Research Article

Reactional leprosy

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Abstract

Background. Reactional leprosy is a clinical modality of acute or subacute presentation with local or systemic involvement as the expression of an inmmune disorder, which appears in the evolutive course of the disease. It may occur in about 30 percent of multibacillary patients (MB): lepromatous and dimorphic or borderline (borderline lepromatous, BL: borderline, BB, borderline tuberculoid, BT). The lack of local published papers on clinical and epidemiological characteristics of reactional episodes (RE) are one of the reasons of this research.
Objetives. To estimate prevalence of RE of leprosy, globally and in each clinical form, identifying them as initial consultation cause, during treatment and/or during follow-up; to characterize clinical polymorphism; and to assess deficiencies/disabilities and therapeutic difficulties (thalidomide- and corticosteroid-dependence).
Design. Retrospective, descriptive of series of cases.
Material and methods. From a total of 276 patients who started leprosy treatment from January 1995 to December 2006, those developing RE (110 patients) were selected and analyzed. Statistical methods used included: prevalence, 95% confidence intervals (95% CI).
Results. Overall RE prevalence: 39.85 percent (110/276). RE prevalence in different clinical forms: lepromatous leprosy (LL) 58.11 percent (86/148); borderline leprosy 22.86% (24/105): BL 29.1 percent, BB 37.5 percent, BT 33.3 percent; tuberculoid leprosy (TT): 0%. Onset of RE: first consultation 32.72 percent (36/110), during treatment: 52.72 percent (58/110), first RE in post-treatment follow-up: 14.5 percent (16/110). Clinical presentation of type I RE: upgrading 83.3 percent (20/24), downgrading 20.83 percent (5/24). Clinical presentation of type II RE: erythema nodosum (EN) 94.19 percent (81/86), acute neuritis 20.93 percent (18/86), erythema multiforme 13.95 percent (12/86), arthritis 12.79 percent (11/86), orchitis 8.14 percent (7/86), Lucio reaction 3.49 percent (3/86), uveitis 2.33 percent (2/86), splenitis 2.33 percent (2/86). Disabilities and sequelae: 30 percent (33/110) of patients. Therapeutic difficulties: thalidomide-dependence: 54.21 percent (45/83) and costicosteroid-dependence: 15 percent (9/60).
Conclusions. Most frequent RE was erythema nodosum leprosum (ENL). Thalidomide-dependence was confirmed in over half of these patients (Dermatol Argent 2009; 15(2):125-130).

Key words: *leprosy, reactional episodes, thalidomide-dependence.*

Introduction

Reactional leprosy constitutes a clinical modality of acute or subacute presentation, local or general, as an expression of complex and diverse immune phenomena occurring during the chronic course of the disease. The reactional episode (RE) may appear before, during or after treatment, and may cause important complications and/or lead to severe disability sequelae.[1]
The local literature does not include works reflecting RE prevalence or RE clinical and epidemiological characteristics of the leprosy patients in Argentina. This information may be of great use to assess requirements and to design therapeutic strategies implemented at national level. The fact that our hospital is a reference center for infectious pathologies, mostly for a population from Great Buenos Aires (57.32 percent), is another motivating reason of special interest for our research, since it represents a significant sample of what may happen in our city, and also in the province of Buenos Aires.
The purpose is to estimate RE prevalence; to identify incidence as first consultation cause, during treatment and/or during post-treatment follow-up; to characterize clinical po-

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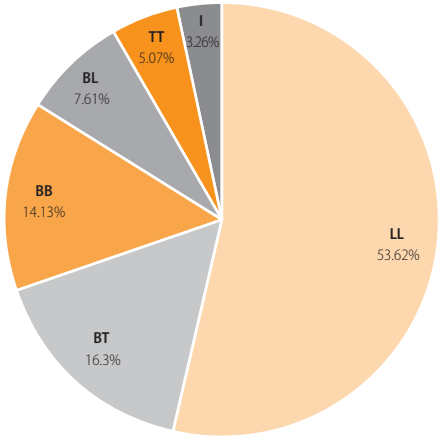

Chart 1. *Percentage of leprous patients according to the clinical classification. Hospital "F. J. Muñiz", years 1996 to 2005.*

Table of values from **Chart 1.**

Clinical form	Number	Percentage
LL	148	53.62
BT	45	16.30
BB	39	14.13
BL	21	7.61
TT	14	5.07
I	9	3.26
	276	100.00

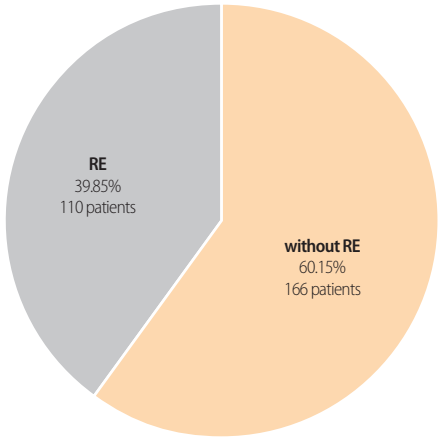

Chart 2. *Global prevalence of RE in 276 patients.*

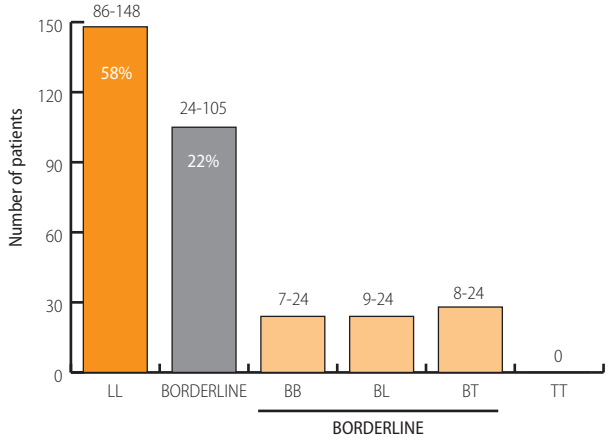

Chart 3. *Prevalence of RE in each clinical form.*

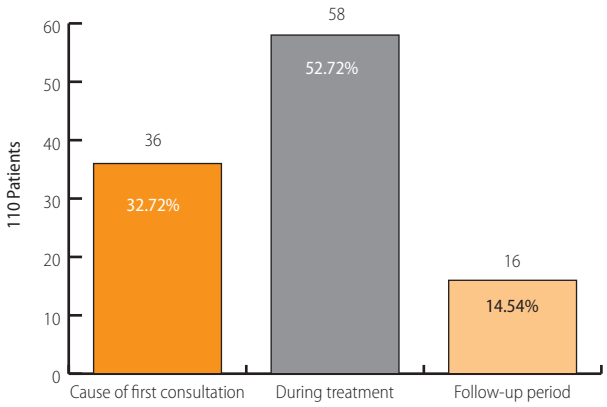

Chart 4. *Identification at the time of RE appearance*

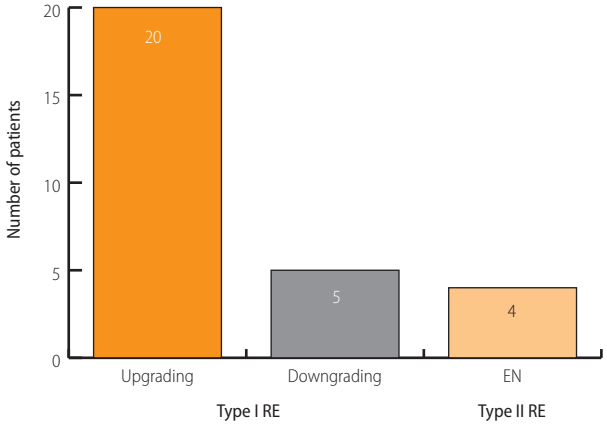

Chart 5. *RE in borderline patients.*

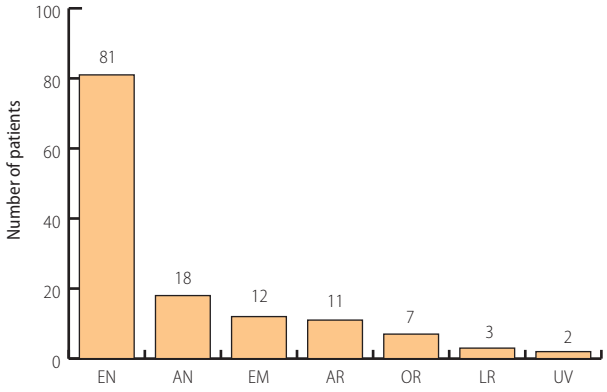

Chart 6. *Type II RE.*

Table of values in **Chart 6.**

Diagnosis	Number	Percentage
E.N.L.	81	94.19
Acute neuritis	18	20.93
E. M.	12	13.95
Arthritis	11	12.79
Orchitis	7	8.14
Lucio reaction	3	3.49
Uveitis	2	2.33

lymorphism; and to assess deficiencies/disabilities and therapeutic difficulties (thalidomide/corticosteroid-dependence).
Therefore, we conducted an observational-descriptive, retrospective study of series of cases encompassing 10 years (1996-2005), on the reactional leprosy population of the Leprosy Section of Hospital "F. J. Muñiz".

Material and methods

From the revision work[2] of 276 patients from the Dermatology Department of Hospital Muñiz with clinical, baciloscopy, and histopathologic diagnosis of leprosy, between January 1996 and December 2005 (**Chart 1**), those developing reactional episodes were exclusively selected and analyzed. Statistical methods used included: prevalence and 95 percent confidence intervals (95% CI).

Results

Global RE prevalence

Of the total of 276 patients, 39.85 percent (110/276) developed RE at some time of the disease evolution, (95% CI: 34.03-45.57 percent) (**Chart 2**).

RE prevalence in each clinical form

RE appeared at some time of the evolution of the lepromatous leprosy patients (LL), 58.11 percent (86 of 148) (95% CI: 50.16-60 percent), as well as 22.86 percent of borderline patients (24 of 105), 95% CI: 14.83-30.8 percent, with similar RE distribution in each borderline subgroup. None of the tuberculoid leprosy patients included in the study showed RE (**Chart 3**).

Identification of time of RE occurrence

In one third of the 110 patients who developed RE, it was the initial cause of consulting (36 of 110 patients), that is, 32.72 percent (95% CI: 24.02-41.42 percent). RE developed for the first time during the follow-up in 14.54 percent (16 of 110) of the patients (95% CI: 7.91-21.08 percent). In the remaining patients (58 of 110), the first RE appeared during treatment, 52.72 percent (CI95%: 43-61.8 percent) (**Chart 4**).

RE in borderline patients

Type 1 RE was found in 22.86 percent (24 of 105) of borderline leprosy patients (BT, BB, BL) (95% CI: 14.83-30.89 percent). In most of them, 83.3 percent (20 of 24), type I RE upgraded during treatment (95% CI: 68.4-98.2 percent).

Only a small percentage, 16.11 percent (4 of 24), also developed type II RE with characteristics of erythema nodosum (EN) (95% CI: 1.7-31.5 percent) (**Chart 5**).

Clinical modalities of type I RE

It encompasses a broad scope of symptoms, both in the upgrading and the downgrading form. In the upgrading episode, preexisting lesions turn erythematous-edematous and infiltrative with appearance of new urticated elements, mainly with eyelid, neck and the external ear involvement (**Figure 1**).
Facial edematous lesions confer some patients a remarkable likeness to lepro-

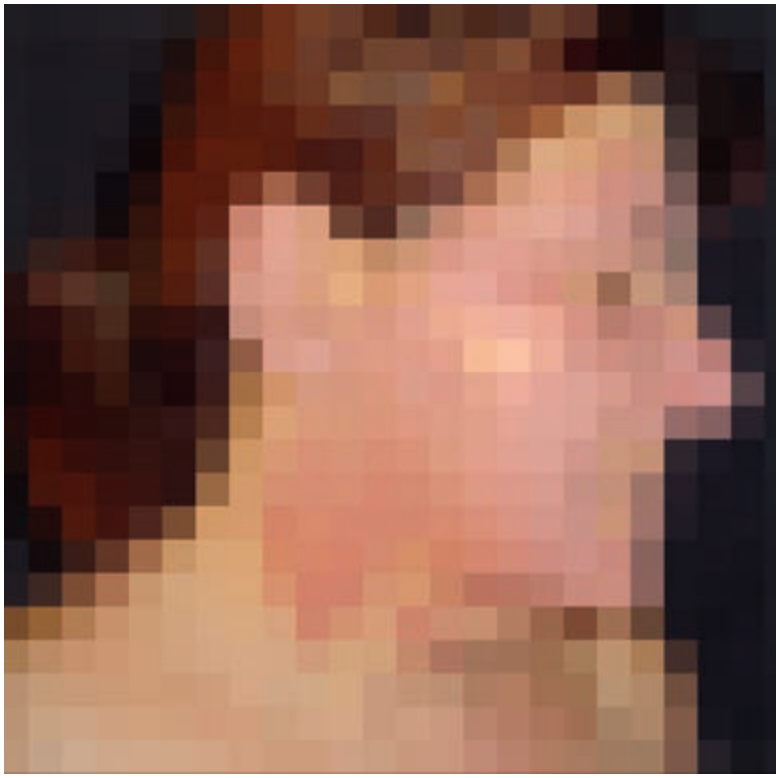

Figure 1. *Type I RE manifestations three months after starting treatment.*

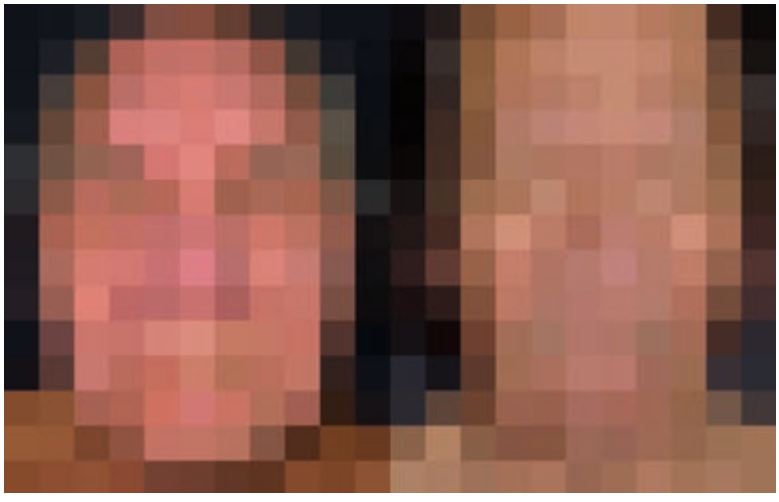

Figure 2. *Leonine and pseudoleonine fascies.*

matous leprosy leonine fascies (**Figure 2**). Patients not exposed to treatment or with discontinuous treatments may develop downgrading RE. In this case, lesions locate similarly to upgrading RE, but with less erythema and edema (**Figure 3**).

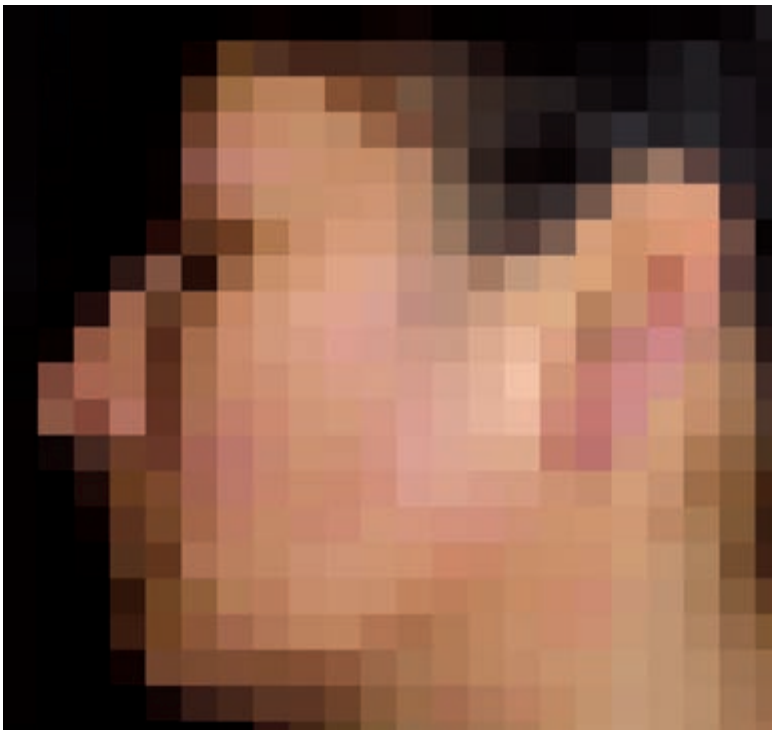

Figure 3. *Downgrading reactional episode.*

Figure 4. *Peripheral facial paralysis in a BB patient.*

RE in lepromatous patients

Clinical modalities of type II RE

Almost all lepromatous patients with RE had EN (81 of 86), 94.19 percent; and the remaining clinical modalities of type II RE in a lesser percentage. In each patient, the REs appeared in isolated, simultaneous, successive and/or recurrent form (**Chart 6**).
Second RE in frequence was neuritis, 20.93 percent, with most severe sequelae in the borderline group (**Figure 4**).
Erythema multiforme (EM) and arthritis were found with similar frequency in about 10 percent of the cases. Lucio reaction represented 3.49 percent of the cases (3 of 86 patients); it usually starts with irregular purplish maculae that follows vascular courses and evolves to cutaneous infarcts with geographical borders evoking disseminated intravascular coagulation. After of necrotic tissue, stellate ulcers appear (**Figure 5**). Less frequent are After of orchitis, uveitis and splenitis (2 cases).

Disabilities and sequelae

According to the WHO definition, 30 percent (33 of 110) of patients had disability/deficiency, with sequelae such as: chronically ulcerated feet, trophic ulcers, ulnar claw, wrist-drop, stepagge, amputations (**Figure 6**).

Therapeutic difficulties

Of the 83 patients (79 LL, 4 BL) receiving thalidomide, 54.22 percent (45 of 83) showed thalidomide-dependence (95% CI: 43.5-64.9 percent). Dependence means impossibility to discontinue a minimal drug dose to maintan the patient free from RE.
Of the 60 patients (36 LL and 24 borderline) receiving corticosteroids, about 15 percent (9/60) showed corticosteroid-dependence (95% CI: 6.3-24.2 percent). In these cases, outbreaks were continuous and led to complications related to chronic corticosteroid therapy, without preventing severe disability sequelae.

Discussion

A distinctive feature of RE, as an expression of immune phenomenon, is the heterogeneity of the immune response: *not all leprous patients have RE, and only some have recurrent RE*. The situation may occur in about 30 percent[3] of multibacillary patients (MB): lepromatous and borderline (BL, BB, BT).
In this study, of the 276 patients that started multidrug therapy (MDT), about 40 percent had RE

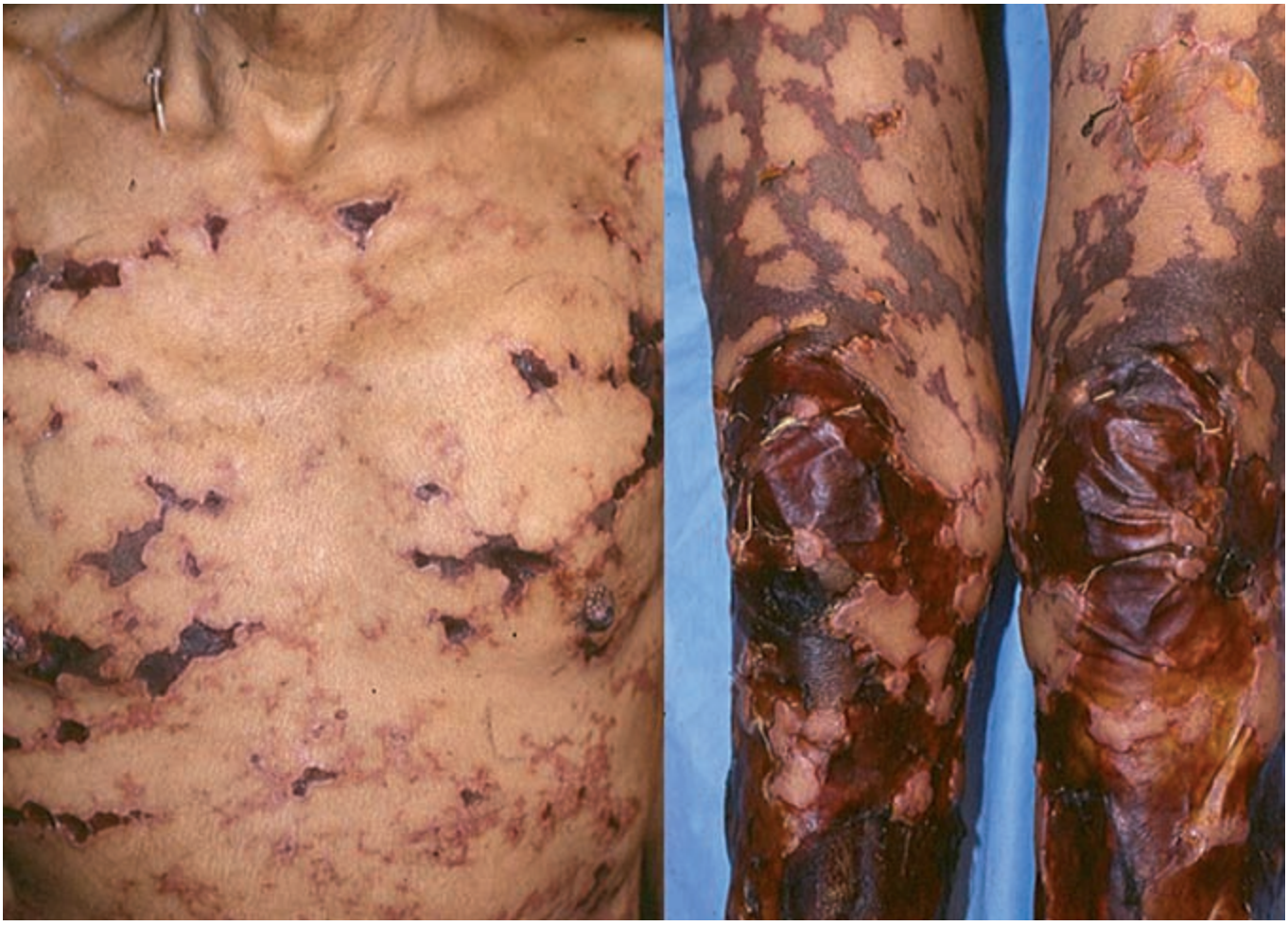

Figure 5. *Lucio reaction.*

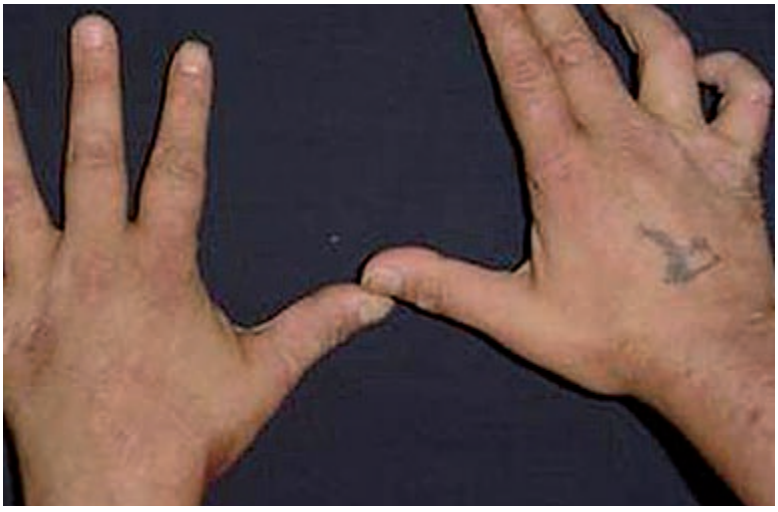

Figure 6. *Sequelae/disability in corticosteroid-dependent patient.*

at some time of evolution, more frequently in lepromatous patients. Occasionally, it may cause delay in disease diagnosis at first consultation. We found it in more than 30 percent of our patients, in contrast to other case-control studies that mention an incidence of 17 percent.[4] Noteworthy, 14.5 percent of patients showed first RE post-treatment.

Borderline RE had a similar distribution in each subgroup (BL, BB, BT), and upgrading RE was most frequent. Some patients showed successive downgrading and upgrading episodes, and ENL was also found in 4 of them.

As regards type II RE, ENL was found most frequently (94.19 percent) among our patients, alone or associated with other reactions such as neuritis, erythema multiforme, arthritis, orchitis, Lucio reaction, uveitis, etc.

In our case-control study, the severity of RE depended on systemic repercussions (2 patients with splenitis), profusion of cutaneous lesions, clinical modality (EM, Lucio reaction) and/or simultaneous reactions.

As regards RE tratment, both thalidomide for ENL and prednisone were the first drugs of choice for our patients.

Thalidomide has been an extensively used drug by latinamerican leprologists, with excellent results and good tolerance. However, this use has raised controversy in other international settings, such as the

United States, where the FDA only authorized the use for EN in 1998.[5,6] Development of thalidomide-dependence was established in our study in 54.22 percent (45 of 83) of the dosed patients. This finding, frequently seen in practice, is seldom mentioned in the treated literature.[7,8] It is hypothesized that these patients may have genetic predisposition to "reacting", thus needing a minimal dose of thalidomide to keep levels of TNF-α sufficiently low to prevent triggering a RE.[9]
Corticosteroid-dependence, with its unwanted effects, did not reach a significant value.

Conclusions

- About 40 percent of patients with leprosy developed RE.
- 58 percent of lepromatous patients had RE.
- 22% of borderline patients had RE, with similar distribution in the different subgroups.
- RE was initial consulting cause in 32 percent of the patients; less than 15 percent showed it for the first time during the follow-up period.
- ENL was the most frequent RE
- Thalidomide-dependence was confirmed in more than 54 percent of ENL patients.

It must be noticed that treatments were effective, although insufficient to prevent severe disability sequelae. The present fndings should be considered in the programming of future therapeutic strategies, in order to adequately prevent and control the possible harmful sequelae of reactive leprosy.

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