifestations of leishmaniasis depend on several factors, particularly the virulence of the causative microorganism and the host immune response. *Leishmania* infection can manifest as a skin disease (cutaneous leishmaniasis, CL) and/or as involvement of mucous membranes (mucosal or mucocutaneous leishmaniasis, MCL) or even internal organs (visceral leishmaniasis, VL).

Leishmania infantum is the major causative agent of leishmaniasis in Southern Europe. In Mediterranean endemic areas, CL accounts for approximately 80–90% of reported cases, MCL for 5–15%, and VL for less than 10%, with Spain being one of the European countries with the highest reported incidence. In immunocompetent individuals, the immunity of the host is capable of controlling the infection, and the natural course of CL is often benign and tends to heal spontaneously (1, 2). Immune suppression may interfere with immune-mediated mechanisms implicated in the control and eradication of the parasite, leading to a reactivation of a latent parasitic disease (3–5).

A polarized Th1 response with reduced Th2 cytokine activity has been associated with infection resistance and disease outcome (5).

Over the past decade, an increased number of biologic drugs have been introduced in the therapeutic armamentarium of different inflammatory and immune-mediated diseases. Treatments targeting tumour necrosis factor-α (TNFα) or interleukins have been identified as risk factors for the development and/or reactivation of several infectious diseases including leishmaniasis. Particularly, TNFα plays a critical role in host defence against various infectious diseases and its relevance in the immune response to *Leishmania* has already been investigated (6–10). TNFα has been implicated in the initial events of the infection, presenting a direct leishmanicidal activity, controlling parasite multiplication and promoting effective acquired immunity (4–6). Moreover, regulatory T cells and Th17 cells also appear to play significant roles in susceptibility and disease resistance (5, 7). In the literature, clinical manifestations of CL in patients receiving biologics have been described as atypical and more severe, frequently characterized by larger and more extensive ulcers, multifocal involvement and, in some cases, disseminated cutaneous disease (8–15).

Additionally, the incidence of leishmaniasis is increasing in endemic regions such as the Mediterranean basin, probably in relation to factors like climate change, expanded travel and population migration (2, 3). A paradigmatic example is the large outbreak that occurred in the Madrid region between 2009 and 2012, which revealed the role of suburban transmission, wild hares as a key sylvatic reservoir of *L. infantum* and immunosuppressed hosts in the emergence of atypical and more complex clinical presentations (16).

This study aims to characterize the demographic and clinical profiles of CL in patients treated with biologic drugs, as well as the clinical approaches adopted by dermatologists in Spain, a country with endemic areas of the disease. Currently, there are no standardized clinical guidelines for the management of CL in patients undergoing biologic therapy, leading to variability in clinical decisions regarding whether to discontinue biologic treatment, perform additional extension studies or select appropriate therapies.

MATERIALS AND METHODS

Study design

We conducted a retrospective study of a prospectively collected multicentre database (CLINI-AEDV registry). Participating dermatology centres were required to include all prospective cases through the CLINI-AEDV platform, created by the Spanish Academy of Dermatology and Venerology (AEDV) (17). All centres followed a standardized data collection protocol implemented through this platform, including shared definitions. Data were collected and managed using the REDCap (Research Electronic Data Capture) system. CL was defined as the presence of one or more enlarging, slow-healing skin lesions caused by *Leishmania,* confirmed by one diagnostic method (histopathology, immunohistochemistry or specific qPCR amplification). MCL was defined as a form of leishmaniasis involving mucous membranes. Patient recruitment commenced on 20 March 2024 and concluded on 30 June 2024, spanning 14 weeks. Invitations to participate were sent to 87 CLINI-AEDV centres, encompassing both hospitals and private practices.

Study population

All patients with confirmed CL or MCL while receiving treatment with biologic agents were included in the study. Dermatologists enrolled patients during routine clinical practice. Both adult and paediatric patients were included in this series, with no upper or lower age limit for eligibility. All patients, or their legal guardians in the case of minors, provided their informed consent. Patients who consented to include clinical images signed a specific informed consent form.

Measures and variables

For each patient, data were collected on the type of biologic therapy, its indication and the duration of treatment. Clinical information recorded included the clinical form of leishmaniasis, number of lesions, size of the largest lesion, its anatomical location and whether there was mucosal or systemic involvement. Diagnostic methods, *Leishmania* species (if identified) and the extent of any diagnostic studies (if performed) were recorded. Treatment regimens and clinical outcomes at the last follow-up were also recorded, with particular attention to patients who discontinued biologic therapy. Treatment failure was defined as either nonresponse, indicated by persistent symptoms at the end of the treatment, or recurrence, defined as the reappearance of clinically compatible lesions within 6–12 months after apparent clinical cure, with microbiological confirmation when feasible.

Statistical analysis

Descriptive analyses were performed using absolute values and percentages for categorical variables, mean±standard deviation (SD) for normally distributed continuous variables, median (interquartile range, IQR)

for non-normally distributed continuous variables. Comparisons of categorical variables were conducted using Fisher exact test, while continuous variables were compared using Student *t*-test (for means) or Wilcoxon test (for medians). *p*-Values <0.05 were considered statistically significant. Statistical analyses were conducted using STATA v.17.0 (Stata Corp. 2021. Stata Statistical Software: Release 17).

RESULTS

Seventy-one patients from 17 centres were included, predominantly from the Mediterranean area. Forty-nine patients (69%) were male, the mean age was 53 years (SD: 15.6). The most frequent underlying condition was inflammatory bowel disease (IBD) in 24 patients (33.8%), followed by psoriasis in 17 (23.9%). Most patients (94.4%) were receiving anti-TNFα therapy, with most therapies lasting for more than 12 months (87.3%). None of the patients included in the series presented immunosuppression related to HIV infection or solid organ transplantation. However, 58 out of 71 patients (81.7%) had received other immunosuppressive treatment in the context of their underlying inflammatory disease.

Sixty-three patients (88.7%) presented with CL, and 8 patients (11.3%) had MCL. One patient (1.4%) with CL subsequently developed visceral involvement. The most common lesion types were plaques in 29 (40.9%) and nodules in 28 cases (39.4%). The mean size of the largest lesion was 2.9 cm (range: 0.5–10 cm). The most affected areas were the arms and forearms, followed by the head and neck. Two or more lesions were observed in 27 out of 63 patients with CL (42.9%).

Leishmaniasis was diagnosed through direct observation of amastigotes in routine histopathological examination in 59 patients (81.9%) and by *Leishmania* polymerase chain reaction (qPCR) positivity in skin samples in 46 patients (64.8%). In 29 patients (40.9% patients), the species of *Leishmania* involved could be identified, reflecting limited access to species-level PCR in some centres and the use of alternative diagnostic methods. As expected, the most frequently found species was *L. infantum* in 26 patients (36.6%), followed by *L. donovani* in 3 patients (4.2%). Extension studies varied upon clinicians: complete blood tests in 54 (76.1%), abdominal ultrasound in 31 (43.7%) and bone marrow aspiration in 7 patients (9.9%).

The most common local therapy was intralesional antimonials in 49 patients (69%), followed by cryotherapy in 6 (8.5%). Cryotherapy was mainly used as an adjunctive treatment rather than as monotherapy (in 7 out of 8 patients). Among systemic treatments, amphotericin B (36.6%) and parenteral pentavalent antimonials (9.9%) were the most frequently used agents. Clinical resolution after the first treatment course was achieved in 57 cases (80.3%). The median disease-free follow-up period was 39 months (IQR: 10–60 months). Additional epidemiological, clinical and therapeutic details are summarized in **Table I**.

Nine patients (5 with CL and 4 with MCL) experienced treatment failure, defined either as recurrent (6 cases) or persistent disease (3 cases), as illustrated in **Table II**. Treatment failure was observed in 5 of 63 CL cases (7.9%) and in 4 of 8 cases of MCL (50%). All patients were receiving anti-TNFα therapy, often for prolonged periods (88.9%). All recurrences underwent an extension study, consisting of blood test and/or abdominal ultrasound. Systemic therapy, alone or combined with local treatments, was prescribed in all patients presenting treatment failure. In 4 of 9 cases, biologic therapy was discontinued, with half of these patients experiencing worsening of their underlying immune-mediated condition. Notably, in 2 patients, reintroduction of biologic therapy led to recurrence of CL.

Following diagnosis, biological therapy was continued in 46.5% of patients and withdrawn in 53.5%. As presented in **Table III**, among those who achieved complete cure (26 who continued and 31 who discontinued biologic treatment), no statistically significant differences in outcomes were observed between the two groups (p=0.868). However, worsening of the underlying immune-mediated disease was reported in 17 of 38 patients who discontinued biologic therapy (44.7%).

DISCUSSION

In our cohort, and in concordance with other series (9–15), TNFα inhibitors were the biologic agents most frequently associated with CL (94.4%). Treatment with anti-TNFα is usually prescribed for a wide range of immune-mediated disorders including IBD, rheumatic diseases or psoriasis. Interestingly, psoriasis itself has been linked to an increased risk of CL (18).

This large multicentre study of CL and MCL in patients receiving biologic therapy within an endemic region provides a representative overview of this growing patient population. CL was by far the most reported form of leishmaniasis in patients receiving biologics (88.7%), with previous series ranging from 60 to 90%, followed by MCL (11.3%), varying from 10 to 32% in prior reports (9–12). VL has been reported at variable frequencies, ranging from 1.4 to 33%.19, 20 In agreement with our results, a recent Spanish cohort of patients with IBD who developed leishmaniasis also identified CL as the predominant phenotype (85%), with a small proportion of VL (11%) (15).

Regarding risk factors for VL, age has been identified as the only independent predictor of visceral involvement, whereas biologic therapy,

Table I. Demographic, clinical, therapeutic and outcome features after a median disease-free follow-up of 39.4 months (SD: 40.9 months)

	N (71)	%/SD
Gender		
Male	49	69.0
Female	22	31.0
Age (years), mean (SD)	52.9	15.6
Geographic area		
Mediterranean area[a]	64	90.1
Others (Madrid and Canary Island)	7	9.9
Disease for which receiving biologic		
Inflammatory bowel disease	24	33.8
Rheumatologic disease other than psoriasis	23	32.4
Psoriasis	17	23.9
Others (hidradenitis, atopic dermatitis…)	7	9.9
Type of biologic		
Anti-TNFα	67	94.4
Others[b]	4	5.6
Duration of the treatment		
Less than 6 months	3	4.2
>6 and <12 months	5	7.1
More than 12 months	62	87.3
Unknown	1	1.4
Type of lesion		
Plaque	29	40.9
Nodule	28	39.4
Papule	12	16.9
Others (erysipela…)	2	2.8
Number of lesions		
1	42	60.0
2	12	17.1
3	5	7.2
4 or more	10	15.7
Size of the largest lesion in each patient (cm), mean (SD)	2.9	2.3
Location	*n*=88	
Typical exposed areas[c]	61	69.3
Atypical hidden areas	27	30.7
Type of leishmaniasis		
Cutaneous	63	88.7
Mucocutaneous	8	11.3
Visceral	1	1.4
Local treatment		
Intralesional antimonials	49	69.0
Photodynamic therapy	1	1.4
Cryotherapy	6	8.5
Systemic treatment		
Amphotericin B	26	36.6
Parenteral antimonials	7	9.9
Miltefosine	6	8.5
Fluconazole	5	7.0
Itraconazole	3	4.2
Discontinuation of biological treatment		
No	33	46.5
Yes	38	53.5
Outcome at last follow-up		
Complete cure	57	80.3
Persistence (no initial cure)	3	4.2
Recurrent course (initial cure and relapse)	6	8.5
Unknown	5	7.0
Number of recurrences		
1	5	1.4
2	1	2.8
Worsening of underlying disease		
No	48	67.6
Yes	18	25.3
Unknown	3	4.2
Disease-free follow-up time (months), mean (SD)	39.4	40.9

[a]Mediterranean endemic area includes Catalonia, Valencian community, Balearic Islands and Murcia.
[b]Other biologic drugs included anti-IL 12/23 (1), anti-IL 23 (1) and anti-IL 4 (1).
[c]Typical areas exposed to mosquito bites included arms and forearms, head and neck, legs and hands and wrists. Hidden and atypical areas of LC included thighs, back, abdomen, breast and axilla, buttocks and feet. It is important to note that patients presented with more than one lesion in different locations (total of lesions: 88).

mainly anti-TNFα agents, has been more strongly associated with cutaneous or mucocutaneous forms (15). Together with our findings, this suggests that host factors, particularly advanced age, play a greater role than exposure to biologic therapy in determining visceral tropism, while patients receiving biologics in Mediterranean endemic settings predominantly develop CL or MCL.

A notable finding in our series was the high proportion of extensive and multifocal lesions. Almost half of patients with CL (42.9%) presented two or more lesions, and in most cases (94.4%), lesion size exceeded 1 cm in diameter, with a mean of 2.9 cm. Disseminated forms – defined as the presence of lesions distributed across separate body areas (21) – were observed in 15.7% of patients.

In previous series, immunosuppressed patients frequently exhibited multiple lesions, often exceeding four in number, whereas immunocompetent individuals typically presented with discrete solitary papules or plaques measuring 5–10 mm in diameter (22–26). Similarly, patients treated with anti-TNFα drugs have been reported to develop unusually large, multifocal lesions with little or no spontaneous regression (8, 15).

Accordingly, Palacios-Díaz et al. (8) observed that lesions in biologic-treated patients were predominantly ulcerated plaques (92%), of larger median size (2.5 cm) and requiring a higher number of intralesional meglumine antimoniate infiltrations than controls not exposed to biologics. Another retrospective review of 49 Mediterranean cases of leishmaniasis under anti-TNFα therapy found that 10 of 28 patients with CL presented with multifocal lesions (9). These consistent observations suggest that biologic-induced immunomodulation may alter lesion morphology and healing kinetics, without increasing the risk of visceral dissemination.

The diagnosis of CL or MCL can be particularly challenging, as its clinical presentation often mimics other ulcerative or granulomatous dermatoses, including syphilis, nontuberculous mycobacterial infections and deep mycoses, or even noninfectious conditions such as squamous cell carcinoma (27). The presence of atypical or multiple lesions in this patient population may further complicate the already difficult clinical recognition of leishmaniasis. Consequently, studies like the present one are crucial to better characterize the clinical spectrum of leishmaniasis in this specific setting, aiding clinicians in improving early diagnosis and management. Representative clinical and dermoscopic features of CL in patients with anti-TNFα therapy are illustrated in **Fig. 1**.

The natural history of CL caused by Old World species tends to heal spontaneously, being generally more prolonged for *L. infantum*, which predominated

Table II. Characteristics of failures: persistent and recurrent cases

Pat. No.	Course of failure	Gender	Age at diagnosis	Underlying disease	Type of biologic therapy	Duration of biologic therapy (months)	Lesions, *n*	Type of leishmaniasis	Identified species	Local treatment	Systemic treatment	Treatment withdrawal
1	Recurrent	Female	42	Other	Anti-TNF	>12	1	MCL	*L. infantum*	IAM	Mitefosine, IvAM	No
2	Recurrent	Female	57	Nonpsoriatic rheumatologic disease	Anti-TNF	>12	1	MCL	*L. infantum*	IAM	AnfB	No
3	Recurrent	Male	50	Inflammatory bowel disease	Anti-TNF	>12	1	MCL	*L. infantum*	IAM	AnfB	Yes
4	Recurrent	Male	53	Inflammatory bowel disease	Anti-TNF	>12	3	CL	*L. infantum*	None	Mitefosine, IvAM	No
5	Persistent	Male	79	Non-psoriatic rheumatologic disease	Anti-TNF	>12	5	CL	*L. donovani*	IAM	Fluconazole	No
6	Persistent	Male	73	Psoriasis	Anti-TNF	>12	2	CL	No	IAM	None	Yes
7	Recurrent	Male	74	Nonpsoriatic rheumatologic disease	Anti-TNF	>12	4	CL	No	IAM	AnfB	No
8	Recurrent	Female	64	Psoriasis	Anti-TNF	>12	1	MCL	No	None	Miltefosine	Yes
9	Persistent	Male	56	Inflammatory bowel disease	Anti-TNF	6–12	1	CL	No	IAM, cryotherapy	None	Yes

AnfB: amphotericin B; CL: cutaneous leishmaniasis; IAM: intralesional antimonials; IvAM: intravenous antimonials; MCL: mucocutaneous leishmaniasis.

in our cohort, compared with other species such as *L. major*. Indeed, when lesions are smaller than 5 cm in diameter and are located in areas without risk of disfigurement or functional impairment, simple wound care alone is generally sufficient (1, 25). The reactivation of latent parasites within granulomatous lesions could provide a feasible explanation for the development of leishmaniasis under TNFα inhibitor treatment (3–5).

Although some authors have suggested that discontinuing TNFα therapy improves treatment outcomes (12, 13), our analysis revealed no statistically

Table III. Comparison between patients who continued and discontinued biologic therapy

Variables	Continuation of biologic therapy		Discontinuation of biologic therapy		
	N=33	%	*N*=38	%	*p*-value
Undergoing disease					
Inflammatory bowel disease	13	39.4	11	29.0	0.071
Non psoriatic rheumatic disease	8	24.2	15	39.5	
Psoriasis	6	18.2	11	29.0	
Others (atopic dermatitis, hidradenitis…)	6	18.2	1	2.6	
Type of biologic					
Anti-TNF	30	90.9	37	97.4	0.239
Others[a]	3	9.1	1	2.6	
Duration of biologic treatment					
Less than 6 months	0	0	3	7.9	0.248
>6 and <12 months	3	9.1	2	5.3	
More than 12 months	29	87.9	33	86.8	
Unknown	1	3.0	0	0.00	
Number of lesions					
1	18	54.5	24	64.9	0.121
2	4	12.1	8	21.6	
3 or more	11	33.3	5	13.5	
Type of leishmaniasis					
Cutaneous	30	90.9	32	84.2	0.544
Mucocutaneous	3	9.1	5	13.2	
Visceral	0	0	1	2.6	
Treatment					
Local	23	69.7	26	68.4	0.908
Amphotericin B	12	36.4	14	36.8	0.967
Parenteral antimonials	2	6.1	5	13.2	0.317
Miltefosine	4	12.1	2	5.3	0.300
Fluconazole	2	6.1	3	7.9	0.763
Itraconazole	2	6.1	1	2.6	0.474
Result at last review					
Cure	26	78.8	31	81.6	0.868
Recurrent course	3	9.7	3	8.6	
Persistence	2	6.4	1	2.8	
Number of recurrences					
1	3	100	2	66.7	0.273
2	0	0	1	33.3	
Worsening of underlying disease					
No	29	87.9	19	50	<0.001
Yes	1	3.0	17	44.7	
Unknown	3	9.1	2	5.3	

[a]Other biologic drugs included anti-IL 12/23, anti-IL 23 and anti-IL 4.

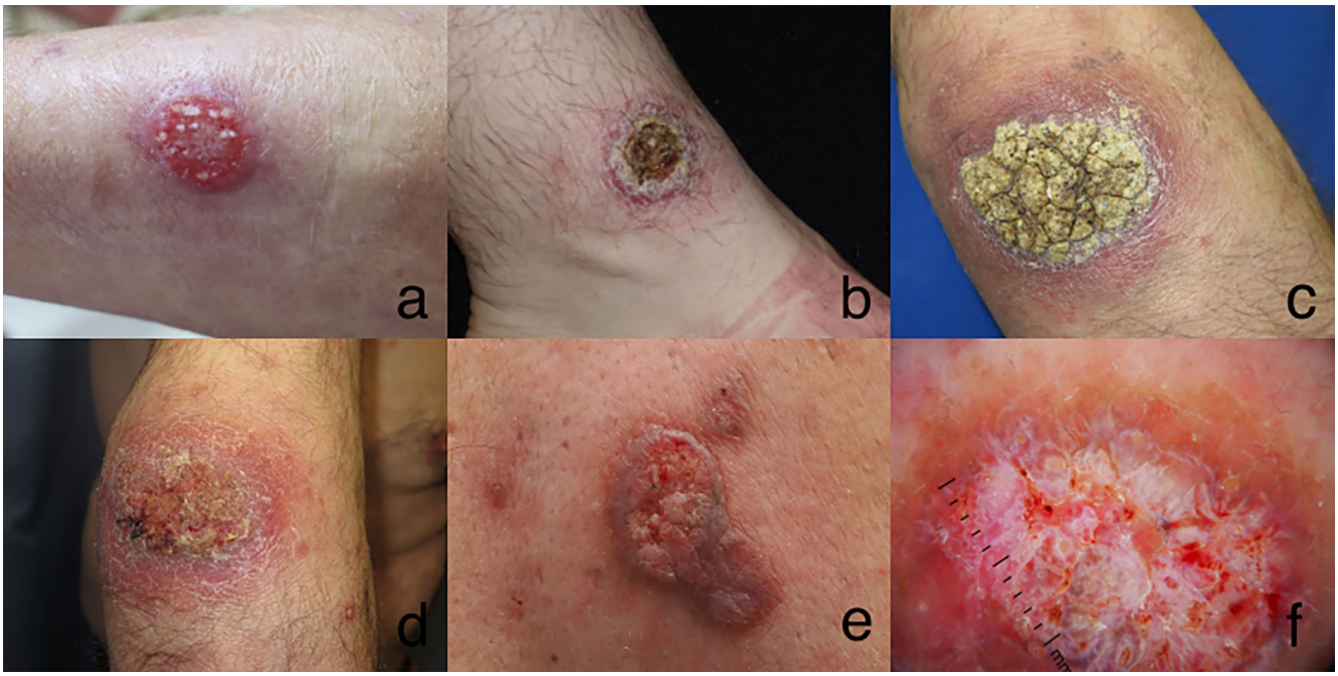

Fig. 1. Clinical features of CL infection. Clinical features of CL infection. (a) Single large plaque with erosive bleeding surface in left arm. (b) Crusted large plaque in right ankle. (c and d) Large hyperkeratotic crust plaque in the elbow of patient with Crohn's disease in treatment with infliximab before and after treatment with intralesional antimonials. (e and f) Clinical and dermoscopic features of a large ulcerated plaque on the back of a patient with suppurative hidradenitis receiving treatment with adalimumab. Note the raised edge and satellite papules.

significant differences in cure rates between patients who continued (78.8%) and those who stopped biologic therapy (81.6%) (p=0.868). However, 44.7% of patients experienced a flare or worsening of their underlying immune-mediated disease after discontinuing biologics, indicating that, with careful supervision, continuation of biologics may be a safe and viable option for non-complicated CL. This observation aligns with other studies reporting no significant differences in clinical outcomes or relapse rates between patients who maintained or discontinued biologic therapy in cases of CL and MCL (8, 15).

There are notable discrepancies in treatment approaches for patients receiving TNFα blockers (8–15). Some reports describe successful outcomes with intralesional antimonials and liposomal amphotericin B used as monotherapy, both leading to lesion resolution without relapses (9). Conversely, other studies have reported poor responses to intralesional meglumine antimoniate in patients on TNFα inhibitors, requiring systemic therapies with intravenous liposomal amphotericin B or intramuscular antimonials (28). In our series, treatment approaches varied: intralesional antimonials were the most used local therapy (69%), while systemic treatments like amphotericin B (36.6%) and pentavalent antimonials (9.9%) were also frequently administered.

Follow-up data, with a median disease-free period of 39 months, indicate that treatments can be effective in many cases, although responses are generally less favourable than in immunocompetent populations (10, 11). Indeed, persistence (4.2%) and recurrence (8.5%) of disease underscore the need for careful long-term monitoring of leishmaniasis in patients on biologic therapies.

In our series, treatment failure, defined as persistent or recurrent lesions after treatment, occurred in 50% of patients with MCL compared to 8% of cases with CL. All MCL cases were treated with systemic therapies including liposomal amphotericin B, miltefosine or intravenous antimonials. Recurrences were consistently associated with prolonged anti-TNFα exposure. After ruling out visceral involvement through blood tests, abdominal ultrasounds and peripheral blood qPCR, a different systemic regimen, often combined with local therapies were the most common approaches for treatment failures. Two-thirds of the patients experienced a relapsing course with various recurrences (associated with biologic reintroduction), suggesting that reinitiating anti-TNFα therapy after a first relapse should be avoided.

For patients with noncomplicated CL, when biologic therapy remains clinically necessary, a reasonable strategy may involve adding a systemic agent such as liposomal amphotericin B or pentavalent antimonials, using local treatments as adjuncts, while maintaining biologic therapy. In patients with very localized CL, particularly when the lesion is small and located in low-risk anatomical areas, it is plausible that

systemic antileishmanial therapy may not be necessary even if biologic treatment is maintained. In such cases, local therapies alone such as intralesional antimonials, cryotherapy or topical agents may provide satisfactory outcomes while avoiding the toxicity associated with systemic agents (29). This tailored approach is especially relevant for patients in whom discontinuation of biologic therapy could lead to significant worsening of their underlying immune-mediated disease. Additionally, close monitoring should be the rule to identify early relapses.

Switching to alternative immunomodulators, such as IL-17 or IL-23 inhibitors – which carry a lower risk of reactivating granulomatous infections – may offer improved outcomes and should be considered. This approach aligns with current recommendations for patients with psoriasis and latent tuberculosis infection who have contraindications for undergoing chemoprophylaxis (25).

Our study has some limitations. The sample size (n=71) limits the statistical power of comparative analyses and should be considered when interpreting subgroup results. Leishmania species identification was achieved in fewer than half of cases, and imported species may display distinct behaviour compared with the endemic strains in our region, potentially influencing outcomes. Furthermore, most cases were retrospectively collected from multiple centres**,** introducing possible selection and measurement bias. Finally, the relatively short follow-up period, particularly for MCL, limits our assessment of long-term relapse risk.

In conclusion, this large retrospective study from an endemic region illustrates current practices in the management of leishmaniasis in patients receiving biologic agents. Continuation of biologic therapy, combined with close and regular follow-up, may be appropriate for most cases of noncomplicated CL. However, consideration of switching to alternative immunomodulatory strategies such as IL-17 or IL-23 inhibitors may be warranted for MCL and CL cases with diffuse, locally complicated or recurrent lesions. Optimal strategies to balance the management of leishmaniasis and the underlying immunomodulatory disease remain to be defined.

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