

Ulcerative necrobiosis lipoidica: case report of an atypical presentation and literature review

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Abstract. – Necrobiosis lipoidica (NL) is a rare chronic granulomatous degenerative skin disease by unknown causes, which is mostly associated with diabetes mellitus, usually presenting with typical plaques of the shins.

Although less common, some ulcerative forms may be seen in clinical practice. The occurrence of an atypical presentation in one of our patients was the occasion to review the pertinent literature.

Key Words:

Necrobiosis lipoidica, Ulceration, Clinical diagnosis, Epidemiology.

Introduction

Necrobiosis lipoidica (NL) presents with sharply demarcated yellow-brown patches or plaques, usually bilaterally on the shins^{1,2}. The plaques can develop an atrophic center with raised borders^{1,2}. The surface is shiny, waxy, with a “glazed-porcelain” appearance, and presents several telangiectasias^{1,2}. Ulceration occurs within 15% to 35% of cases¹⁻³. Ulcerative necrobiosis lipoidica (UNL) can present in two different clinical types, which we have called “classical” and “non-classical”.

Case Report

A 50-year-old man complained of a 6-month history of multiple ulcerated lesions on the medial surface of his left leg (Figure 1). The lesions started a year before as painless erythematous papules, with progressive ulcerative evolution.

The ulcers, each measuring approximately 1 cm in diameter, had a punched-out appearance with heavily inflamed borders and fibrinous tissue at their base.

No symptoms other than a slight burning have been reported. Medical history did not reveal diabetes or other systemic disorders. Routine laboratory tests were within the normal ranges. A color-Doppler ultrasound was negative for peripheral arterial disease or thrombotic vasculopathy. The histological examination revealed necrobiosis lipoidica.

Materials and Methods

A bibliographic search was conducted on PubMed using the key words: “ulcerated necrobiosis lipoidica”, “ulcerative necrobiosis lipoidica”, “necrobiosis lipoidica” AND “ulceration”. We included only articles, out of 173 studies, that met the following criteria: (1) case report or case series, (2) complete clinical presentation of the case by photos or text. Studies that did not fit into the above categories, together with reviews, clinical trials or meta-analysis were excluded. No restrictions on the language or year of publication were applied. According to these criteria, 81 case report were selected.

We defined classical UNL by the presence of at least two of these clinical parameters: yellow-brown patches, atrophy, waxy surface, several telangiectasias (Figure 2). Variables considered for statistical analysis were: age, gender, associations, time to ulceration, localization. About associations, no differences were applied for type 1 or type 2 diabetes. Glucose intolerance was not classified as diabetes.

Mean and standard deviation (SD) for continuous variables, percentage distribution for categorical variables were calculated. For statistical analysis of categorical variables, the chi-square



Figure 1. Atypical presentation of UNL on the medial surface of our patient's left leg.

test (χ^2), with Yates's correction (YC) where relevant, was used. A p -value of less than 0.05 was considered statistically significant.

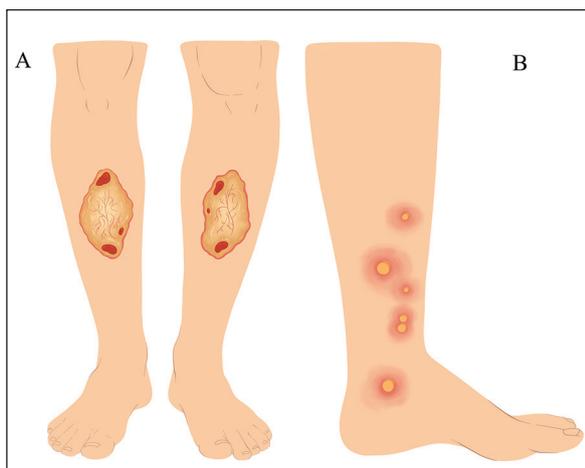


Figure 2. A, Classical UNL characterized by yellow-brown patches, atrophy, waxy surface, several telangiectasias. B, Picture of non-classical UNL.

Results

We found 62 cases (76.5%) of classical UNL and 19 cases (23.5%) of non-classical UNL according to our criteria (Table I).

The patients' age at presentation ranged from 13 to 85 years with a mean age of 46.2 ± 19 years. The mean age at onset of disease was 39.4 ± 19.2 years, while ulceration occurred on average at 43.4 ± 18.9 years. No significant differences of age were between patients with classical or non-classical type. Age at onset and at ulceration was not reported in all cases and mean and SD were calculated on available data. Women were more than men, and the risk of classical UNL was higher in female group (F:M=4:1). There were not relevant gender differences for the risk of non-classical UNL (F:M=1.3:1).

Diabetes was the most common association of UNL (65.4% of patients with UNL) and patients with non-classical type were as likely to be diabetic as patients with the classical type ($p=0.81$). Presence of associated diabetes was not specified in one case, while in another case blood sugar levels were altered but the diagnosis of diabetes was not confirmed. Glucose intolerance was present in three cases.

Hypertension was the second most frequent association (9 cases). Hypertension was more frequent in non-classical than in classical types. This difference was statistically significant ($p < 0.01$).

In classical UNL cases, ulceration arose on average 54.5 months later the onset of NL. In the majority of non-classical UNL cases, necrobiosis was diagnosed after the onset of ulceration; it was not possible to determine exactly if and for how long there was necrobiosis. In fact, a previous diagnosis of necrobiosis was made more frequently in classical UNL than in non-classical UNL cases ($p < 0.001$).

Legs (71 patients, 87.6%), in particular shins (64 patients, 79.0%), were the favorite sites of UNL. Other preferred sites were ankles, particularly the malleolar region (6 cases), followed by upper limbs and feet (5 cases each), thighs and penis (3), knees (2), and cheeks (1). Other localizations than legs were found in 11% of total cases, while no leg involvement was seen in 13.6%. No legs involvement was more frequent in non-classical UNL ($p < 0.05$). Ulcers on penis and cheeks were seen only in non-classical types.

Bilateral NL was present in 55.5% of cases. Cases presenting with unilateral ulcers were observed with the same percentage: it means that necrobiosis most often involved both sides, while

Table 1. Differences between classical and non-classical UNL.

	Classical UNL (n = 62)		Non-classical UNL (n = 19)		
	No.	%	No.	%	
Sex					<i>p</i> > 0.05
Women	50	80.6%	11	57.9%	
Men	12	19.3%	8	42.1%	
Diabetes	41	66.1%	12	63.1%	<i>p</i> > 0.05
Hypertension	3	4.8%	6	31.6%	<i>p</i> < 0.01
Previous diagnosis of NL	46	74.2%	3	15.8%	<i>p</i> < 0.001
No legs involvement	5	8.1%	6	31.6%	<i>p</i> < 0.05
Symmetry of NL					<i>p</i> > 0.05
Monolateral NL	25	40.3%	11	57.9%	
Bilateral NL	37	59.7%	8	42.1%	
Simmetry of ulceration					<i>p</i> > 0.05
Monolateral ulcers	33	53.2%	12	63.2%	
Bilateral ulcers	29	46.7%	7	36.8%	
Number of ulcers					<i>p</i> > 0.05
Single ulcer	15	24.2%	5	26.3%	
Multiple ulcers	47	75.8%	14	73.7%	
Pain	20	32.2%	7	36.8%	<i>p</i> > 0.05

ulcers appeared more often only at one side. Ulcers were also more multiple than single.

Finally, classical and non-classical forms were not significantly different with regard to the number of ulcers or symmetry of presentation. The borders of the ulcers were generally defined as “raised”, “inflamed”, “undermined”, “punched-out” or “ragged”. Only non-classical UNLs had a “punched-out” presentation. About one-third (33.3%) of all cases were painful, equally in classical and non-classical types. Symptoms were not described in the majority of cases. Previous traumas were reported only in 7 cases, one of these being a non-classical UNL.

Discussion

We present a case of UNL, which shares an atypical clinical presentation with other 19 cases in literature. To the best of our knowledge, ours is the largest collection of studies providing data about the onset of ulceration. Ulceration occurred on average at 42.8 years, while Franklin et al⁴ reported a mean age of 32.6 years at time of ulceration in a series of 10 cases.

Erfurt-Berge et al⁵ described the time between skin lesions and the occurrence of ulceration, which was about 6 months or longer. We considered cases in which the time of onset of

necrobiosis and ulceration were both known, thus recording a latency of about 54.5 months.

Dwyer et al³ pointed out that the only male of their series had an ulcerated form, as well as Erfurt-Berge et al^{5,6} found that ulceration was predominant (about two-fold) in male patients. In our study, we found a female prevalence in classic forms of UNL. A male predominance was seen in non-classical UNL group, in which ulceration was the most representative of NL clinical features. Our case concerned a male patient.

The rate of diabetes in UNL is reported between 54.5%⁵ and 70%⁴. Our results were consistent with previous studies. High diabetes rates may mean there is an association between ulceration and diabetes. Erfurt-Berge et al⁶ suggested that diabetic microangiopathy may explain ulceration. The role of tyrosine kinase receptors, a receptor superfamily which mediates the effects of excessive amount of insulin, should be investigated⁷.

Hypertension was found as the second most frequent association in our study. This was in agreement with the observations of Erfurt-Berge et al^{5,6} (38% and 40.4%) and Franklin et al⁴ (60%) for UNL.

In particular, we found that hypertension was a specific comorbidity of non-classical UNL.

With regard to localization, lower legs appeared to be the most common site as described in literature, even if other localizations have been described^{1,8}.

Finally, the isolated involvement of sites other than legs seemed to be due exclusively to the non-classical forms of UNL.

Up to date, there is not a study that investigates the symmetry of ulcerations in UNL: we found that they were more commonly unilateral and that ulcerated lesions were more frequently multiple than single. Therefore, the clinical image of the UNL may include multiple localized ulcerations on a bilateral or less commonly unilateral fashion, as we saw in our case report.

Regarding symptoms, we found pain in one-third of cases, and this was in agreement with the rate reported by Hashemi et al⁸ (25.5%).

Trauma has been recognized as a risk factor for the development of ulceration¹⁻⁴. However, in our study, this datum seemed to be reduced. In our opinion, the trauma may favor ulceration when atrophy is already present, but it is not the primary cause of ulceration and cannot explain the ulceration in the earlier stages.

Conclusions

A diagnostic delay commonly occurs in atypical forms of NL, when small lesions, unusual localization and severe ulceration are present, especially in cases of UNL. Further studies focusing on the characteristics of uncommon pictures may help clinicians to recognize UNL earlier, thus providing a better management of the condition.

Conflict of Interest

The Authors declare that they have no conflict of interests.

Consent to Participate

The patient gave the permission to use his clinical image and data.

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