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Cutaneous Leishmaniasis

«Clinical Myths and Realities»

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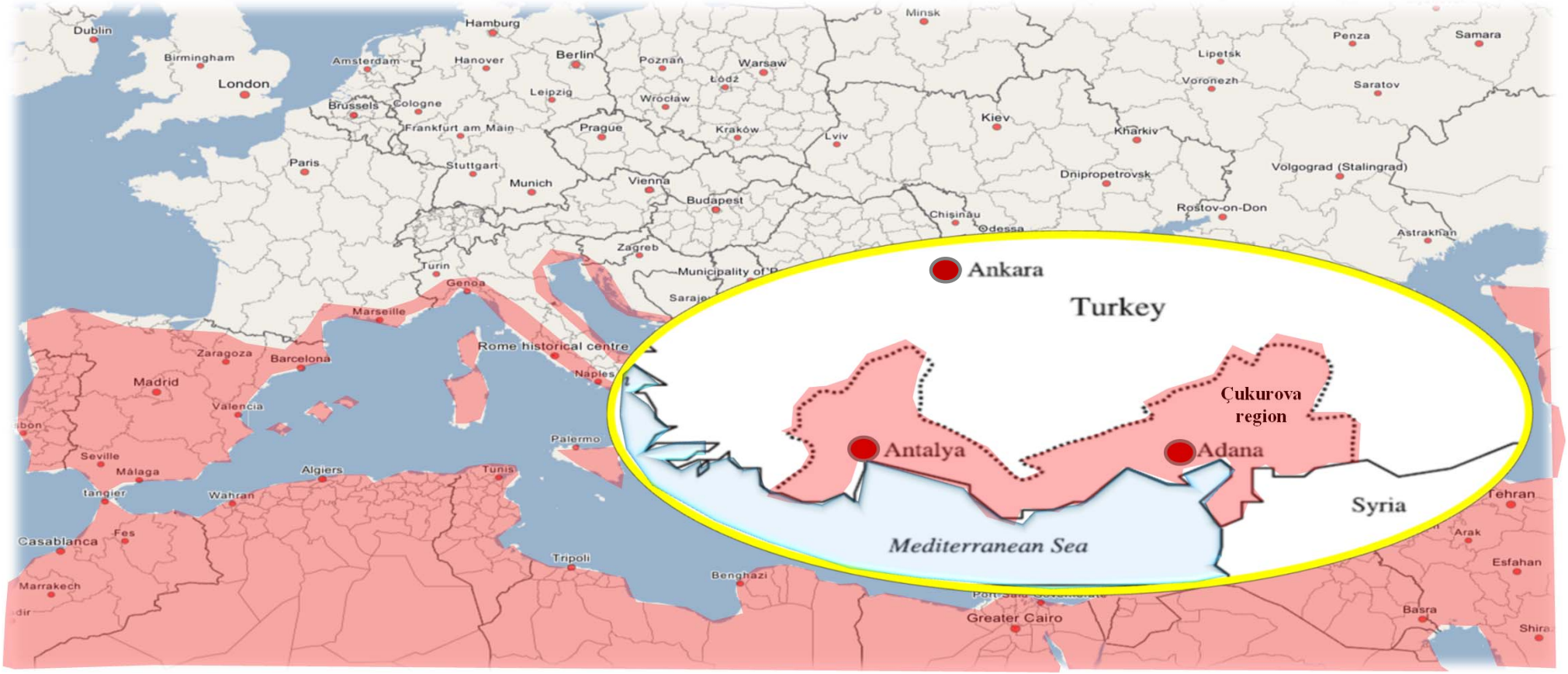
Old World Cutaneous Leishmaniasis



British Journal of Dermatology 1999; 140: 347–350.

Cutaneous leishmaniasis: evaluation of 3074 cases in the Çukurova region of Turkey

S. UZUN, C. USLULAR, A. YÜCEL, M. A. ACAR, M. ÖZPOYRAZ AND H. R. MEMIŞOĞLU*
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J. Parasitol., 90(4), 2004, pp. 853–859

CLINICAL FEATURES, EPIDEMIOLOGY, AND EFFICACY AND SAFETY OF INTRALESIONAL ANTIMONY TREATMENT OF CUTANEOUS LEISHMANIASIS: RECENT EXPERIENCE IN TURKEY

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ABSTRACT: A total of 1,030 patients, 40.2% men and 59.8% women, identified during the period of October 1998 to November 2002 as having cutaneous leishmaniasis (CL), were studied; 1,431 lesions were identified in the 1,030 patients. One lesion was present in 80.7% of the patients. The size of the lesions (longest axis) was 13.6 mm (standard, 12.1 mm; range 3–150 mm). Most of the lesions were of the papular type (51.2%), although several atypical clinical presentations of CL were observed. The duration of the disease ranged between 1 and 72 mo (mean duration, 10.8 mo). The clinical suspicion of CL was confirmed by the observation of amastigotes on lesion tissue samples stained by Giemsa. The test was positive in 851 of 1,030 patients (82.6%). Intralesional meglumine antimonate solution (85 mg Sb/ml, 0.2–1 ml, depending on the size of the lesion) weekly until complete cure or up to 20 wk was used for first-line therapy of 890 patients (86.4%). We found that this regimen of intralesional Sb has an efficacy of 97.2% with a low relapse rate of 3.9% and no serious adverse side effects.

Cutaneous leishmaniasis (CL) is a major, worldwide health problem caused by species of *Leishmania*, which are transmitted by the bite of infected female sand flies (Herwaldt, 1999). Although CL is well known in certain areas of the tropics and of the world since the ninth century, its epidemiol- treatment are incompletely under- lence of CL was

CL was defined as a chronic skin lesion(s), with parasites identified by the methods listed below.

Diagnosis

CL cases were parasitologically confirmed by Giemsa staining of direct smears. Briefly, in solid lesions without an ulcer, after the lesions were cleaned with 70% alcohol swab, a small incision was made at the edge of the lesion, and tissue was scrapped through the incision. In lesions, smears were made from tissue pulp aspirated from after removal of the overlying crust. The smears

Syrian Refugees in Turkey

4 million refugees

Thousands of patients with CL

Travel Medicine and Infections Disease (2015) 13, 443–444

Available online at www.sciencedi

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journal homepage: www.elsevierhealth.

EDITORIAL

Syrian refugees and infectious disease challenges

The on-going conflict in Syria has led to the destruction of health care facilities, a breakdown and destruction of childhood immunization programmes, a shortage of drugs, and a lack of access to clean water. These sad circumstances have resulted in significant emerging health problems in Syria [1]. It is estimated that some 6.5 million people are displaced within the country. More than 4.2 million Syrians have crossed borders; Turkey hosts more than 2.1 million refugees, Lebanon 1 million, Jordan 630,000 and Iraq 235,000 and there are approximately 682,000 asylum applications in Europe [2].

Health care problems and specifically infectious diseases are a major burden for the refugees. In Turkey, some of the refugees are in camps while others are distributed to the cities. Re-emerging major infectious disease challenges include polio, cholera, typhoid fever, tuberculosis, and leishmaniasis.

The World Health Organization (WHO) reported 37 polio cases in the Syrian Arab Republic as of March 20th, 2014. Regional spread was confirmed by a report of a case from Iraq, the first polio case in that country since 2000. Genetic sequencing indicated that the virus is most closely related to the virus detected in the Syrian Arab Republic and the virus was also isolated from the index child's three-year old sister, who did not develop symptoms [3]. Turkey, which has started to vaccine all Syrian

Cutaneo
and it has
countries a
cities havi
cases with
of Leishma
linked to S
and the fli
CL should
merly, una
Patients
reported in
infrastructi
infections
tuberculos
carry thes
Bacterial
hepatitis A
challenges
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been contr
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infections

The new situation of cutaneous leishmaniasis after Syrian civil war in Gaziantep city, Southeastern region of Turkey

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ABSTRACT

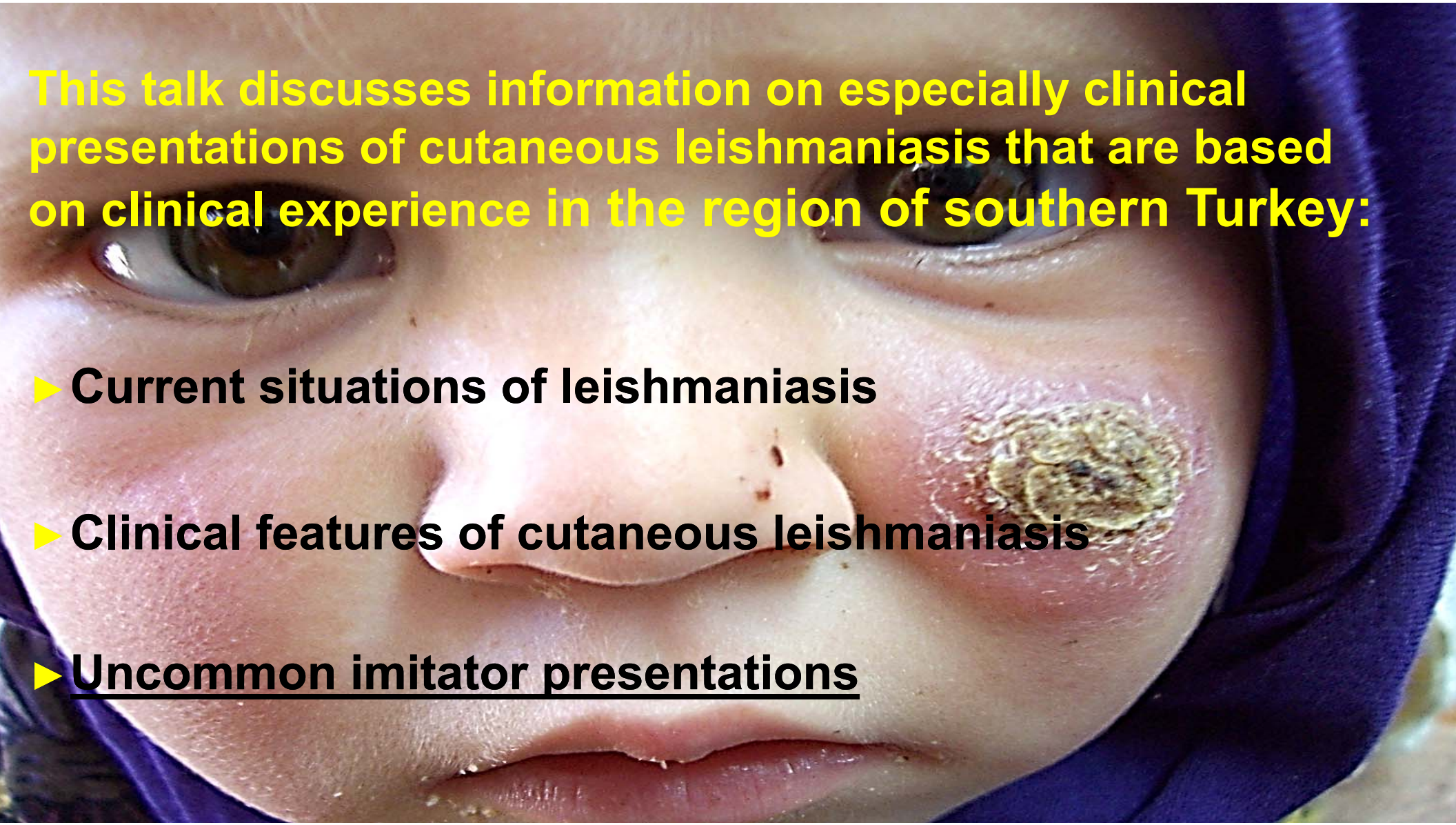
Cutaneous leishmaniasis (CL) is an important public health problem with around 2,000 au
reported cases each year in Turkey. Due to the civil war in Syria, Turkey received around
refugees and they are mainly located at either camps or homes in south/southeastern part
the present study, we aimed to collect samples from CL suspected patients admitting to S
in Gaziantep City and perform parasitological and DNA-based techniques for diagnosis as w
identification of the parasite for better understanding the prevalence of each species amo
Syrian patients in the region.

The collection of samples was carried out between January 2009 and July 2015. The le
samples were taken and stained with Giemsa stain followed by microscopical examinati
logical diagnosis. After the DNA extraction from Giemsa stained slides, real time and se
both targeting ITS1 region were performed for molecular diagnosis and species identific

A total of 567 people were admitted to the hospital with the suspicion of CL and 263
were found to be positive by parasitological examination. One hundred seventy-four (66.1
and 1 (0.38%) of them were Turkish, Syrians and Afghan, respectively. Slide samples o
CL suspected patients were analyzed by PCR and 20 of them were found positive. Eigh
and 13 Syrians) of the positive samples were identified as *L. tropica*, while two (1 Turk
of them were *L. infantum*.

In conclusion, the effects of Syrian civil war on the epidemiology of CL in Gaziantep cit
in the present study. The use of molecular tool in the diagnosis of leishmaniasis is effec
time saving which will enable the species typing. Species typing of the causative agen
will bring valuable data to epidemiological knowledge.

Turkey is an endemic country for leishmani
are mostly reported in south/south eastern reg
reports of Ministry of Health of Turkey, more th
1990 and 2010 (MoH, 2

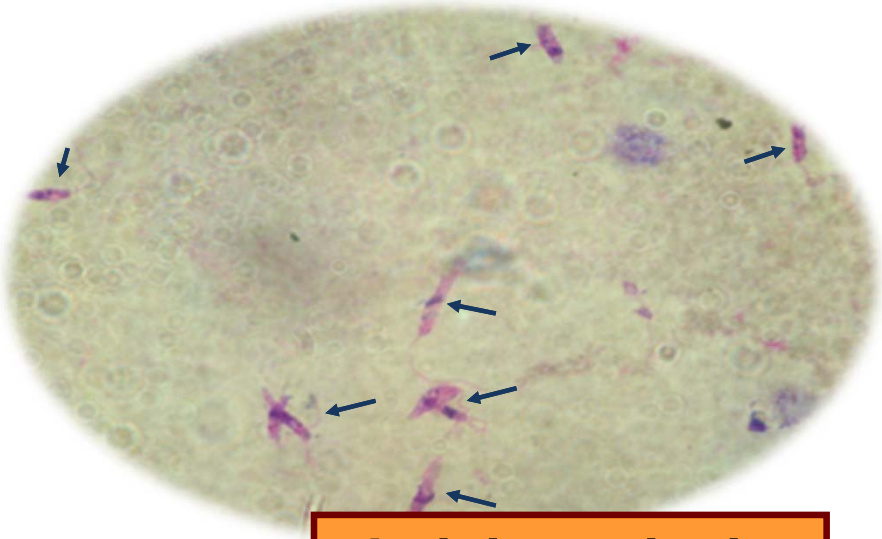


This talk discusses information on especially clinical presentations of cutaneous leishmaniasis that are based on clinical experience in the region of southern Turkey:

- **Current situations of leishmaniasis**
- **Clinical features of cutaneous leishmaniasis**
- **Uncommon imitator presentations**

“Leishmaniasis is caused by a parasite belonging to the genus *Leishmania*”

20 *Leishmania* species are pathogenic for human!



Leishmaniasis

- **Cutaneous**
  - **Old World** → ***L.tropica*** ***L.major*** ★ ***L.infantum*** *L.aethiopica*
  - **New World** → *L. braziliensis* *L.mexicana* *L.amazonensis* *L.venezuelensis* *L.[V] guyanensis* *L.[V] peruviana* *L.[V] panamensis*
- **Mucocutaneous** → *L. braziliensis* *L.[V] guyanensis* *L.[V] peruviana* *L.amazonensis*
- **Visceral** → *L.donovani* *L.infantum* *L.tropica* *L.chagasi* *L.amazonensis*

The emergence of *Leishmania major* and *Leishmania donovani* in southern Turkey

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Transactions of The Royal Society of Tropical Medicine and Hygiene, Volume 108, Issue 3, March 2014, Pages 154–158, https://doi.org/10.1093/trstmh/trt119
Published: 20 January 2014

Abstract

Background

In southern Turkey, *Leishmania tropica* and *L. infantum* are both the causative agents of cutaneous leishmaniasis (CL) and visceral leishmaniasis (VL), respectively. However, *L. major* and *L. donovani* were known to exist after the influx of Syrian refugees.

Methods

Between the years of July 2003 and July 2013, a total of 167 smears and 113 bone marrow samples were taken from CL and VL-suspected cases, respectively. Samples were analysed through real-time PCR and ITS1 DNA sequencing.

Results

One hundred and seven 64% (107/167) smears and 56% (63/113) bone marrow samples were positive for leishmaniasis according to the real-time PCR. Three different *Leishmania* species were found in the 107 CL cases by real-time PCR: 42% (45/107) *L. tropica*, 36.5% (39/107) *L. infantum* and 21.5% (23/107) *L. major*. In addition, three different *Leishmania* species were identified in the 63 VL cases: 60.3% (38/63) *L. infantum*, 30.2% (19/63) *L. donovani* and 9.5% (6/63) *L.*

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Leishmaniasis in Turkey: first clinical isolation of *Leishmania major* from 18 autochthonous cases of cutaneous leishmaniasis in four geographical regions

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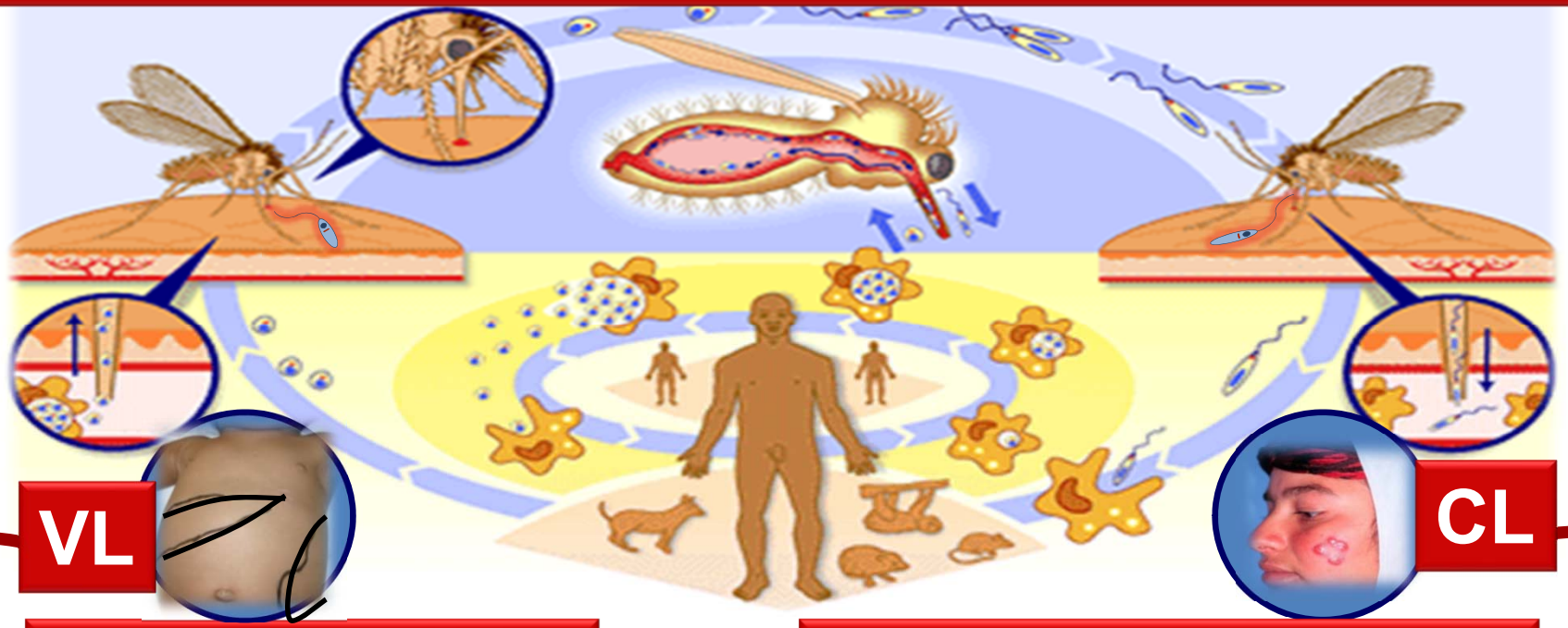
Leishmaniasis

A group of diseases caused by Leishmania parasites transmitted by the bite of the sand fly..



VL

Visceral Leishmaniasis

CL

Cutaneous Leishmaniasis

«Cutaneous Leishmaniasis»

CL

New World CL

“Espundia”
“Chiclero ulcer”

Old World CL

“Oreintal sore”
“Aleppo boil”

Leishmaniasis: current situation!

12 million cases
infected

350 million
people
at risk

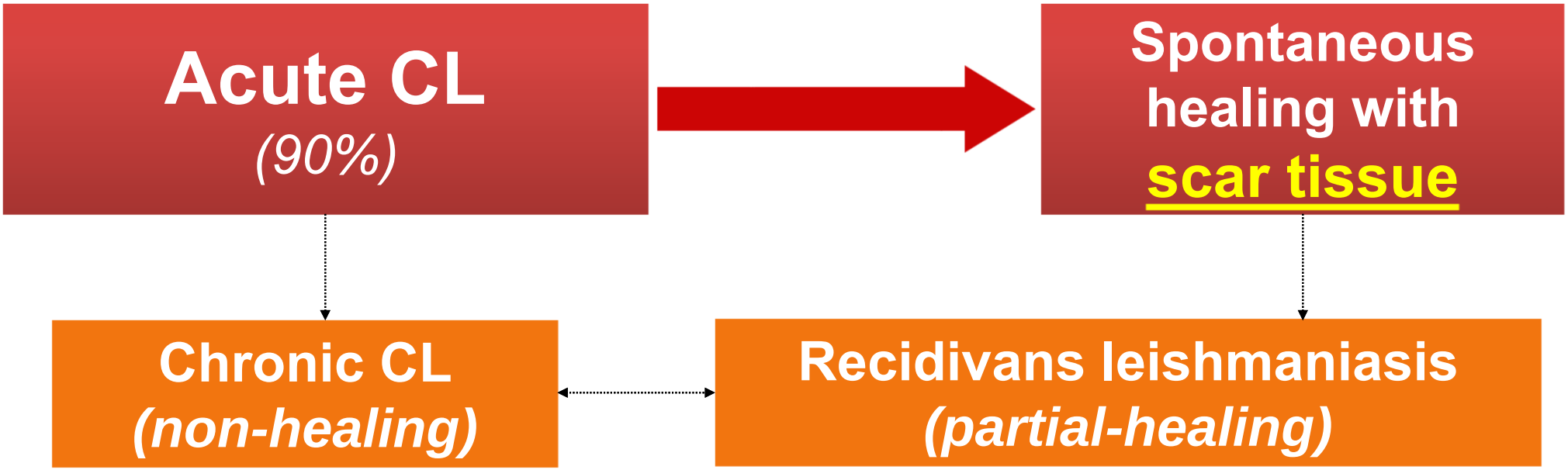
2 million new patients every year
(1.5 million CL, 500.000 VL -70.000 deaths)

Highly endemic countries for CL (90% of cases)

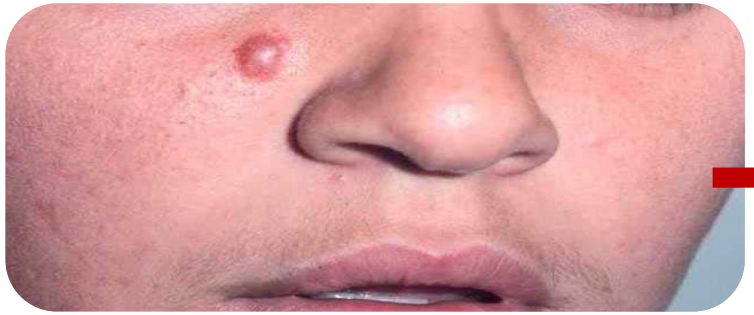
New World
- Peru
- Brazil

Old World
- Afghanistan
- Pakistan
- Iran
- Syria
- Saudi Arabia
- Algeria
- Turkey

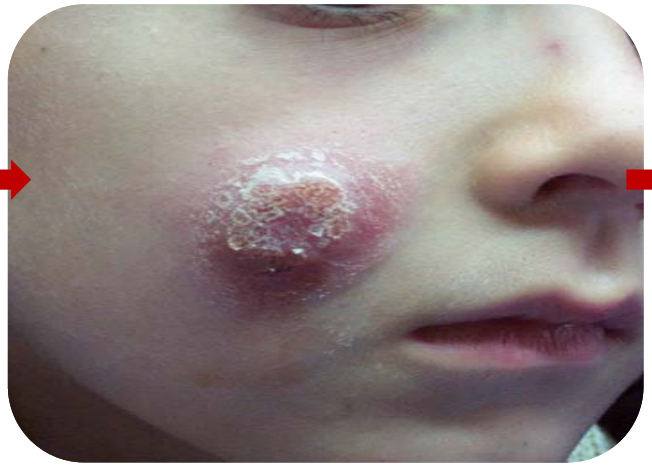
Clinical course of CL



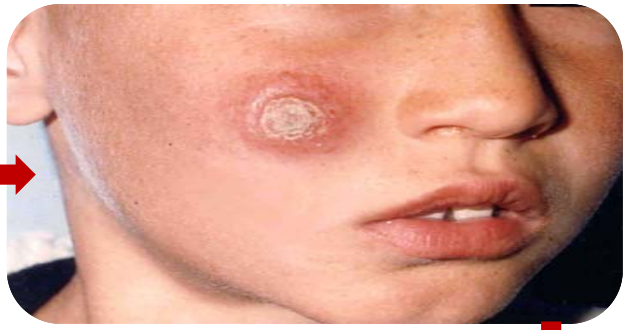
Natural history of acute CL



..starts as an erythematous papule



.. gradually enlarges



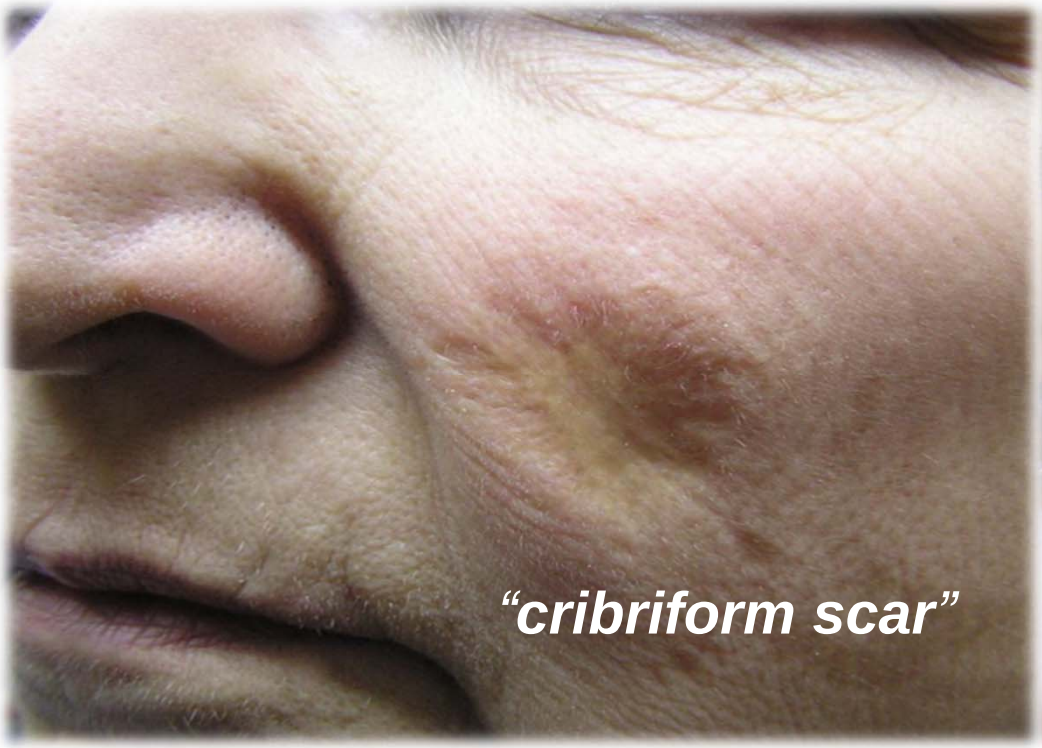
and then ulcerates

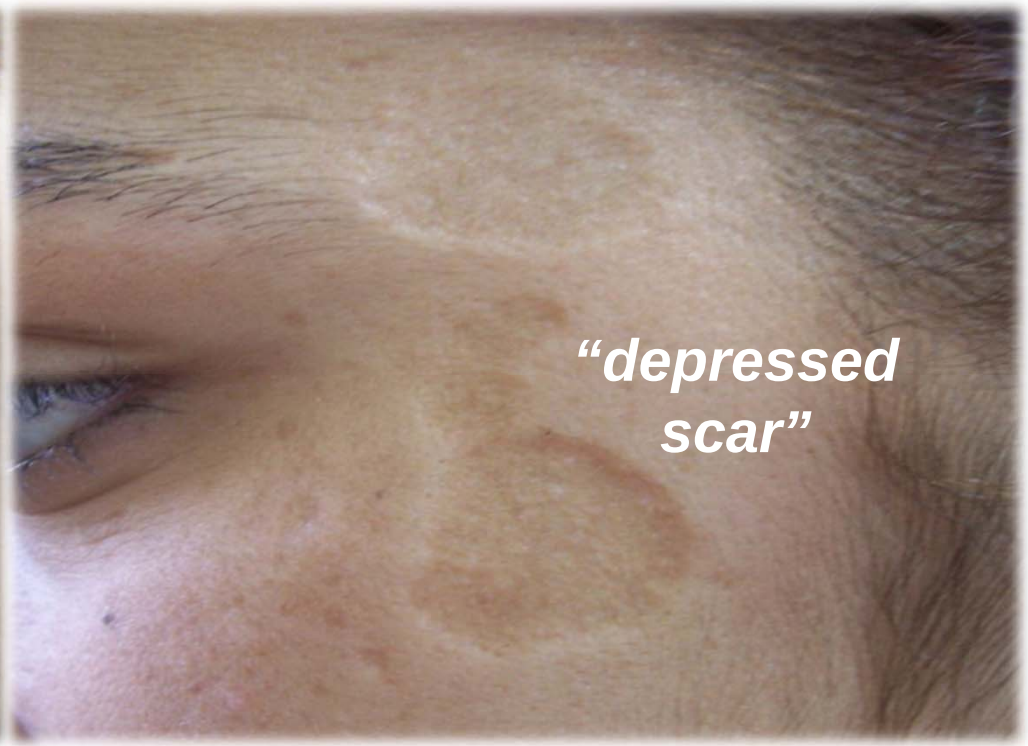
ulcer is **painless** with necrotic base and indurated margin and is frequently **covered by a firmly adherent crust**.

time to self-cure is variable;

6-15 months *(L.tropica),* 2-6 months (*L.major*)

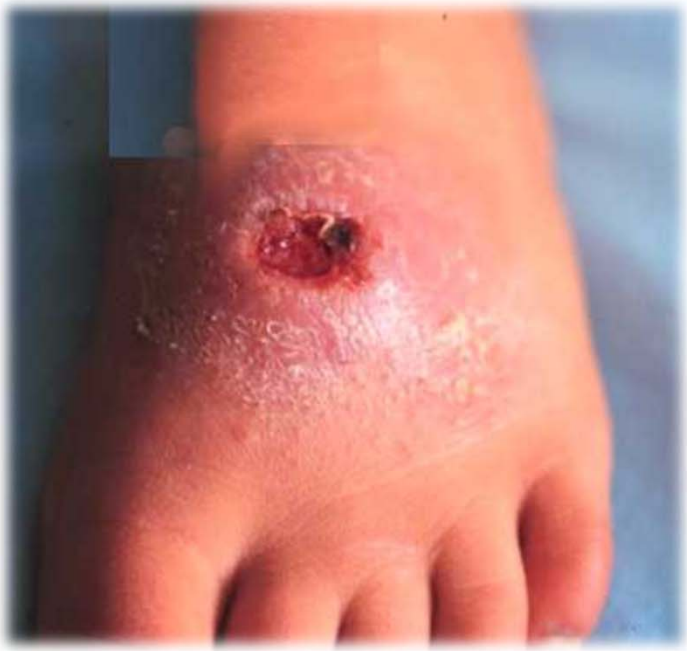
lifelong cutaneous scar / lifelong prevention

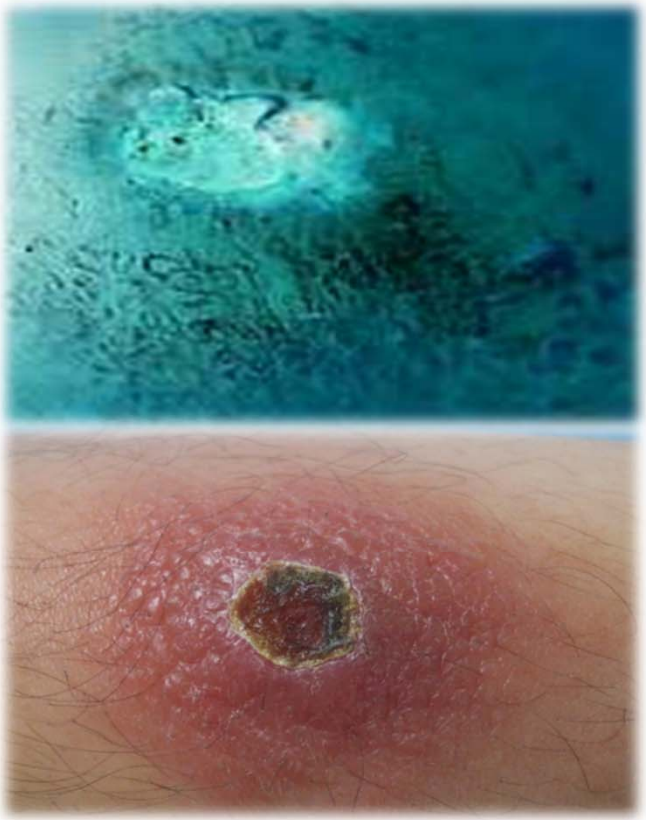


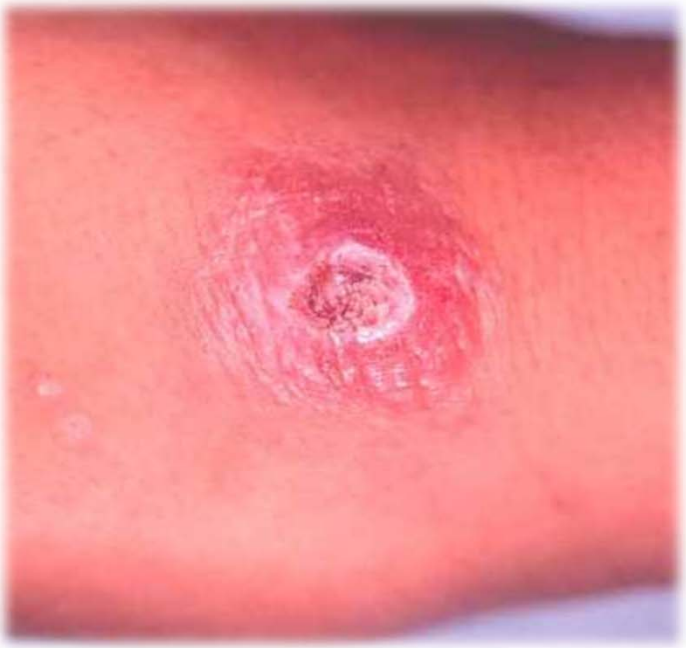


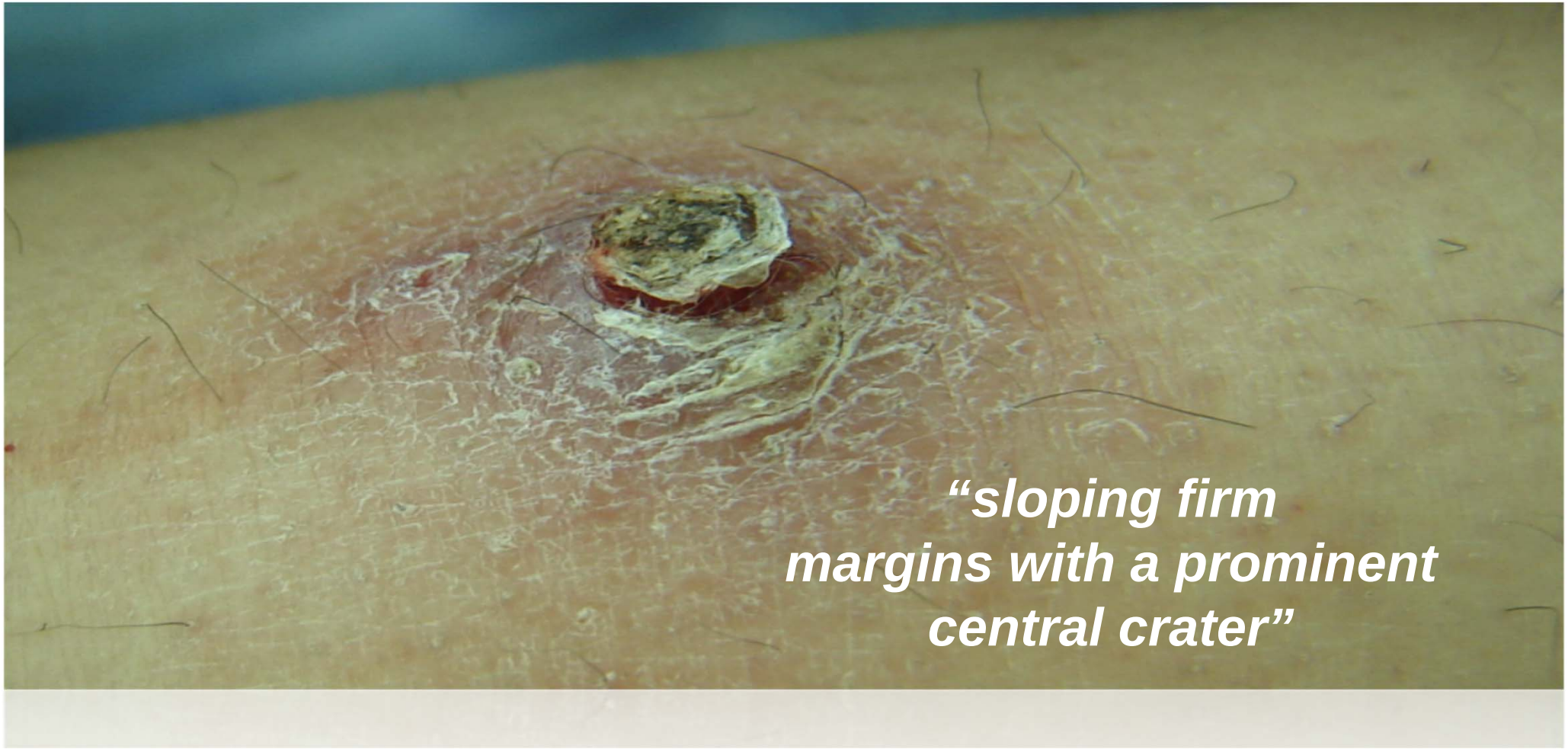
physical signs presented at ulcer stage

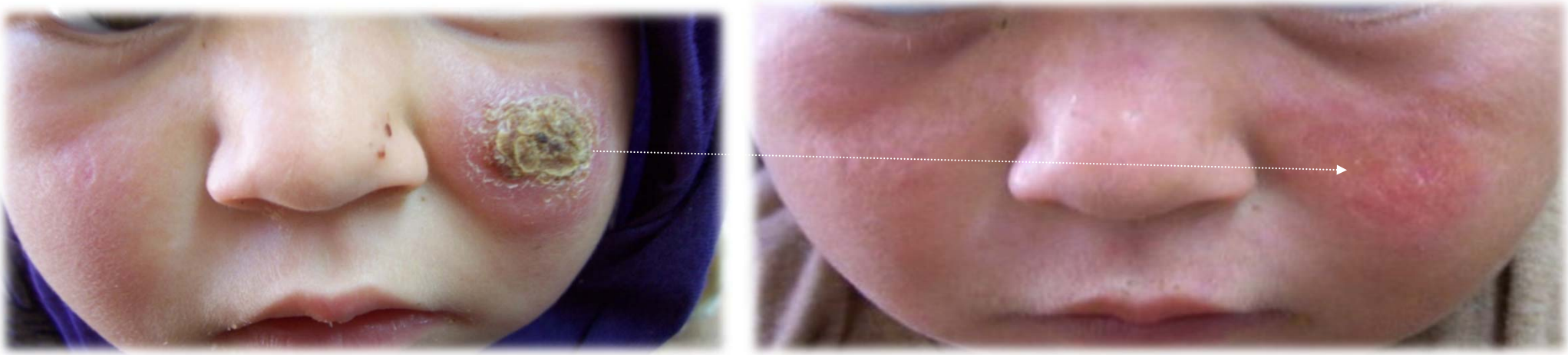
“the volcano sign”



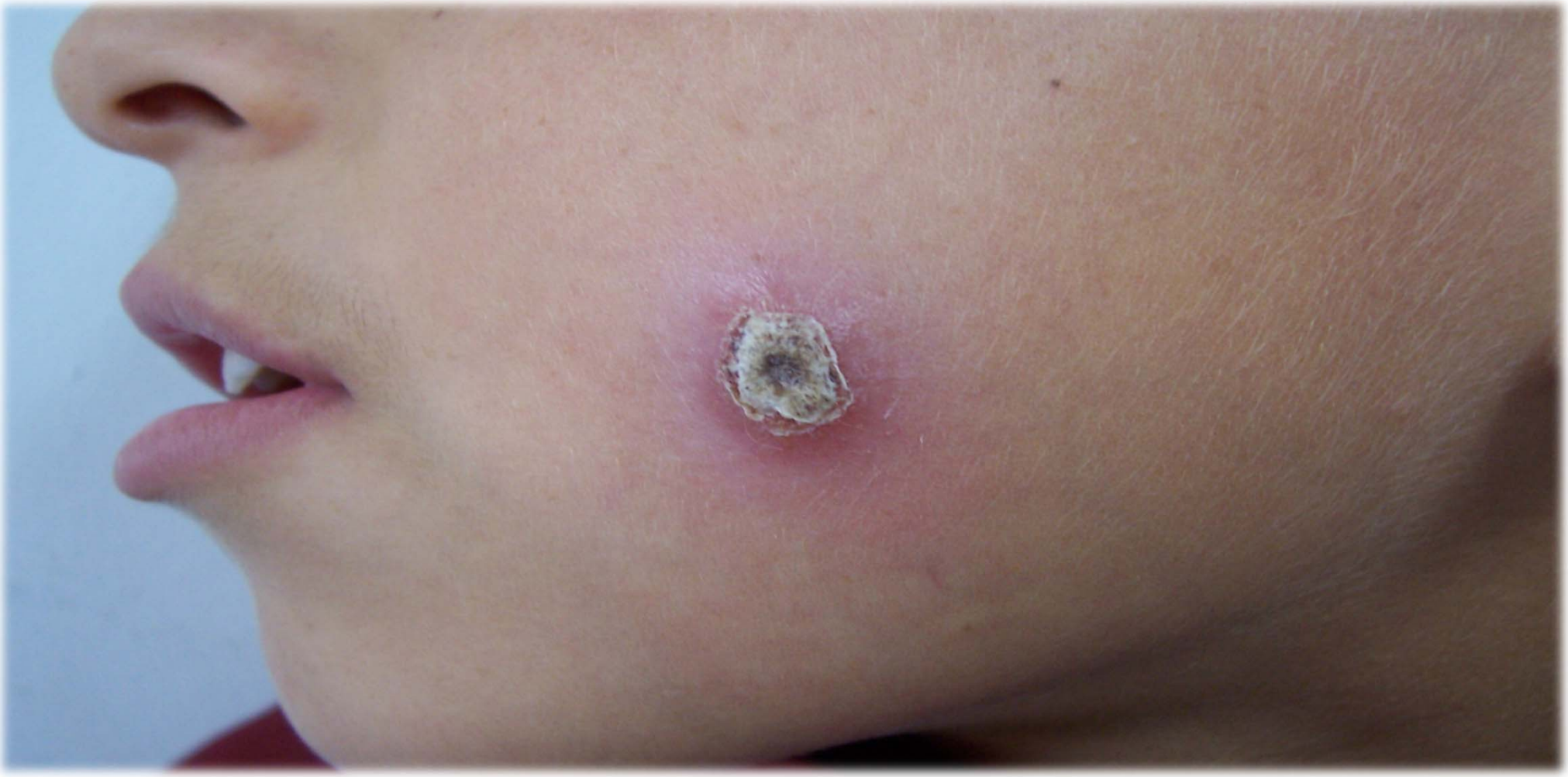





“sloping firm
margins with a prominent
central crater”

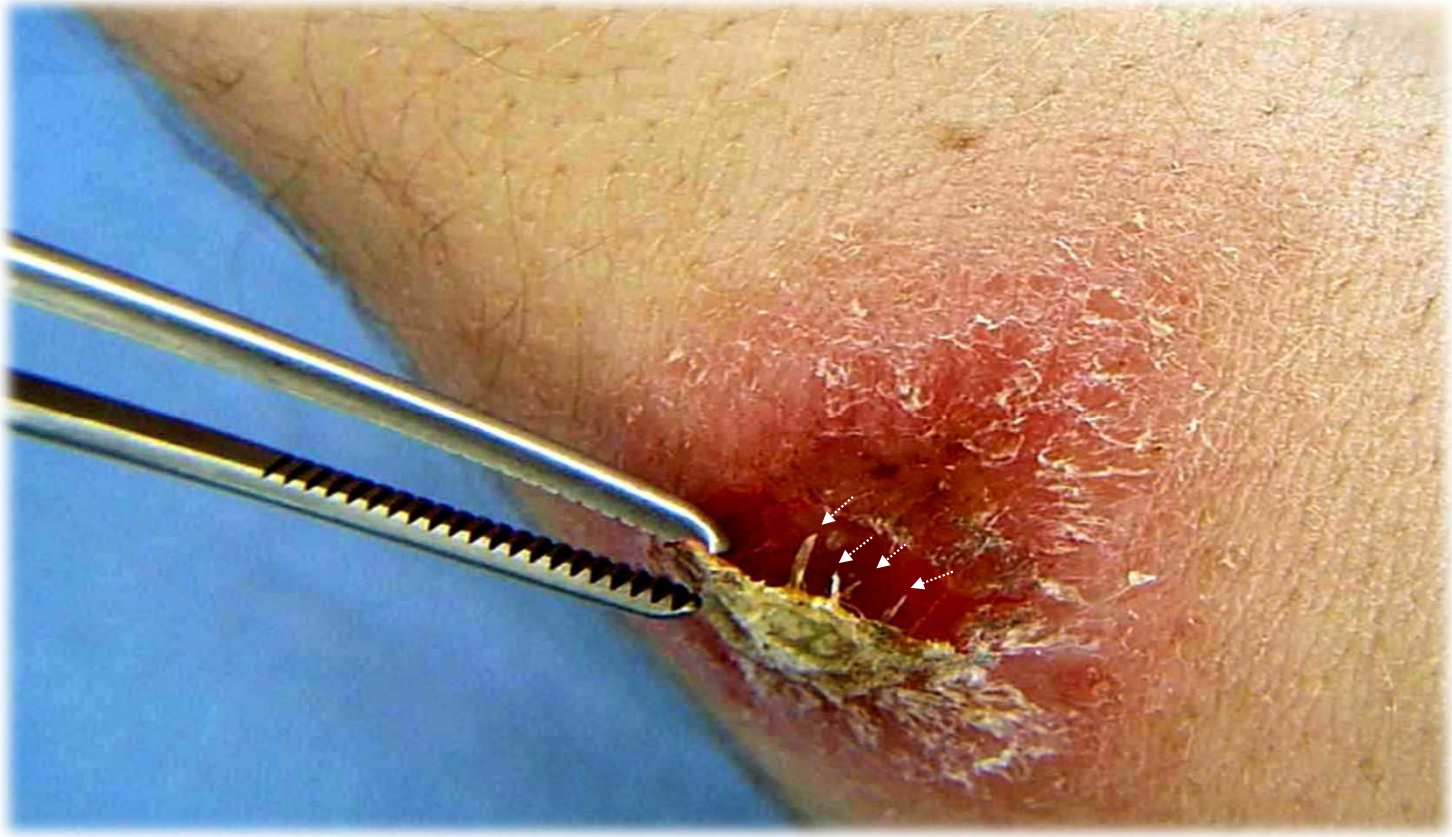


After treatment with IL antimony

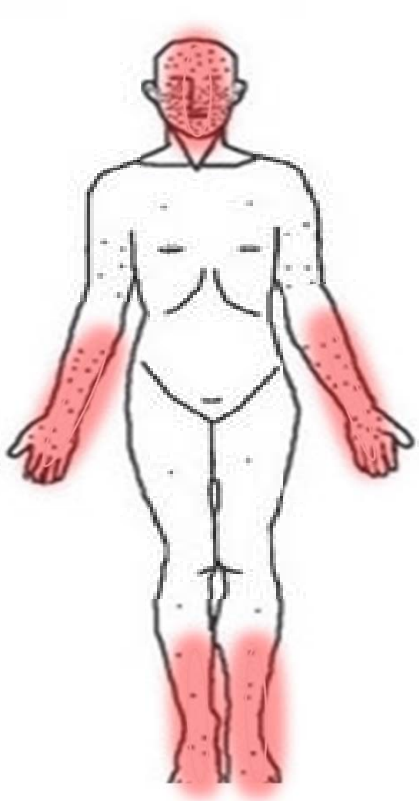


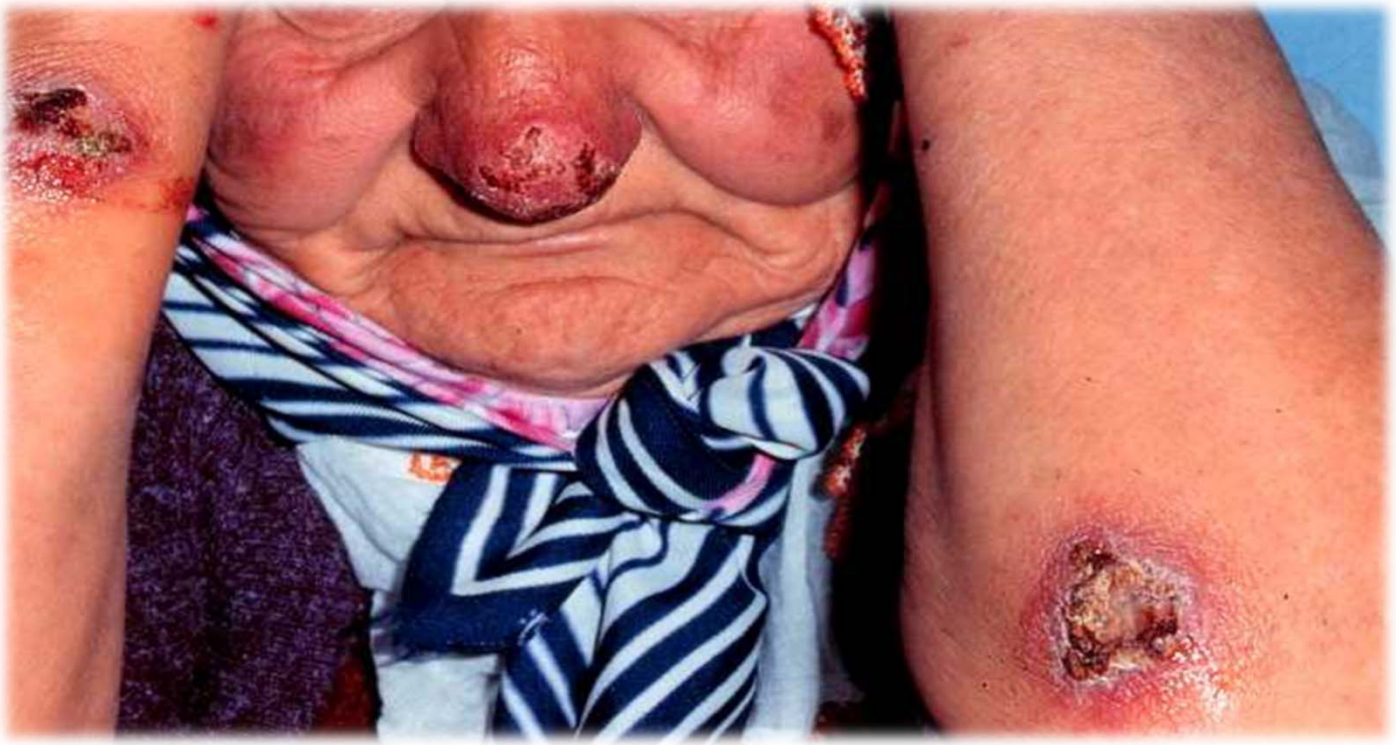
“tin-tack” sign

“spiny projections under-surface of the detached crust”

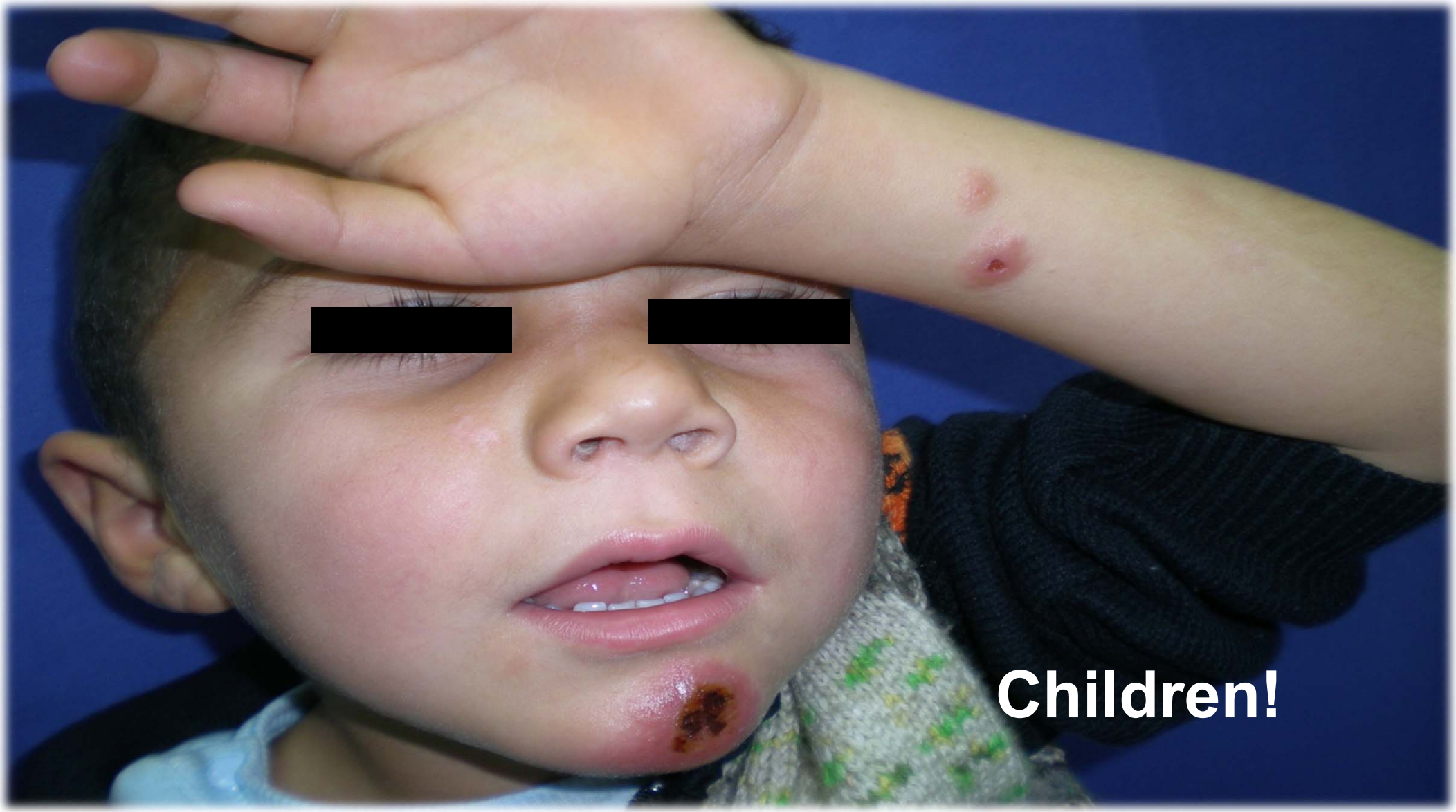


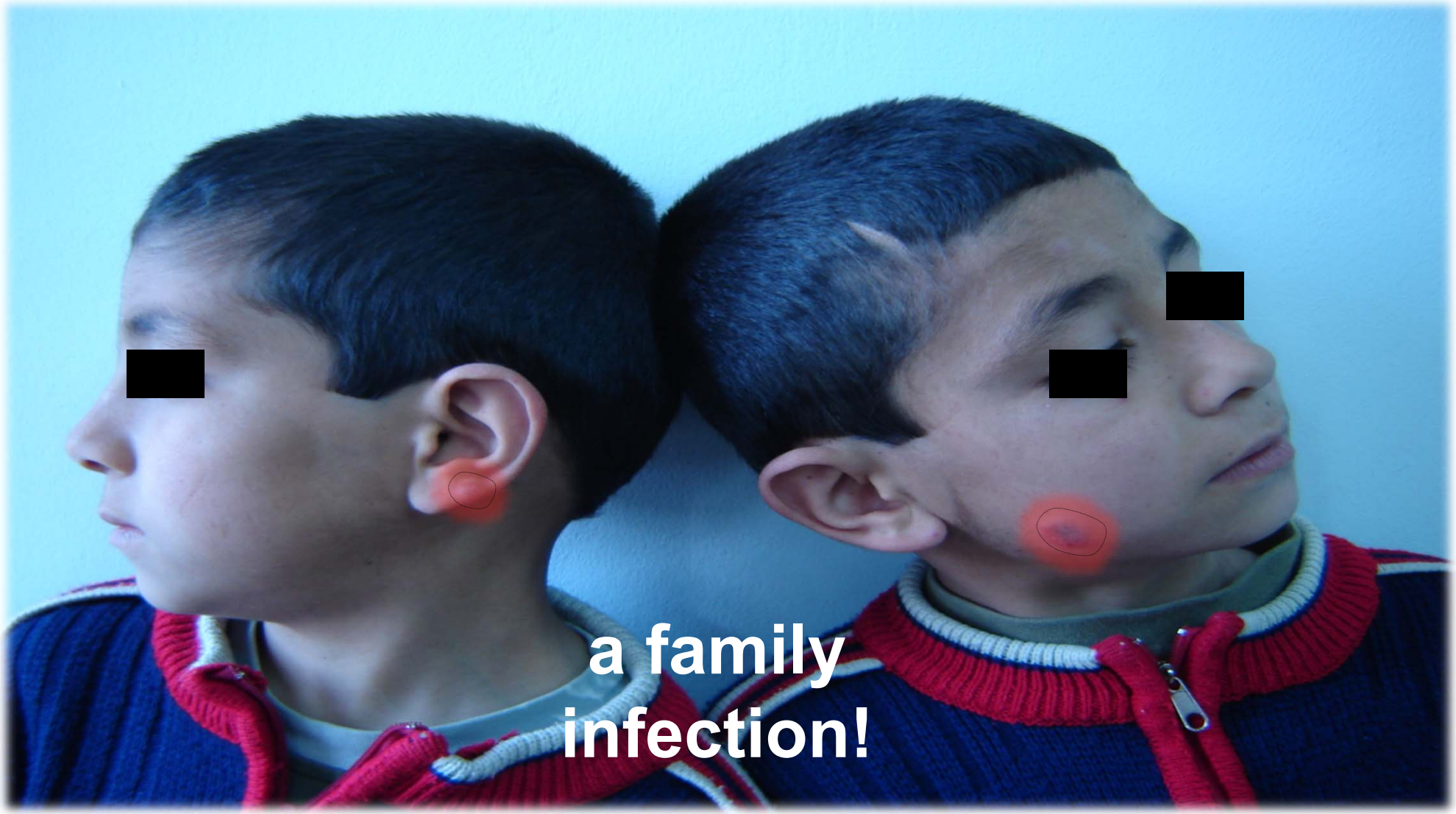
..most of the lesions are located on uncovered areas of the body *(more than 90%)*



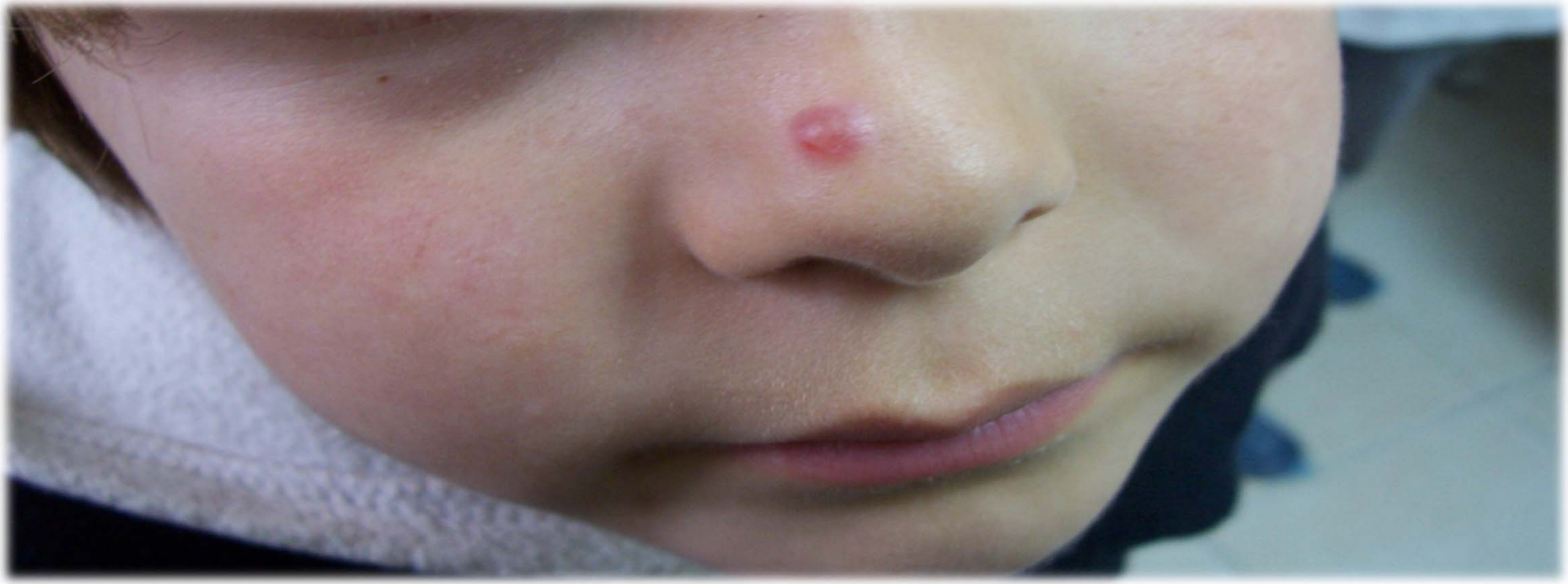


Head and neck sites:≈60%


Children!

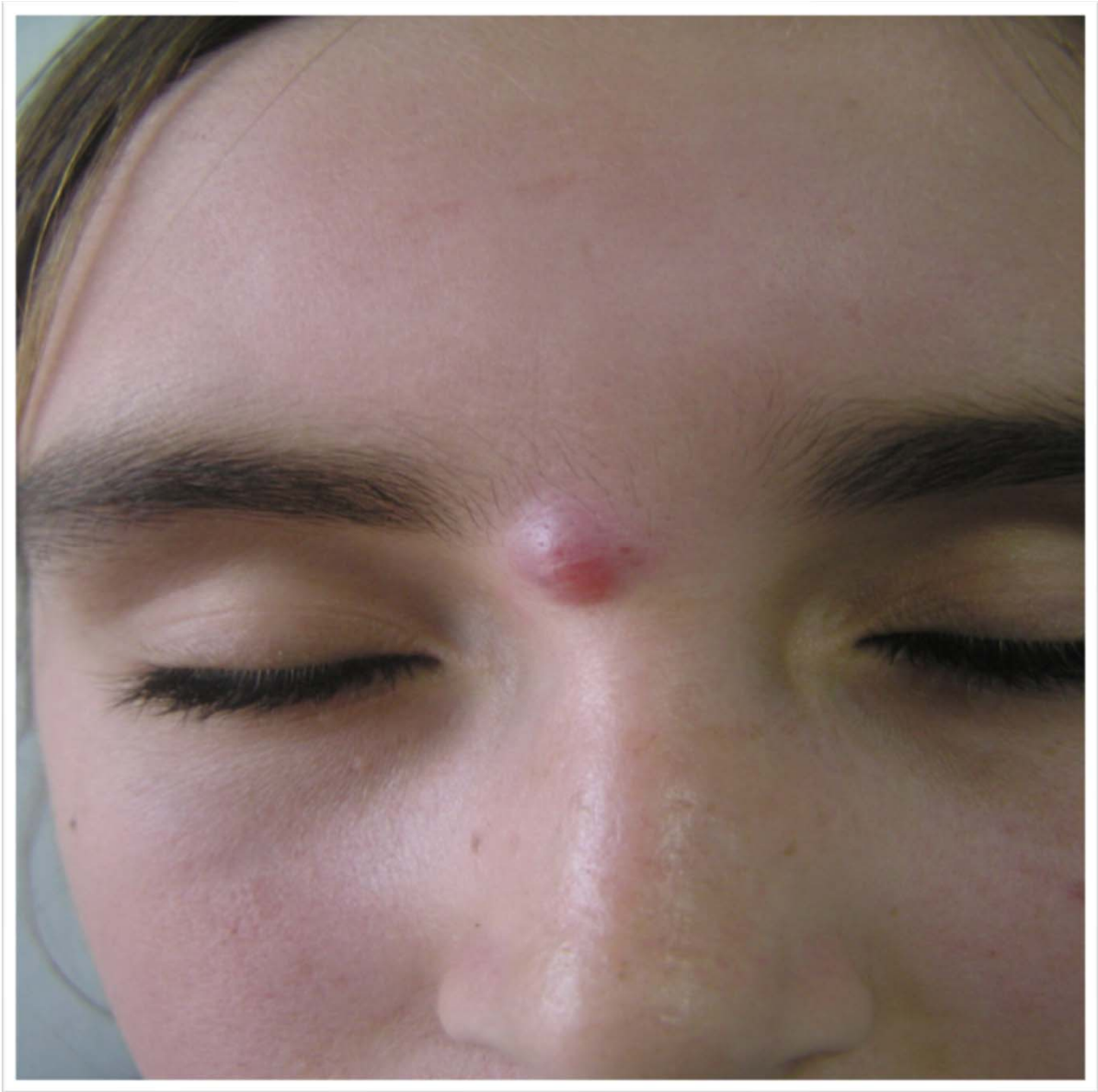

a family
infection!

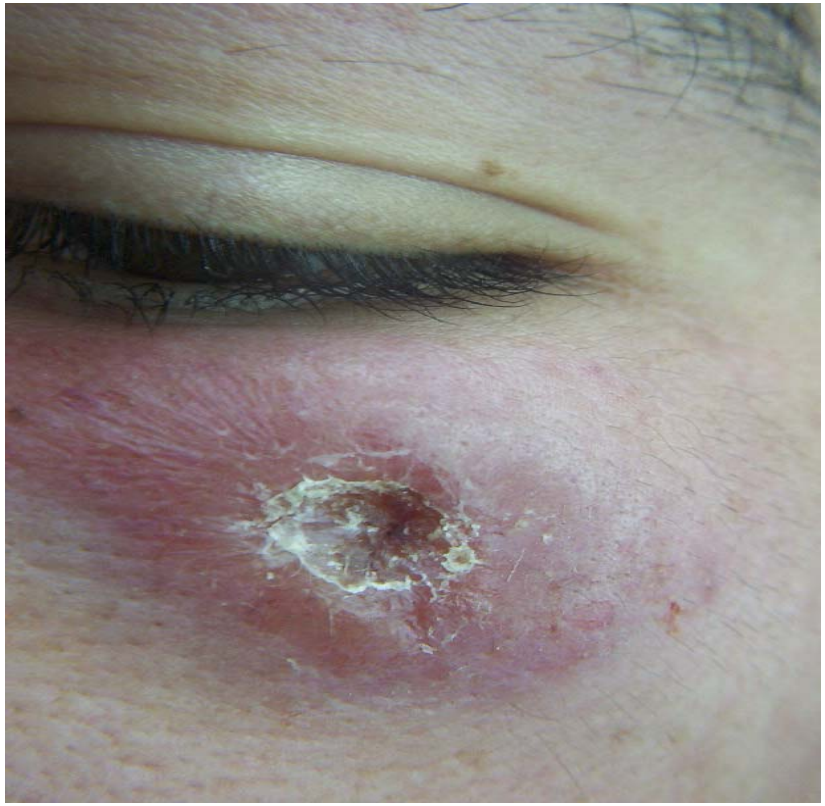
Common clinical presentations of acute CL

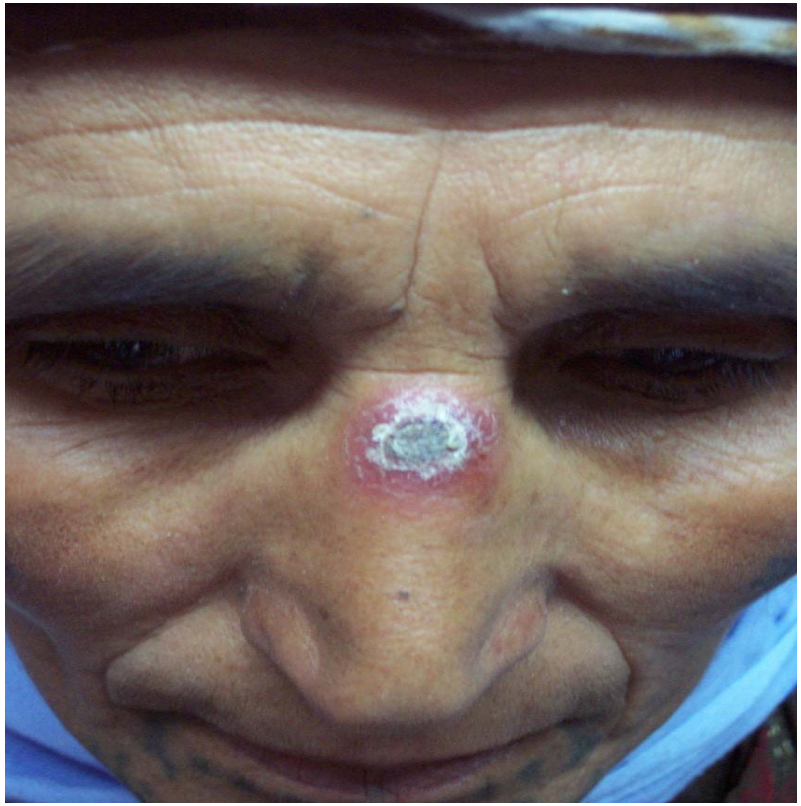


Papular

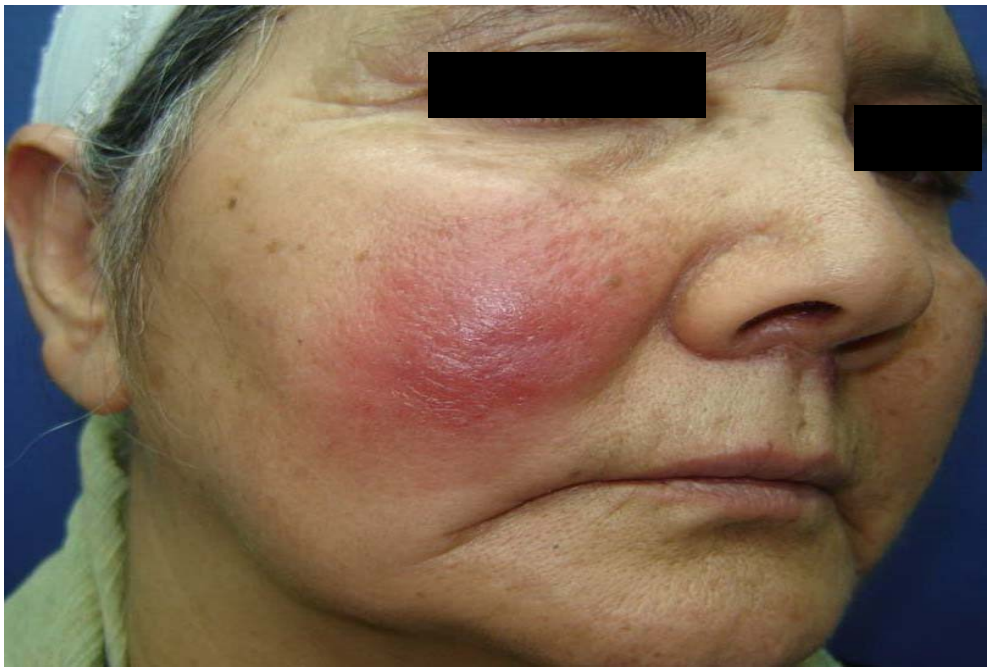
nodular

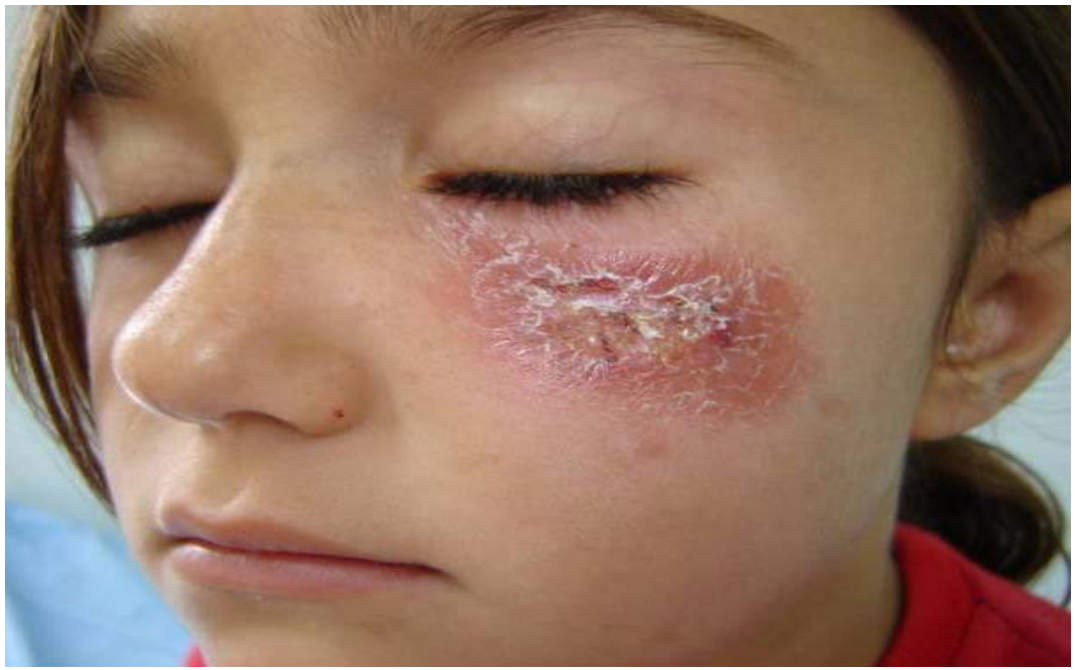




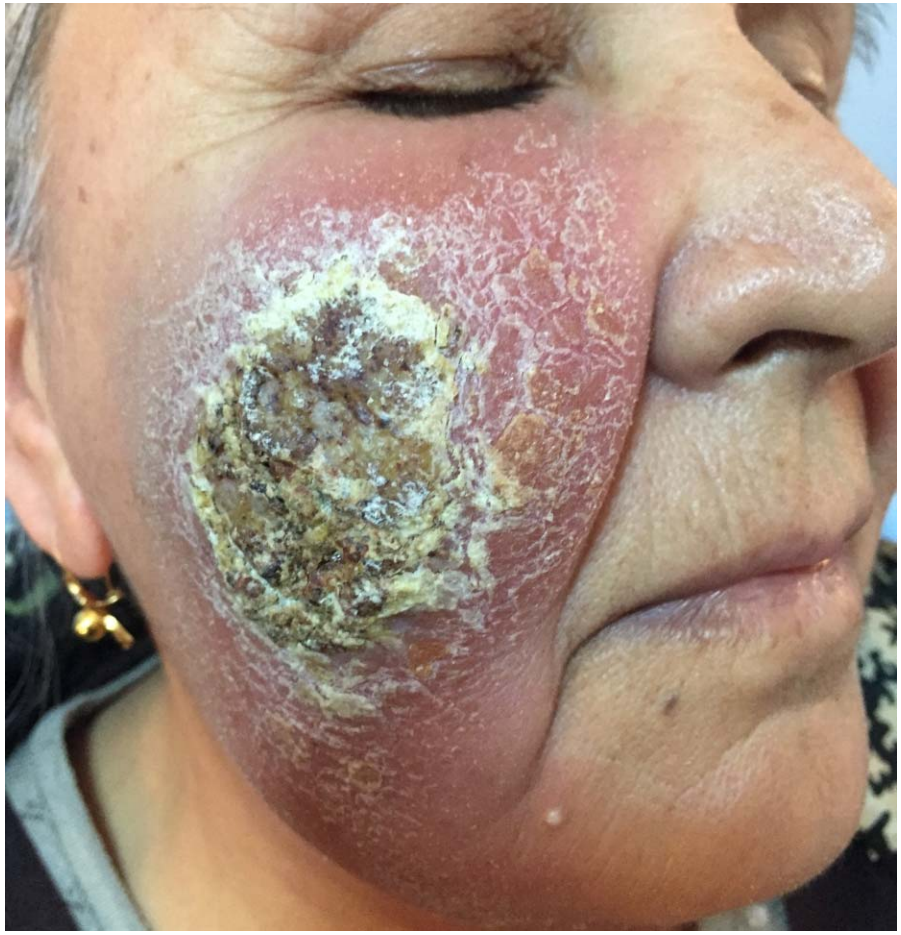


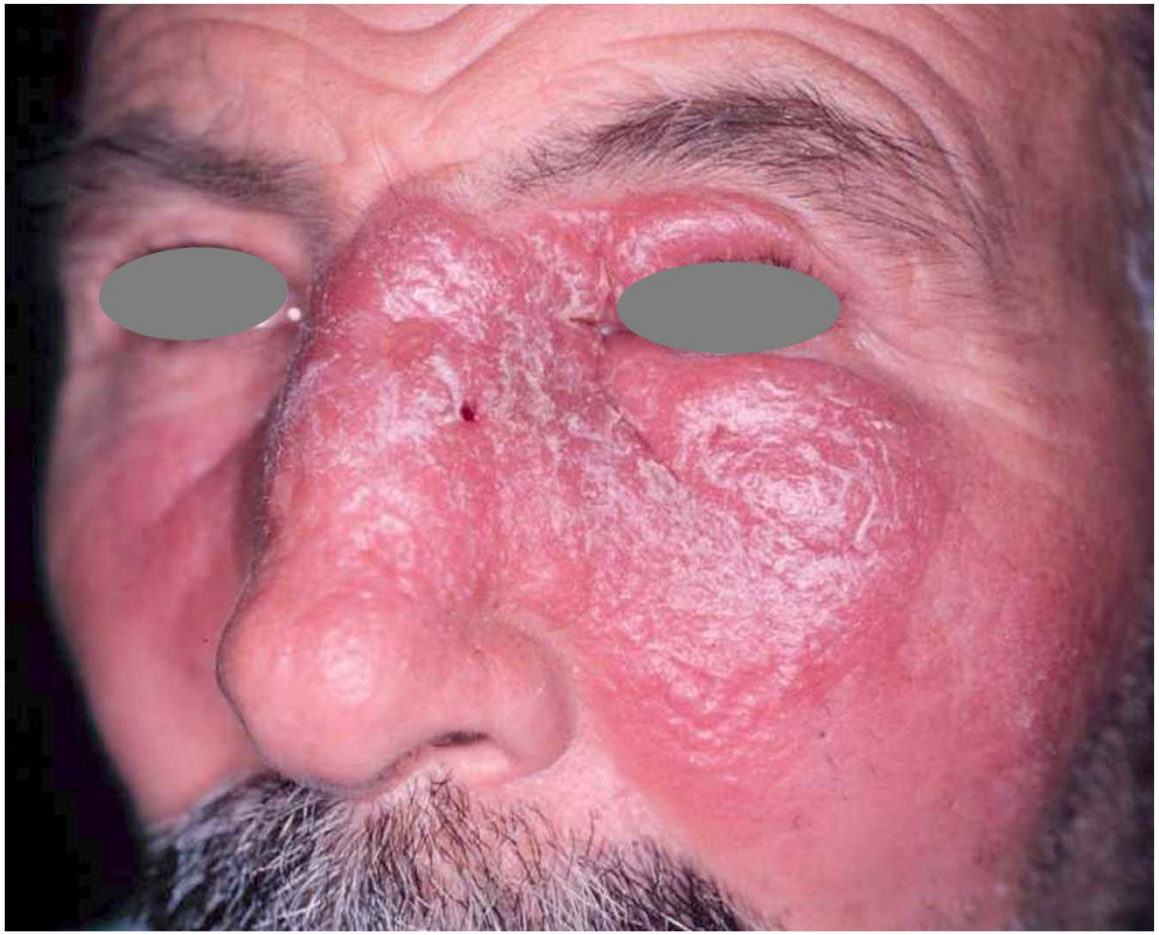
noduloulcerative

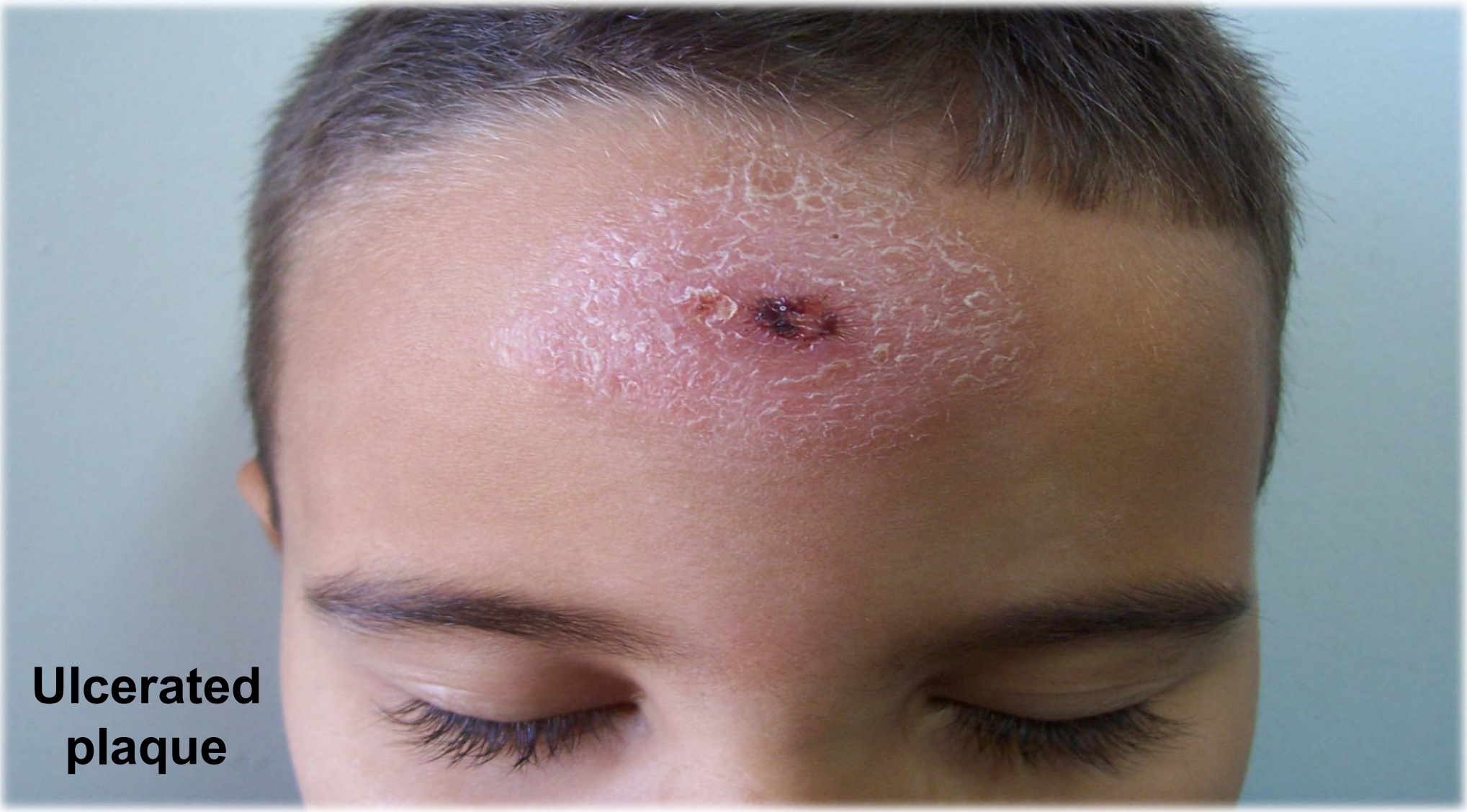


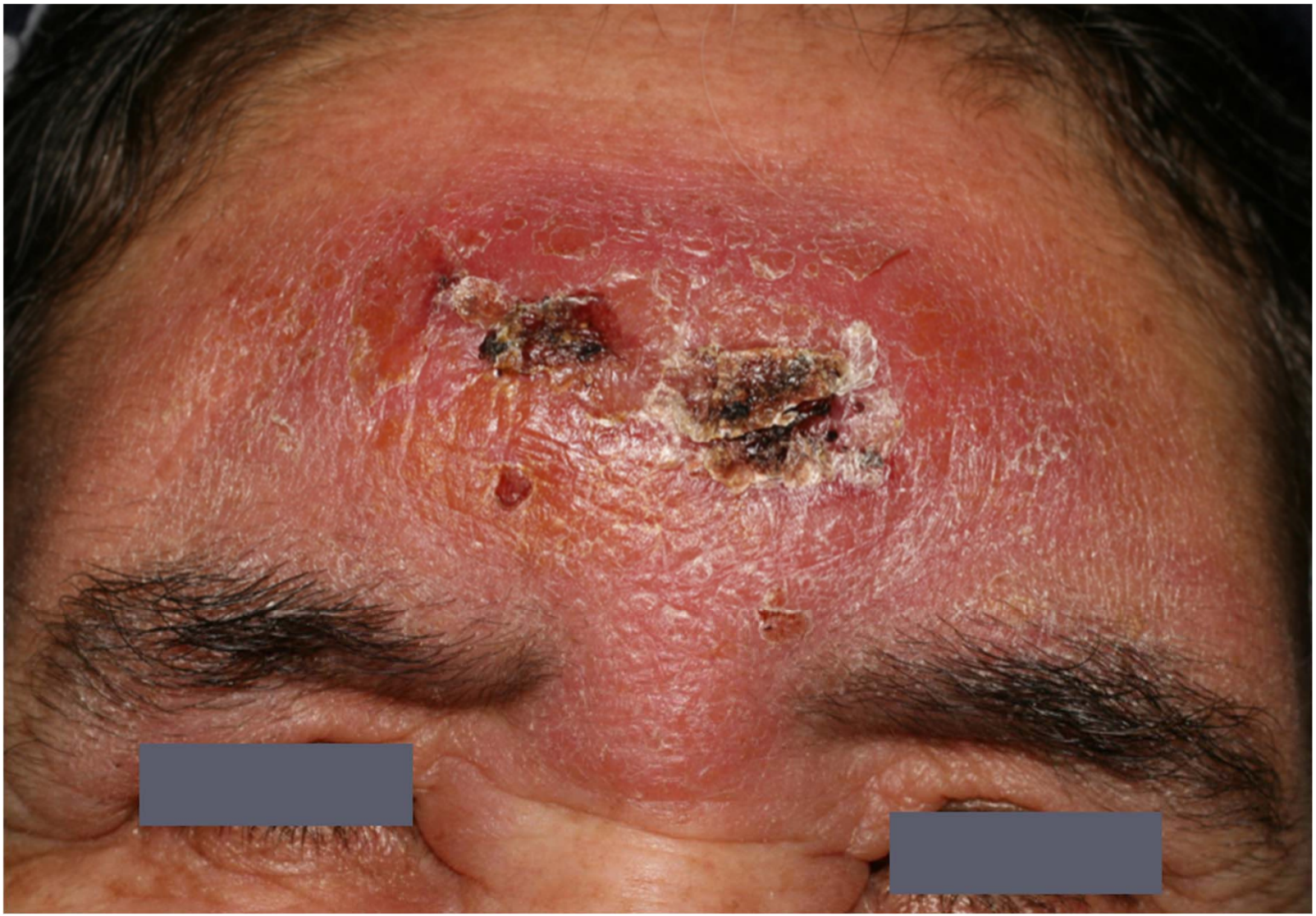


plaque






Ulcerated
plaque



Acute CL	Chronic CL and Leishmaniasis Recidivans
Insect bite	Lupus vulgaris
Impetigo	Leprosy
Furuncle	Syphilitic gummata
Ecthyma	Sarcoidosis
Kerion	Granuloma faciale
Wart	Jessner's lymphocytic infiltrate
Orf	Lymphocytoma cutis
Molluscum	Discoid lupus erythematosus
Tuberculosis cutis	Psoriasis
Syphilitic gummata	Wegener's granulomatosis
Yaws	
Pyogenic granuloma	
Blastomycosis	
Paracoccidiomycosis	
Sporotrichosis	
Chromoblastomycosis	
Swimming pool granuloma	
Foreign body granuloma	
Keratoacanthoma	
Basal cell carcinoma	
Squamous cell carcinoma	
Lymphoma	
Leukemia, Cutaneous metastases	

Differential diagnosis of CL

"there are a number of mimics of CL"

CL can mimic a number of skin diseases

“the great imitator”

J Cutan Pathol 2012: 39: 251–262
doi: 10.1111/j.1600-0560.2011.01844.x
John Wiley & Sons. Printed in Singapore

Journal of
Cutaneous Pathology

Cutaneous leishmaniasis mimicking inflammatory and neoplastic processes: a clinical, histopathological and molecular study of 57 cases

Background: Cutaneous leishmaniasis displays considerable variation in its histopathological and clinical presentation. Clinically, it progresses from a papule into a painless ulcerated and crusted nodule/papule. Microscopically, it progresses from sheets of amastigote-filled histiocytes to granulomatous inflammation.
Methods: The study was conducted on 145 skin biopsies from untreated patients with histopathological and/or clinical suspicion of cutaneous leishmaniasis in Lebanon, Syria and Saudi Arabia (1992–2010). The pre-biopsy clinical diagnosis and demographic data were collected. Biopsies were evaluated for the major microscopic pattern, and the parasitic index (PI) was also determined. Diagnosis was confirmed by polymerase chain reaction (PCR) followed by molecular sub-speciation.
Results: Of the 145 patients, 125 were confirmed as cutaneous leishmaniasis by PCR. Eighteen cases presented with a pre-biopsy clinical diagnosis other than cutaneous leishmaniasis that ranged from dermatitis to neoplasm. Of the 125 cases, 57 showed a major histopathological pattern other than cutaneous leishmaniasis. Identification of amastigotes was equivocal (PI ≤1) in 38 of the 57 cases. Of interest, all the 18 cases with a pre-biopsy clinical diagnosis other than cutaneous leishmaniasis also showed atypical histopathology for cutaneous leishmaniasis.
Conclusions: The manifestations of cutaneous leishmaniasis are broad and may mimic other inflammatory and neoplastic diseases. Pathologists and dermatologists should be aware of such pitfalls and can utilize PCR to confirm the diagnosis of leishmaniasis.

Keywords: cutaneous leishmaniasis, mimic, molecular sub-speciation, simulant

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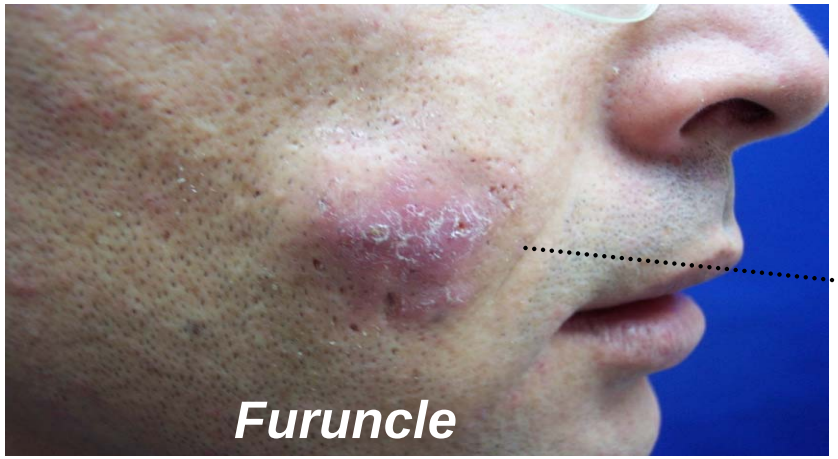
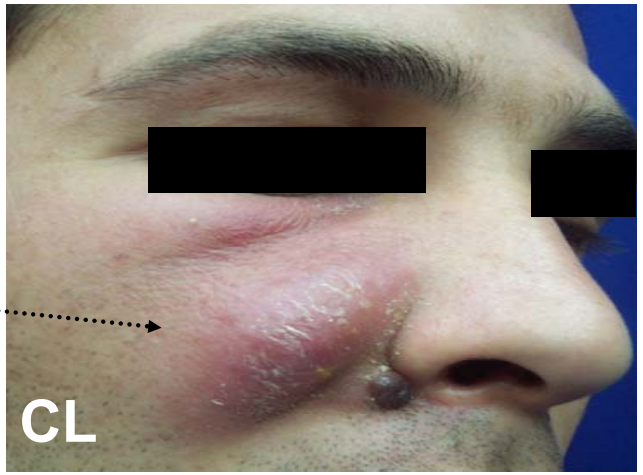
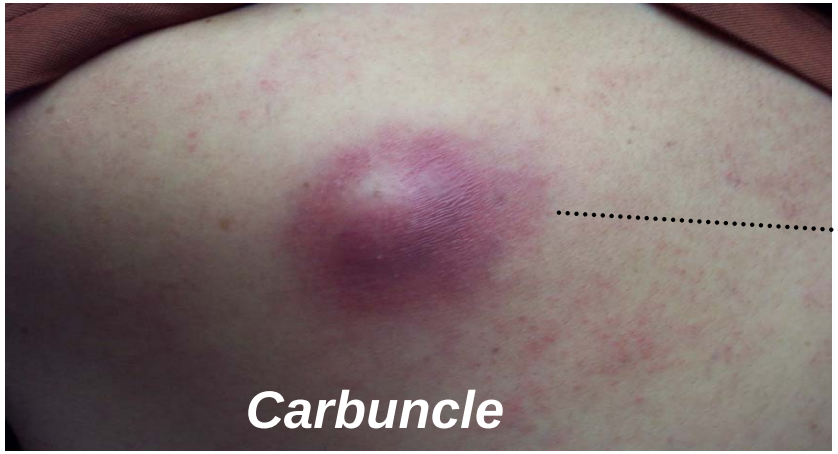
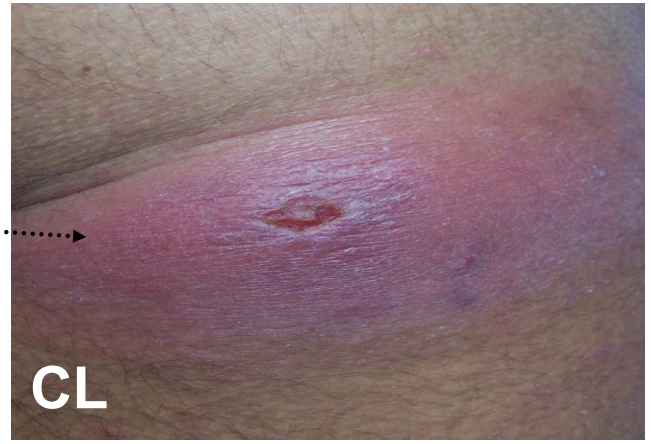
Bacterial skin infections

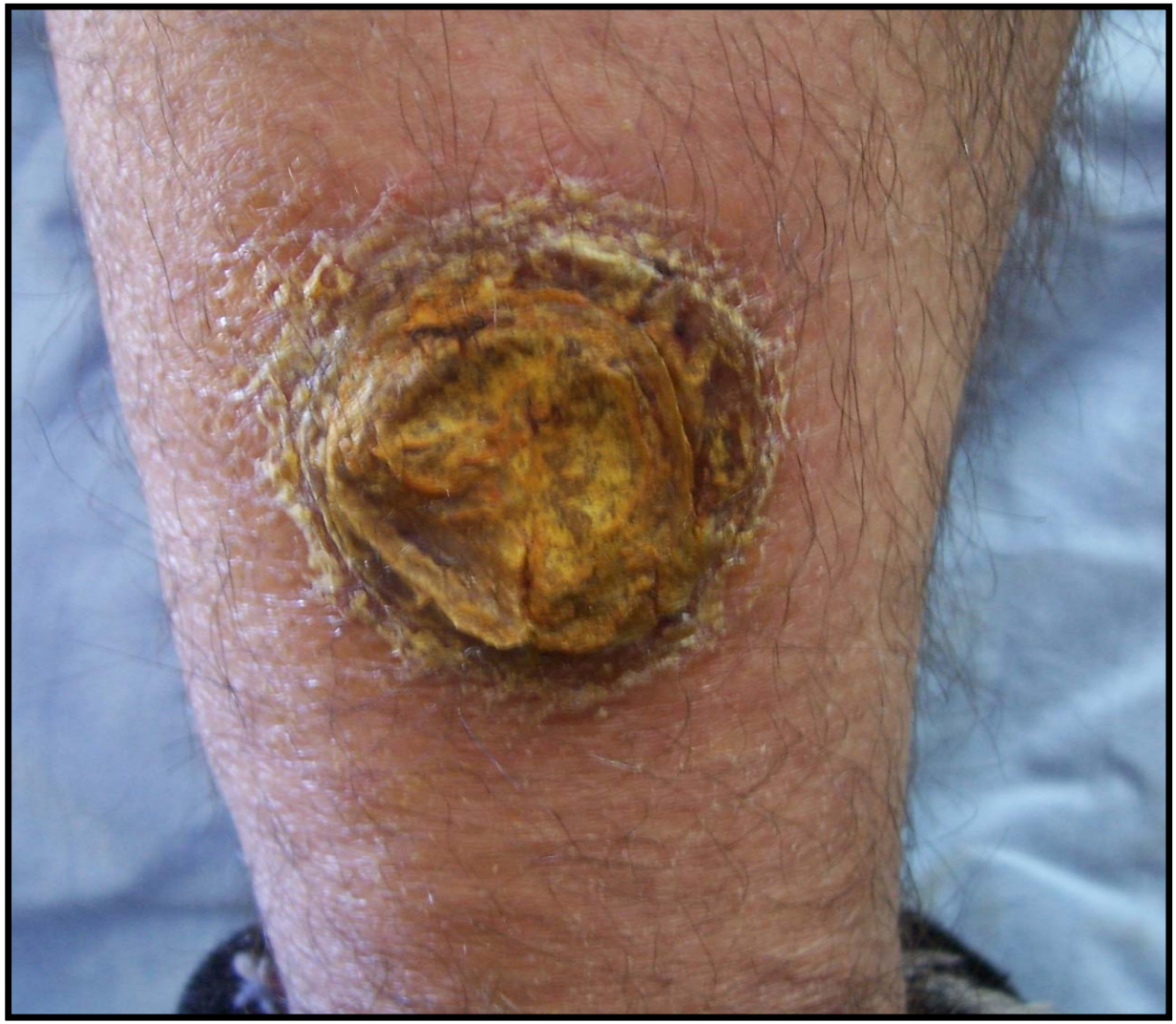


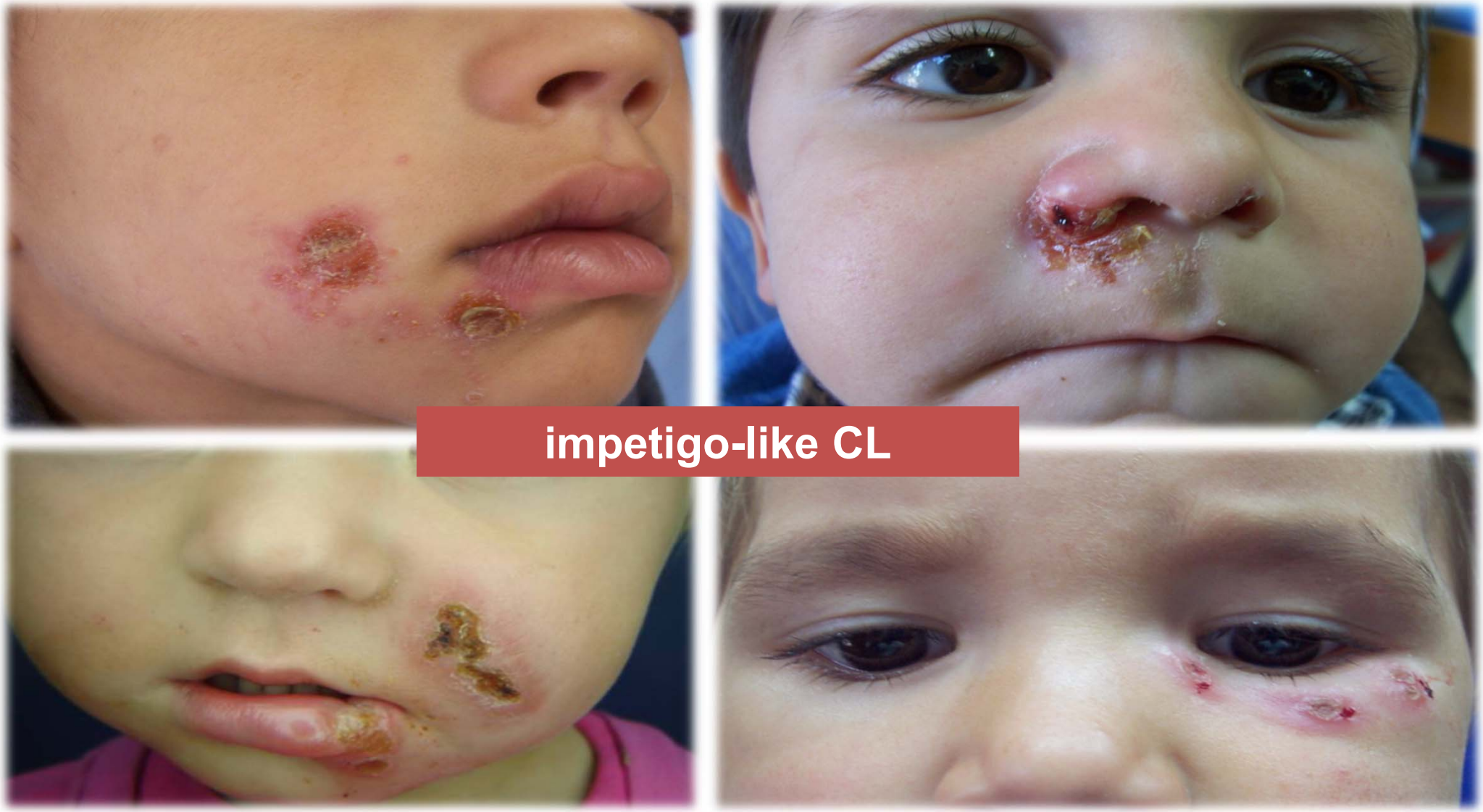




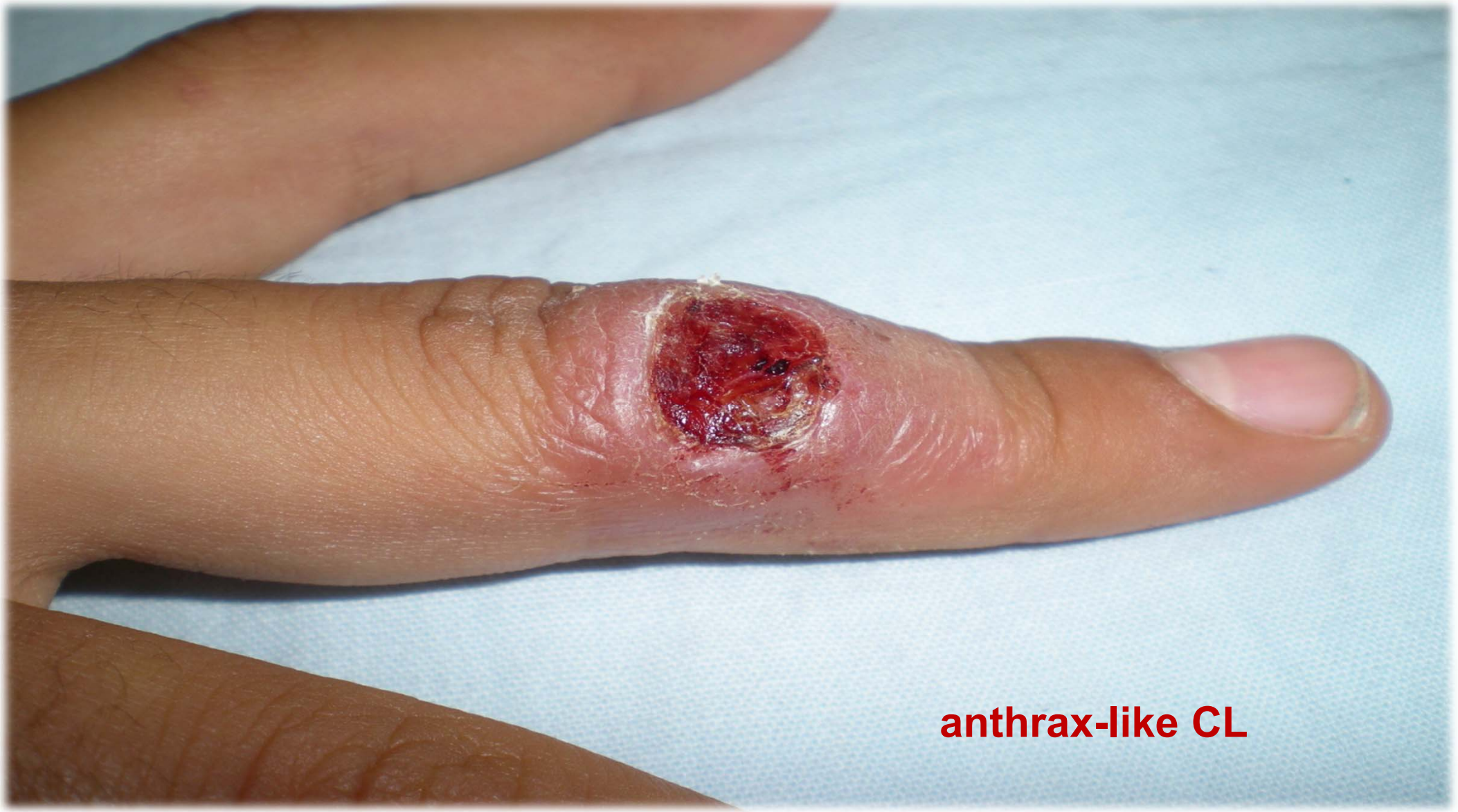


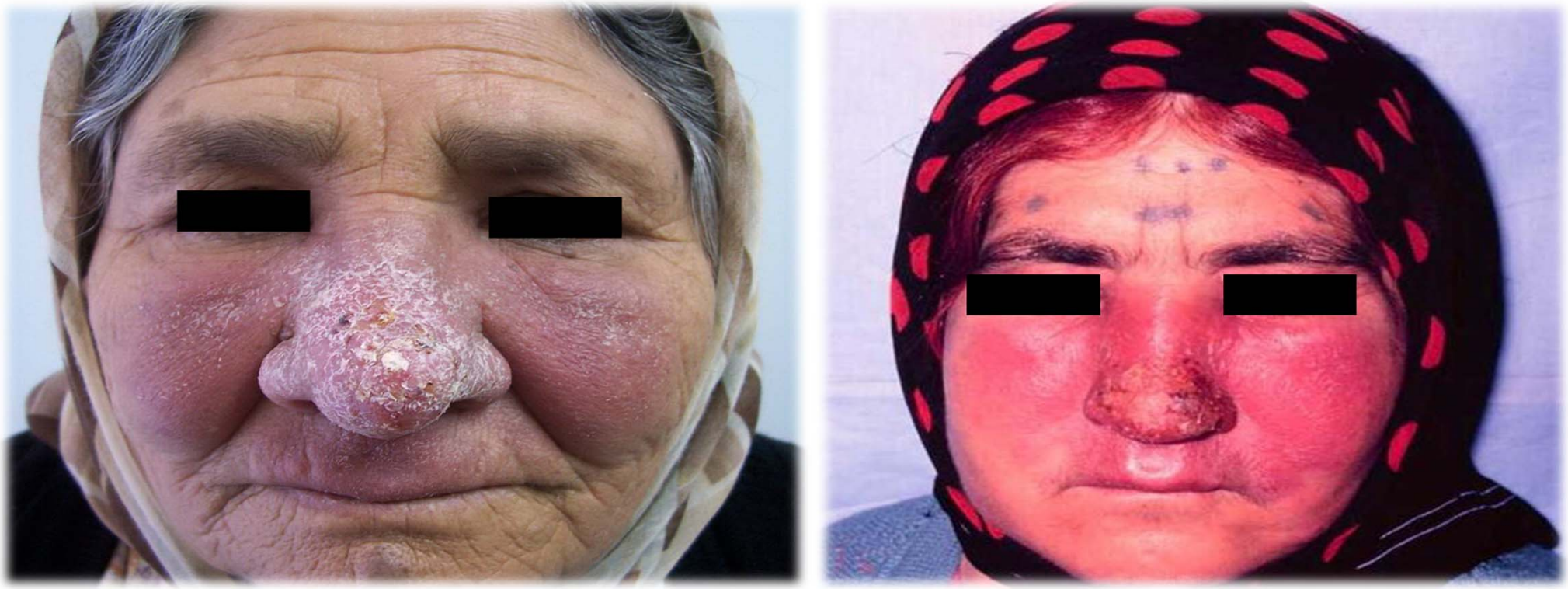
ecthyma-like CL



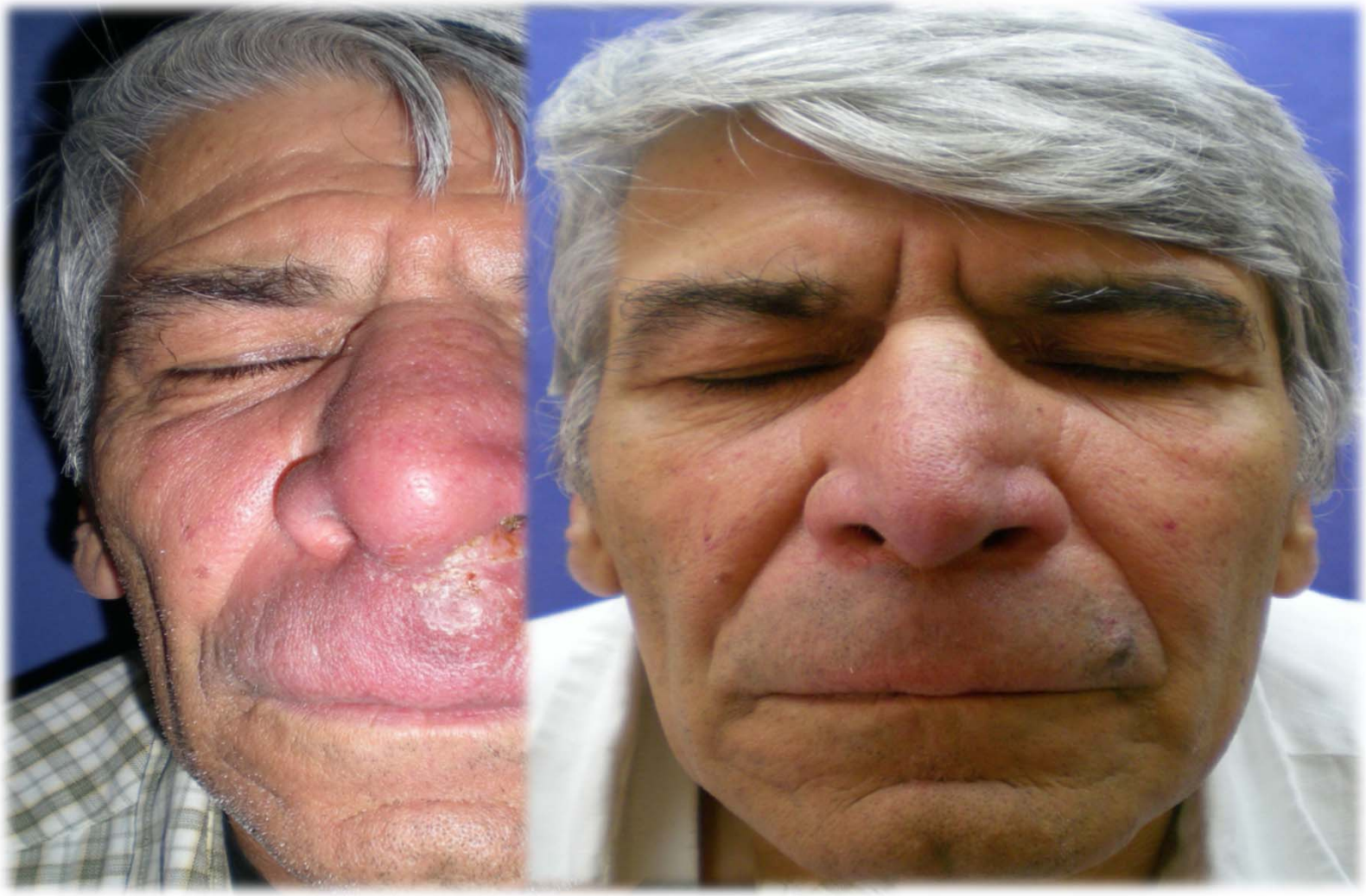


impetigo-like CL


anthrax-like CL

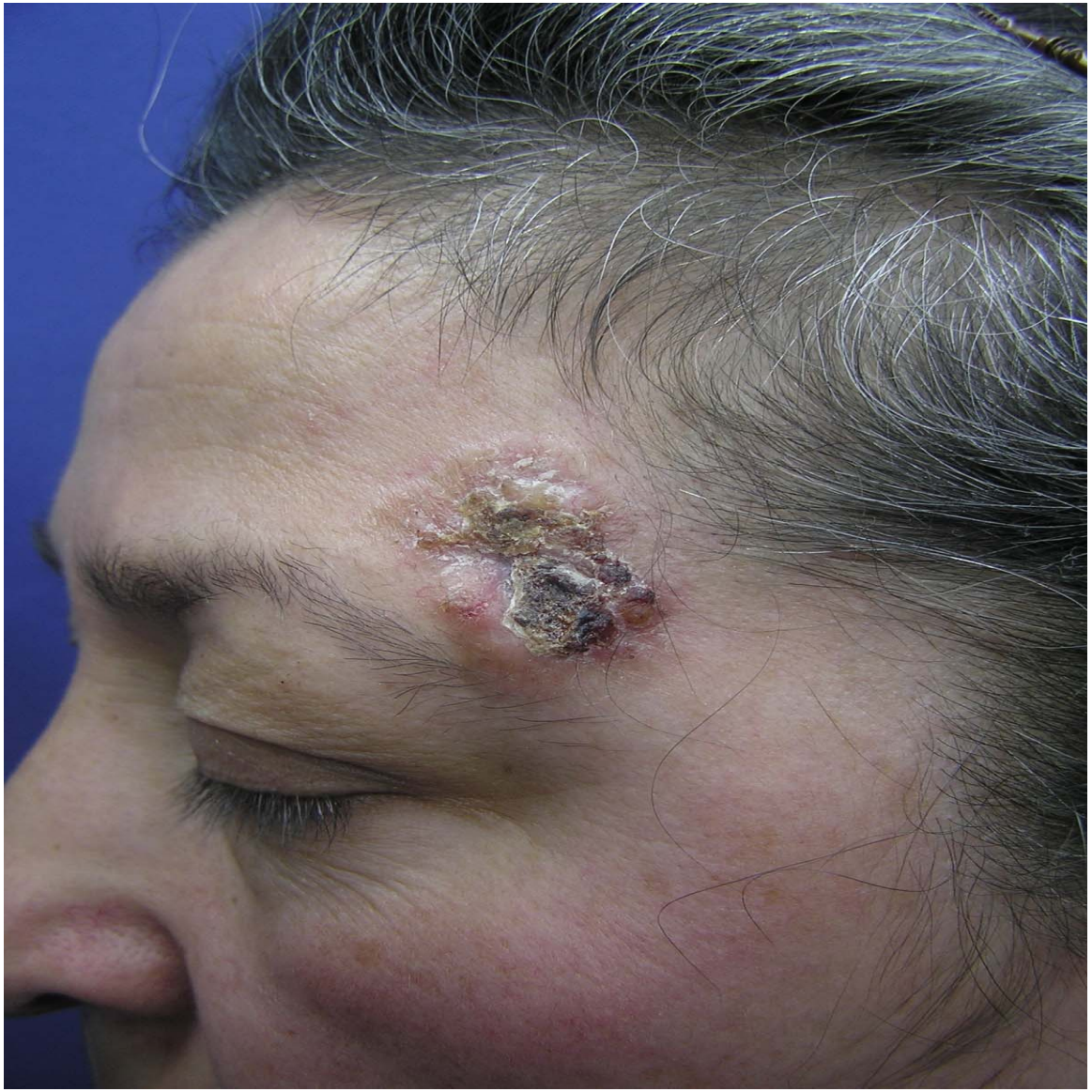


erysipeloid CL *(Erysipelas-like CL)*



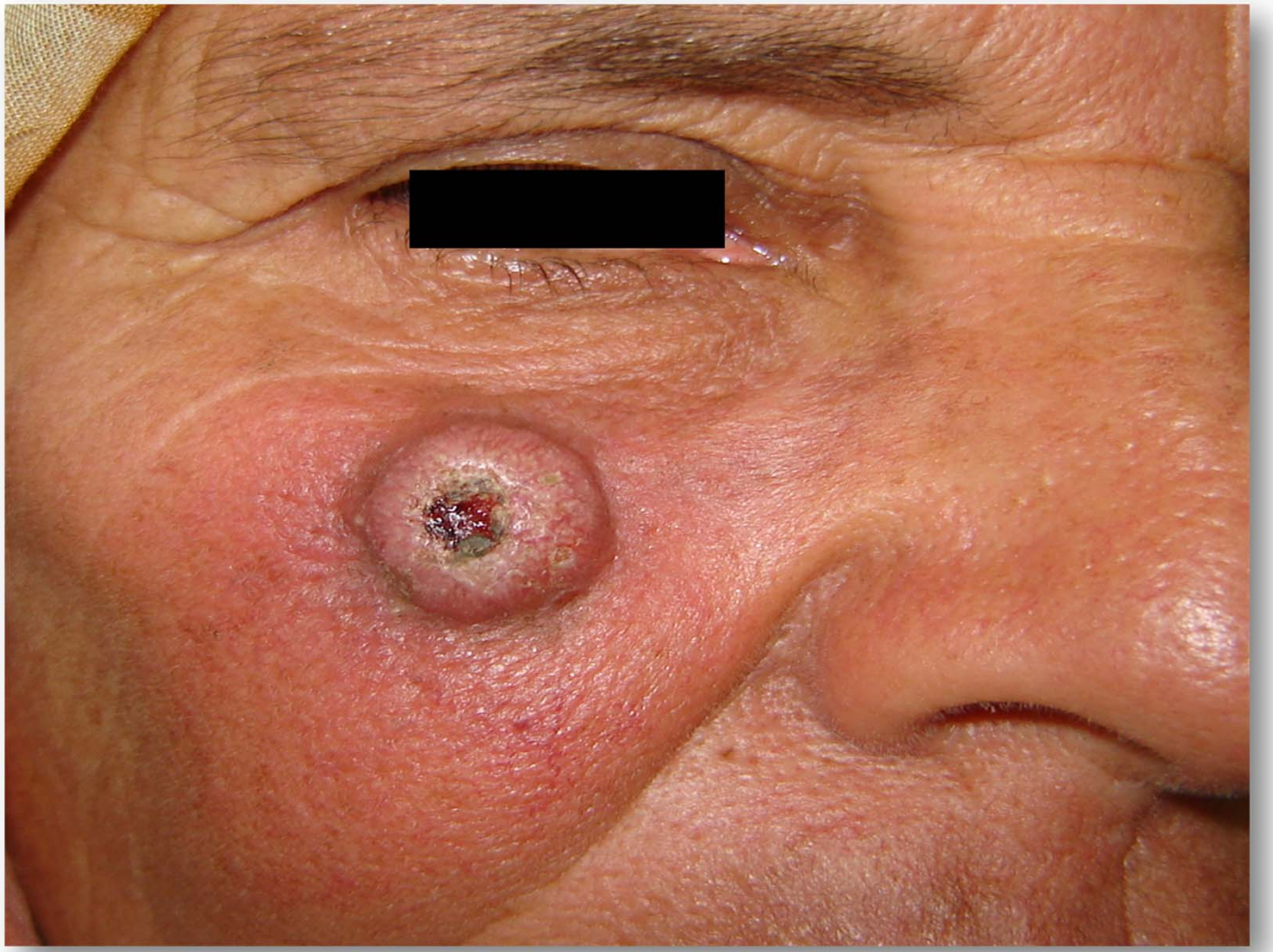
Erysipelas-like CL

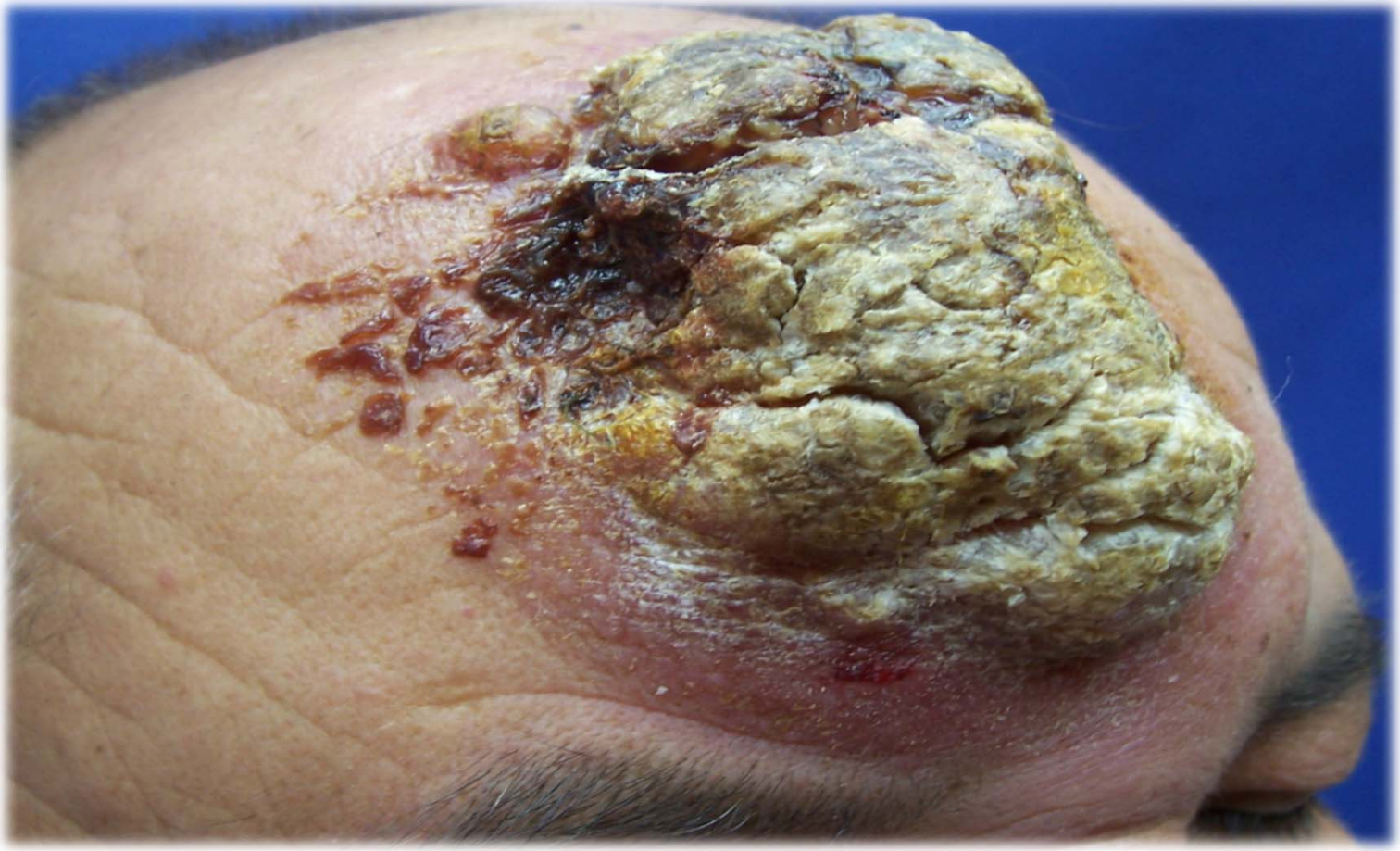
After systemic antimony treatment



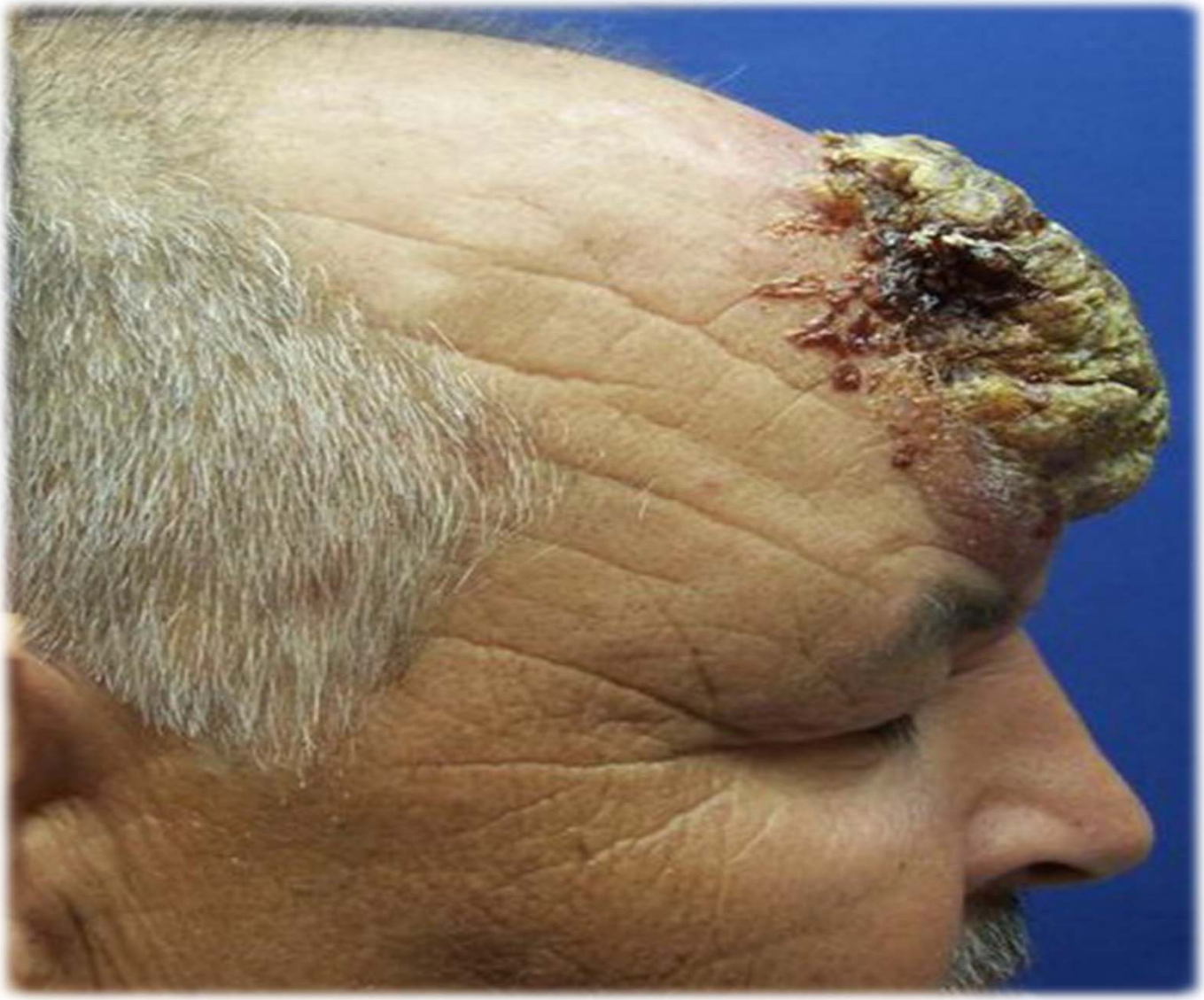
basal cell carcinoma-like CL

Keratoacanthoma-like CL



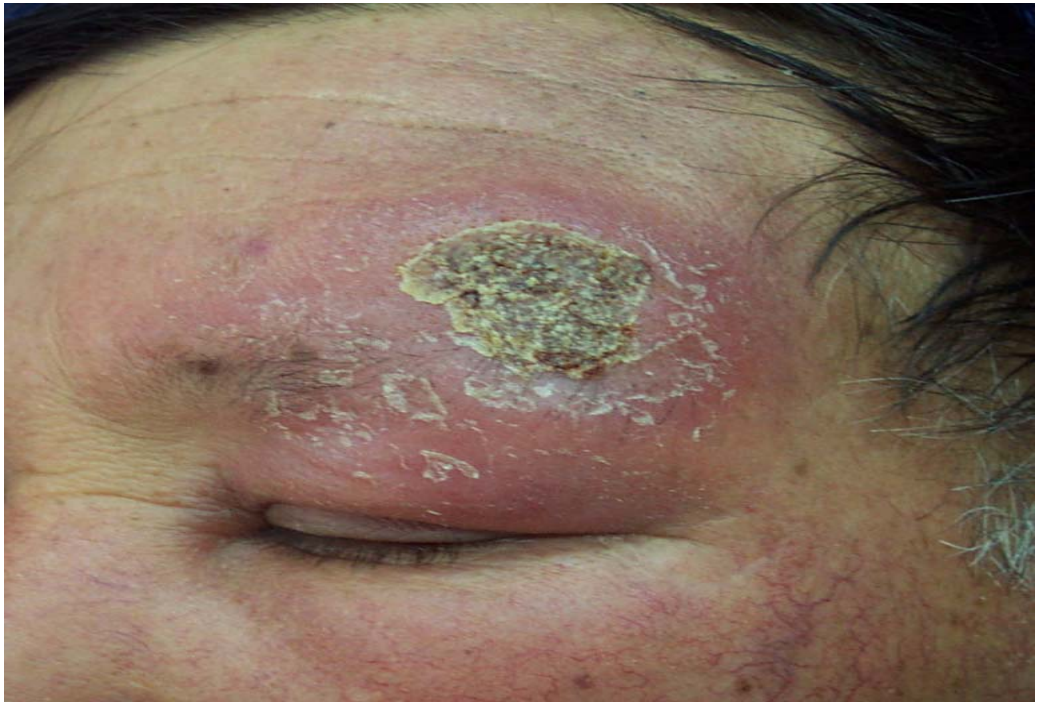


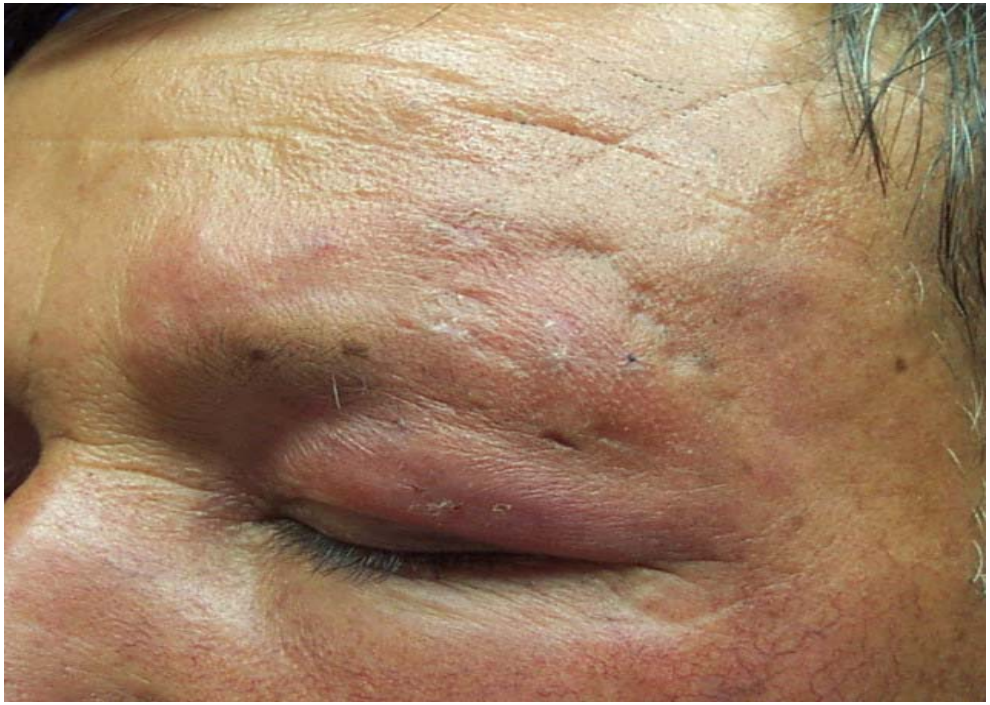
squamous cell carcinoma or cutaneous lymphoma-like CL



after first cure of systemic antimony treatment

cutaneous lymphoma-like CL

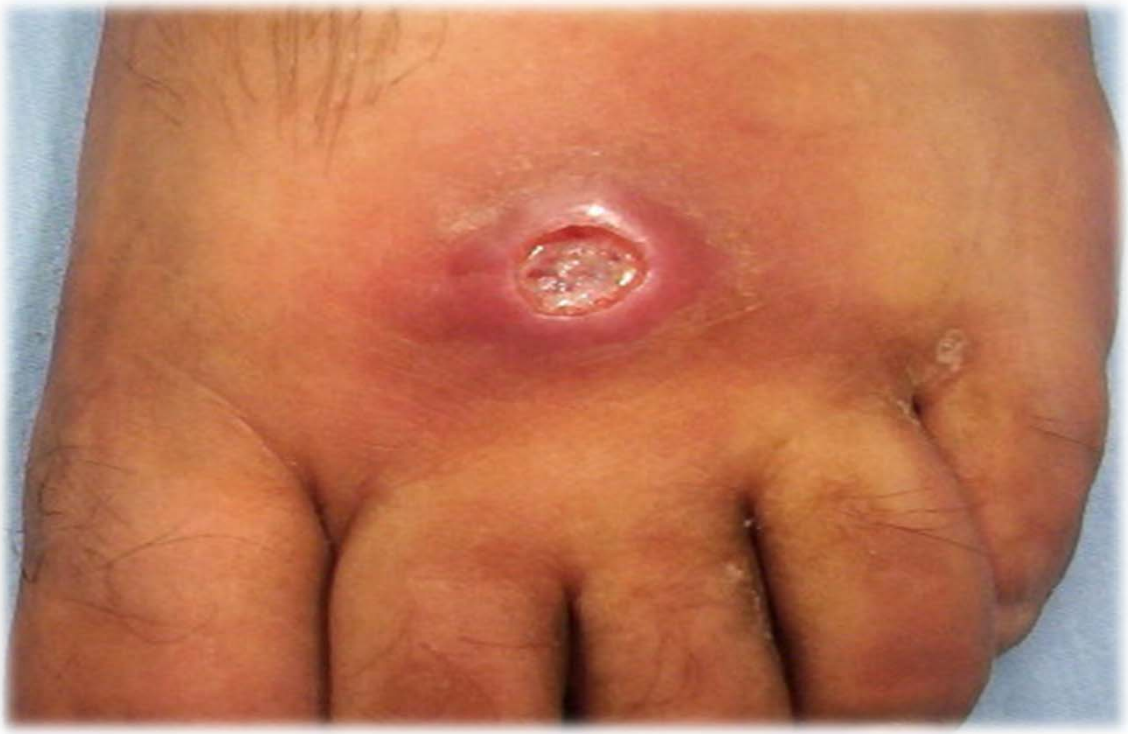


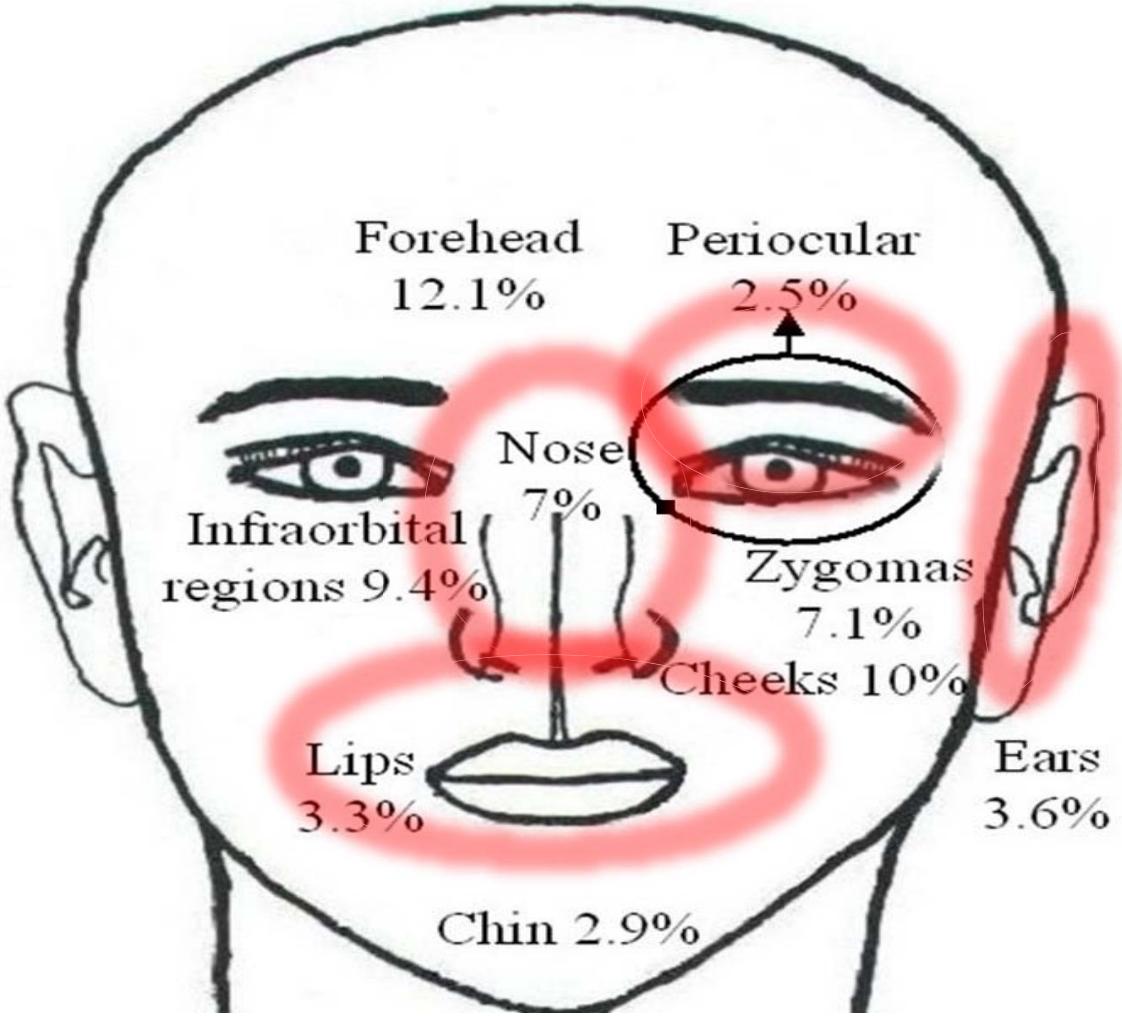


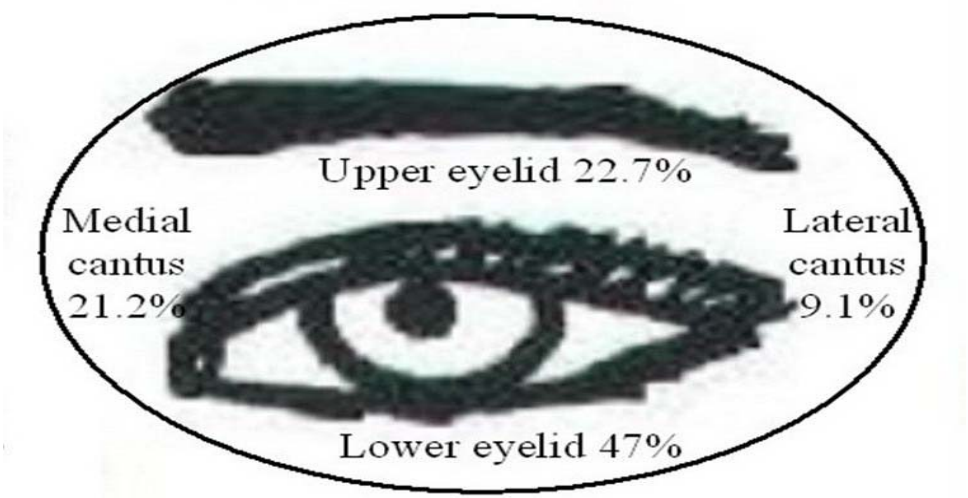
After IL antimony treatment

Duration of the disease

from onset to the diagnosis ranges between **1 mo and 5 yr** (**mean duration,11 mo**)




Forehead
12.1%
Periocular
2.5%
Nose
7%
Infraorbital
regions 9.4%
Zygomas
7.1%
Cheeks 10%
Lips
3.3%
Ears
3.6%
Chin 2.9%



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ORIGINAL ARTICLE

Periocular involvement in cutaneous leishmaniasis

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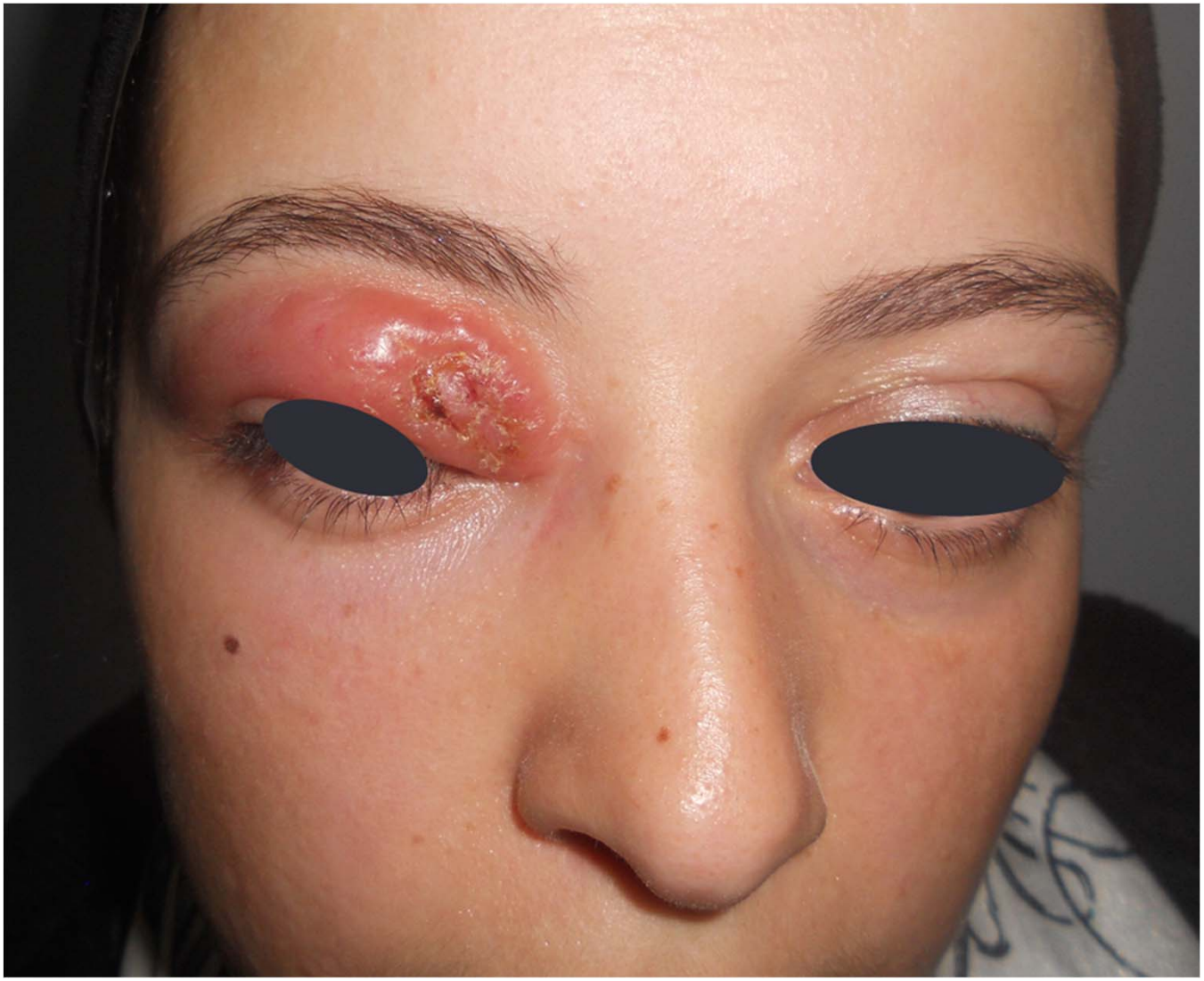
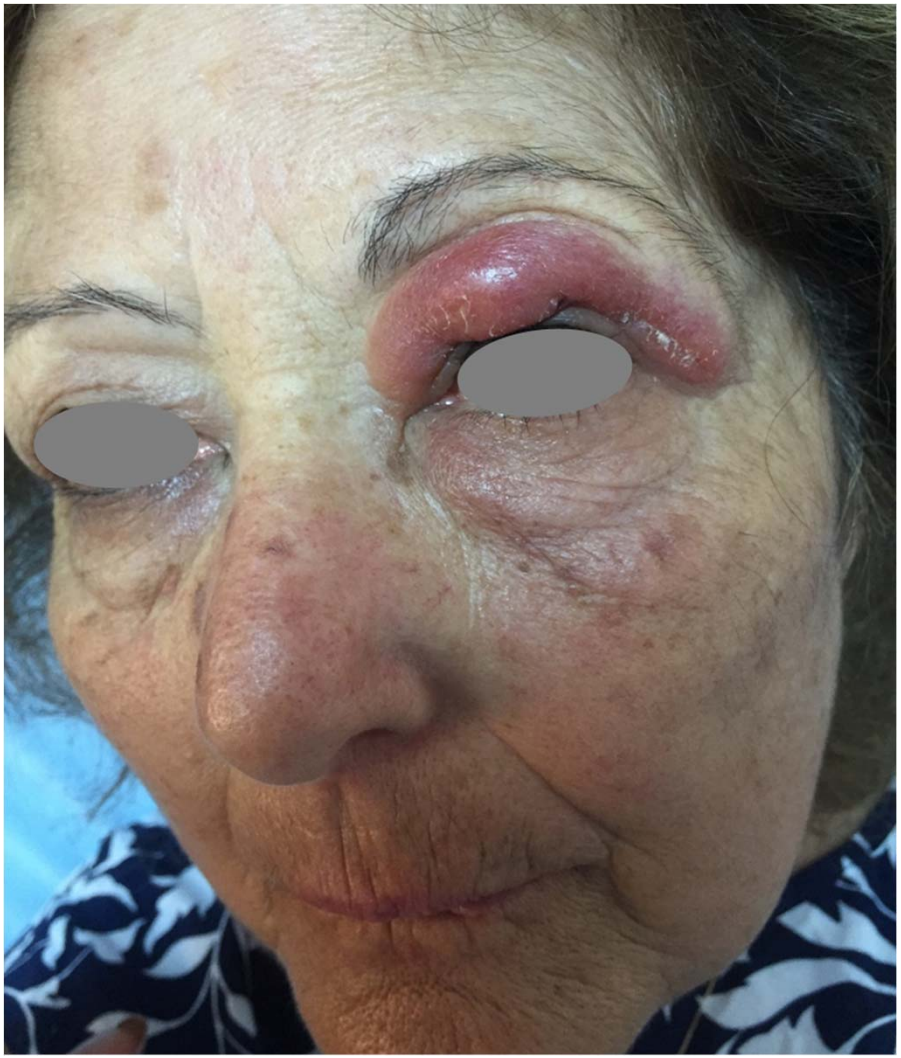
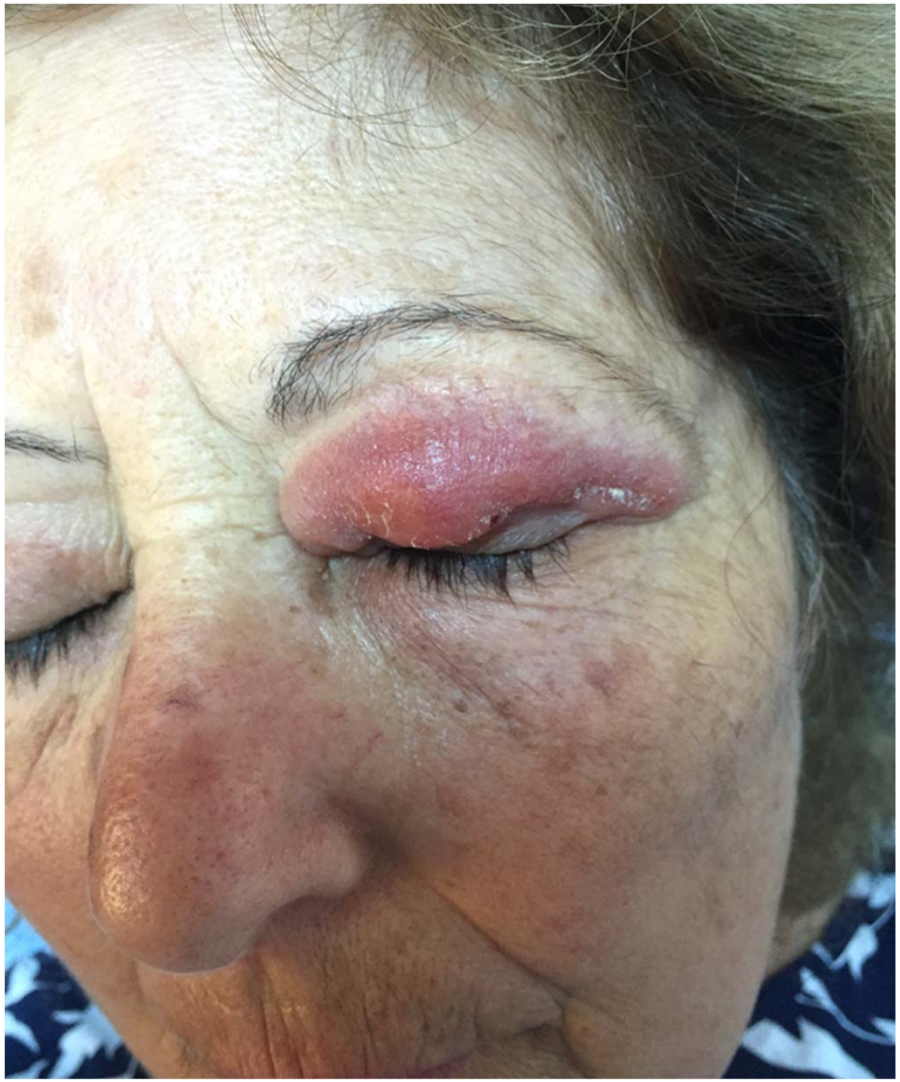
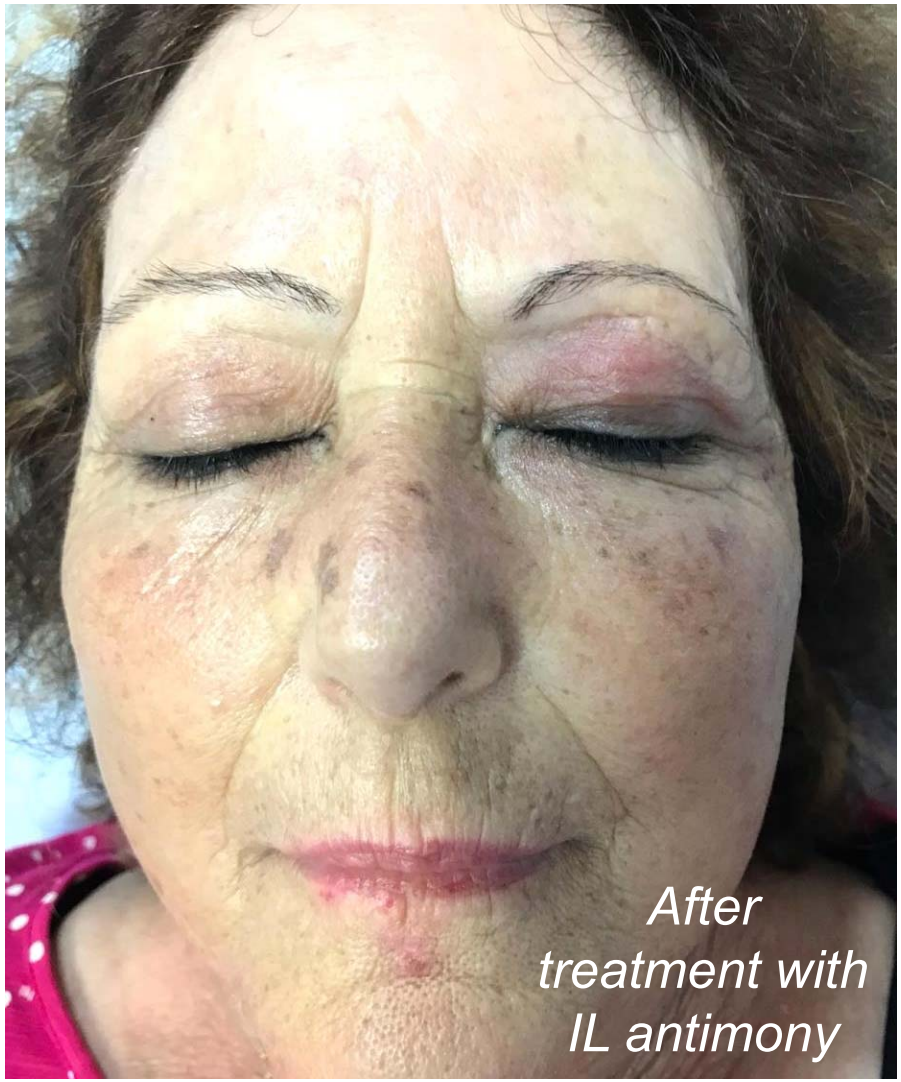
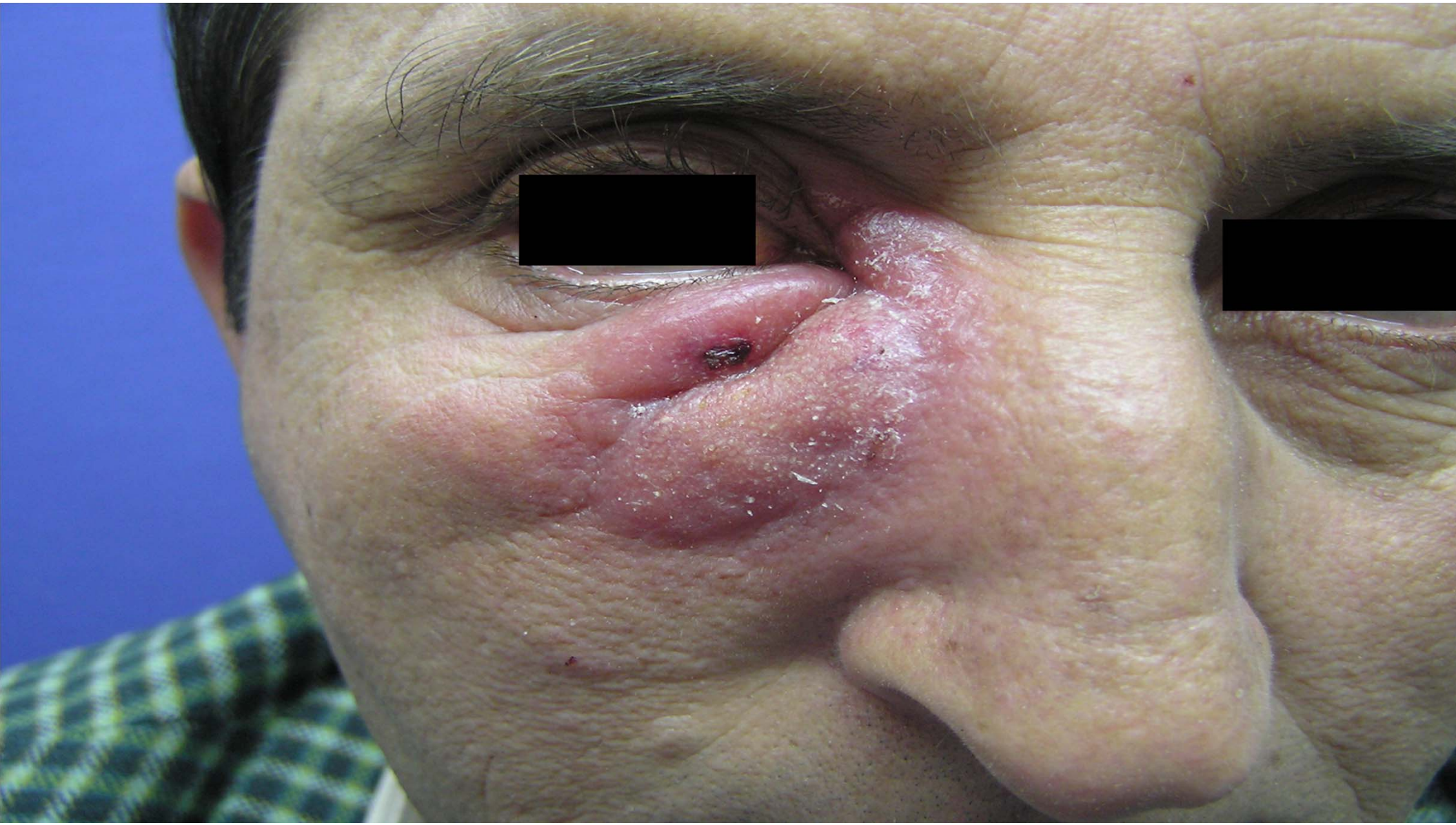


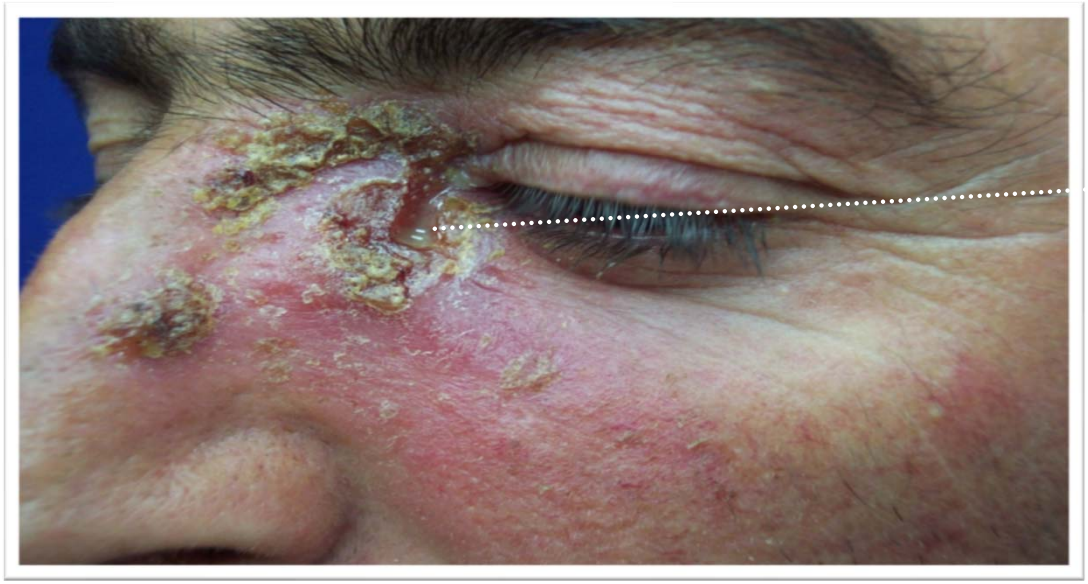


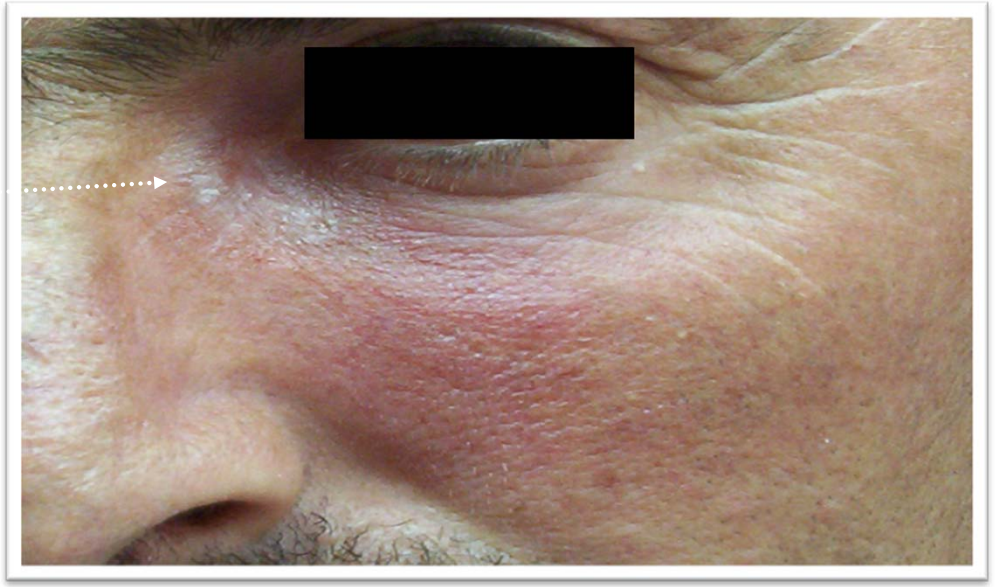



After
treatment with
IL antimony

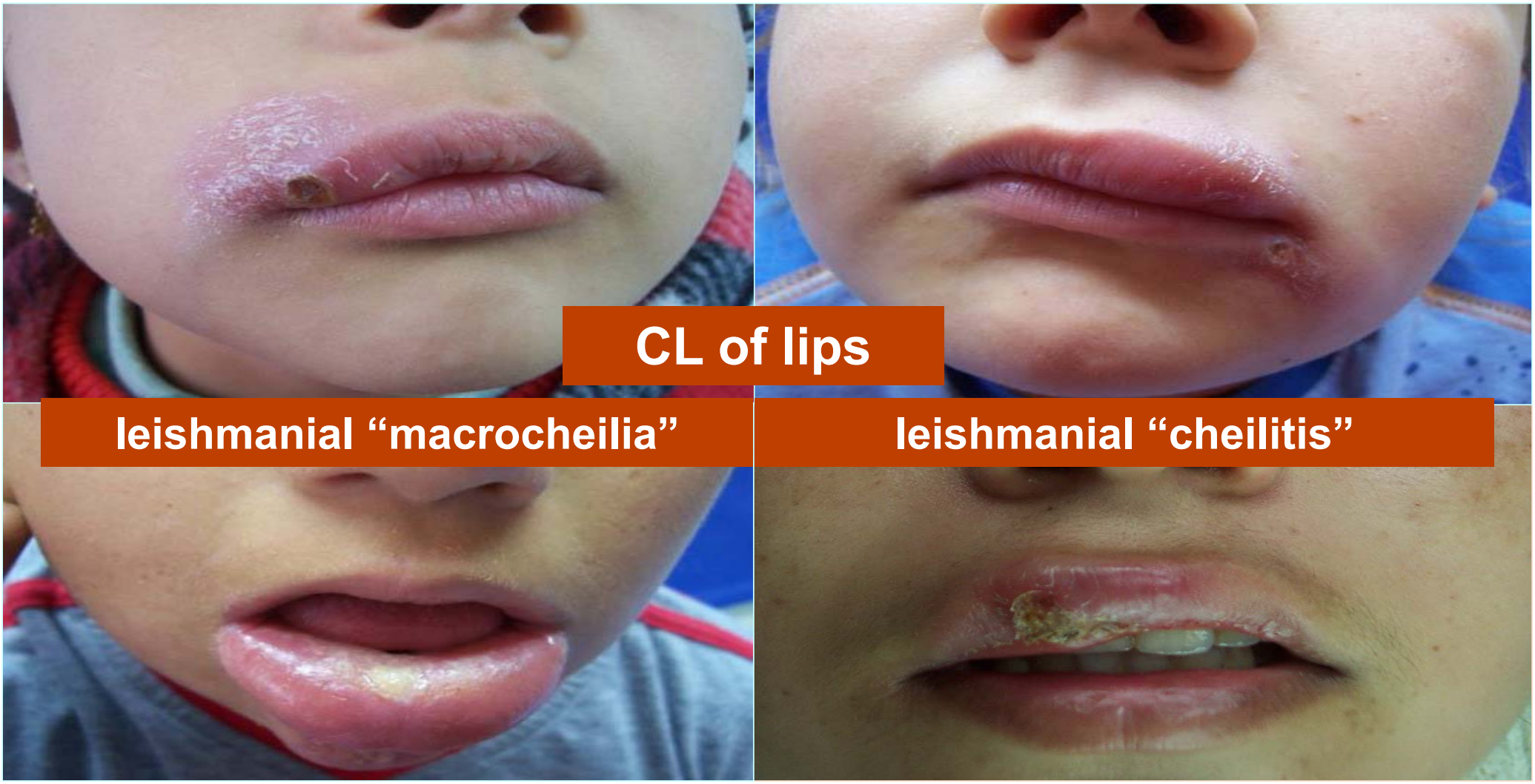


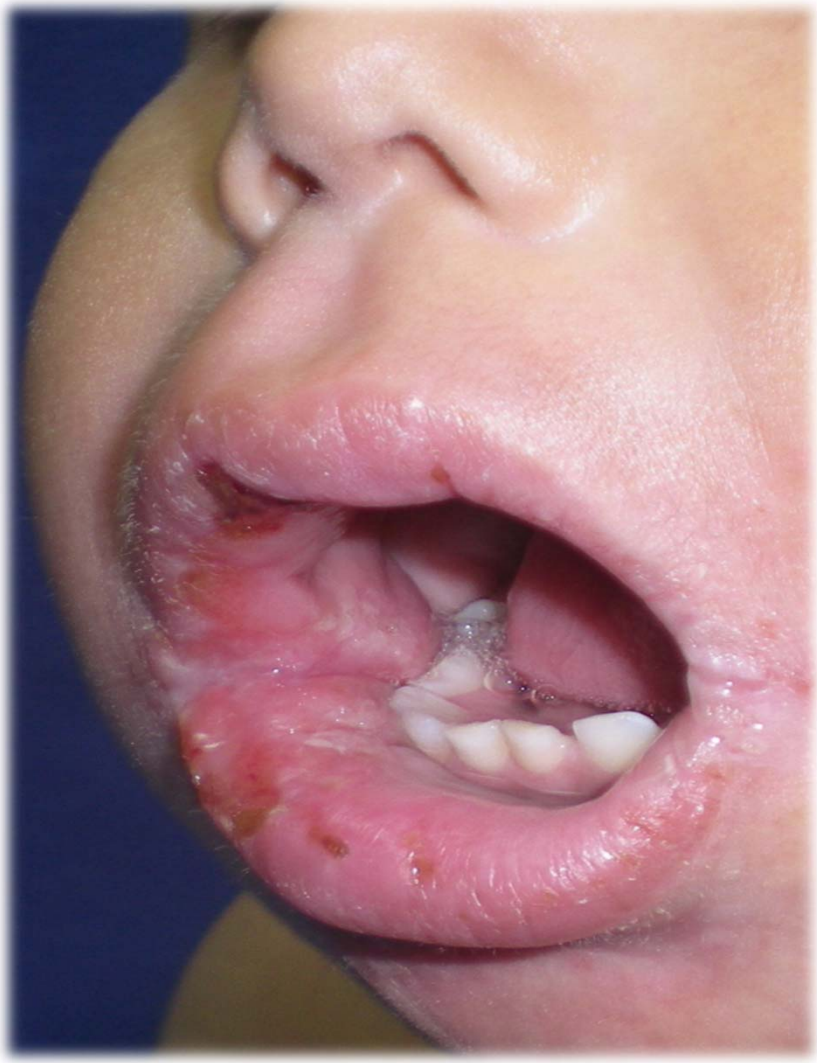
leishmanial dacryocystitis

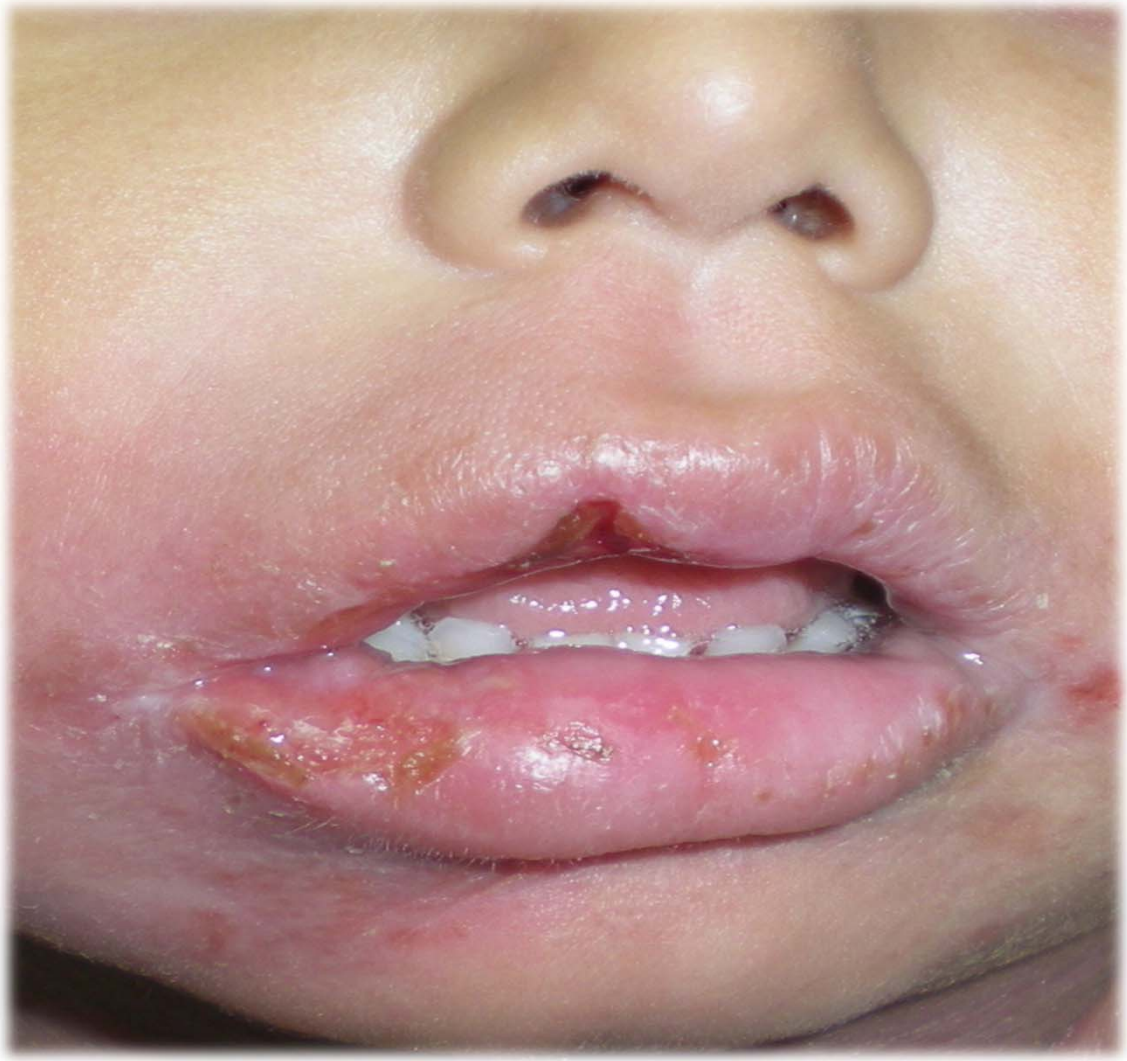


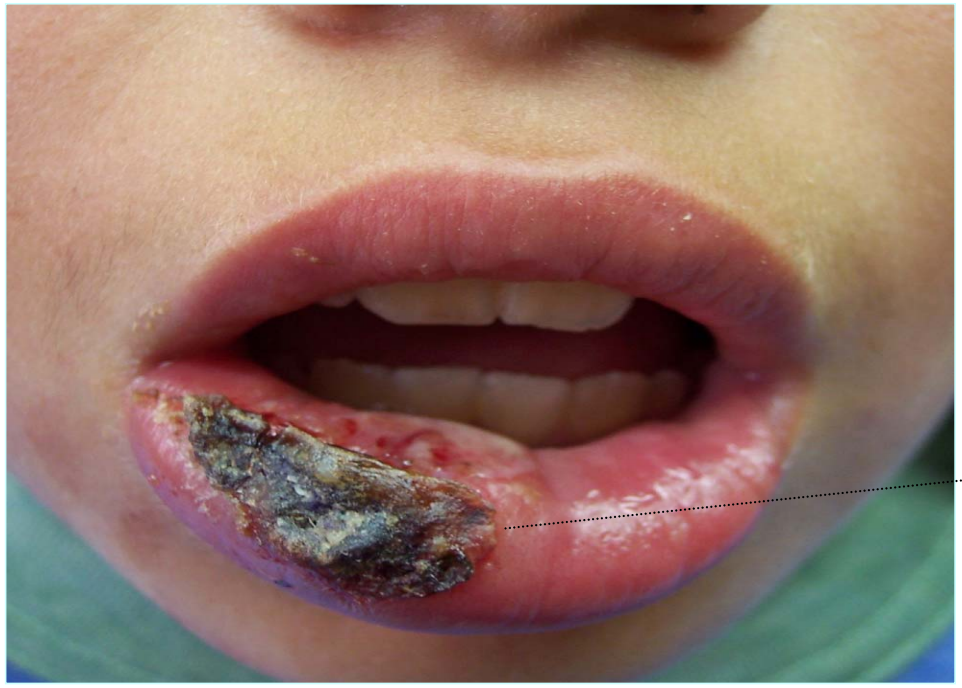


After treatment with IL antimony


CL of lips
leishmanial “macrocheilia”
leishmanial “cheilitis”

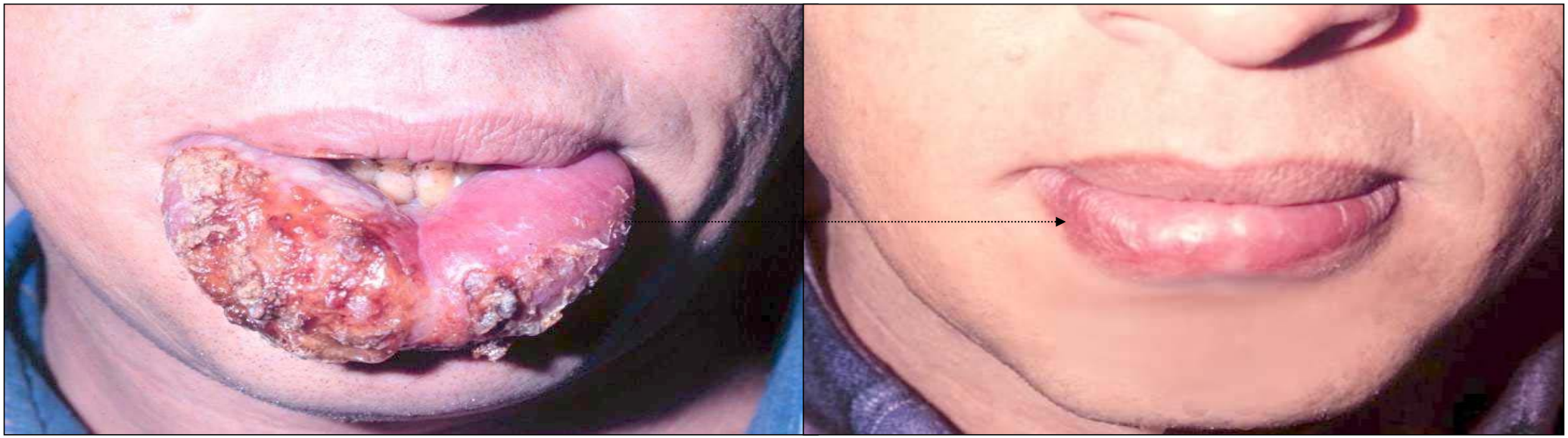






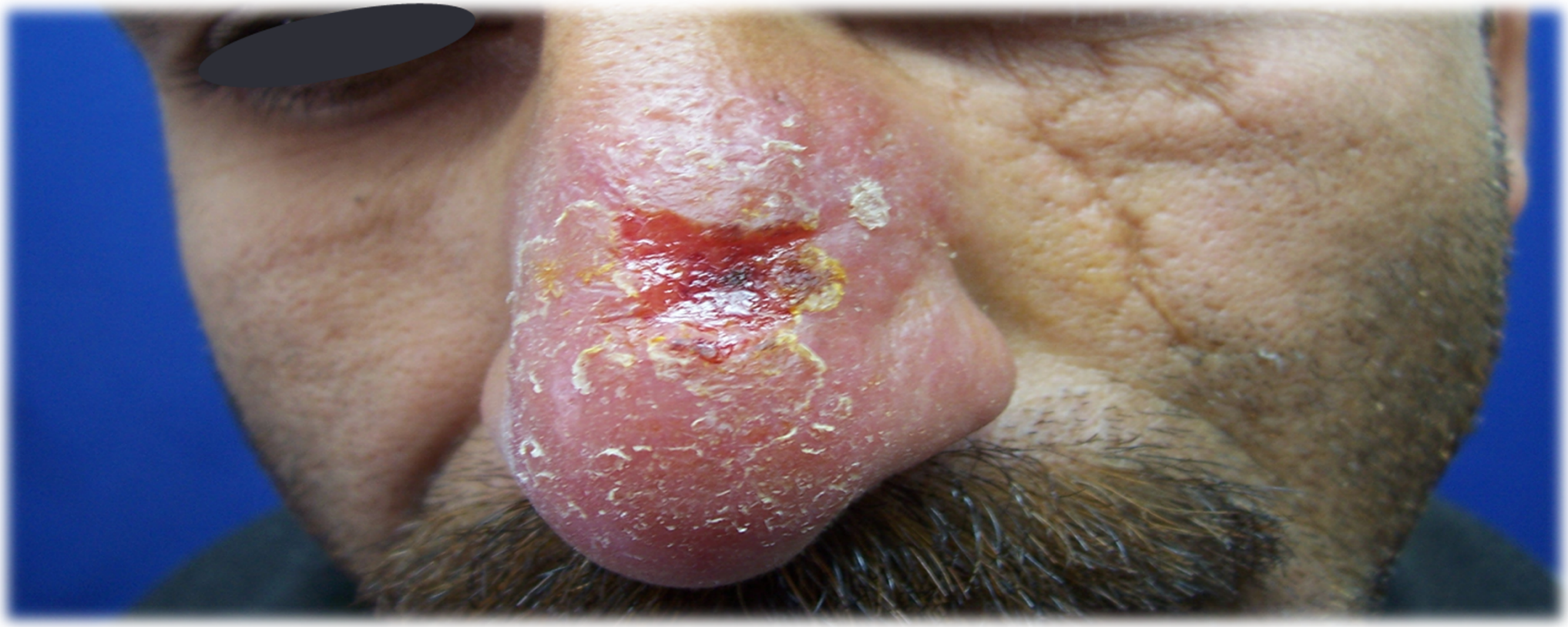
squamous cell carcinoma-like lip involvement of CL

After treatment with systemic antimony

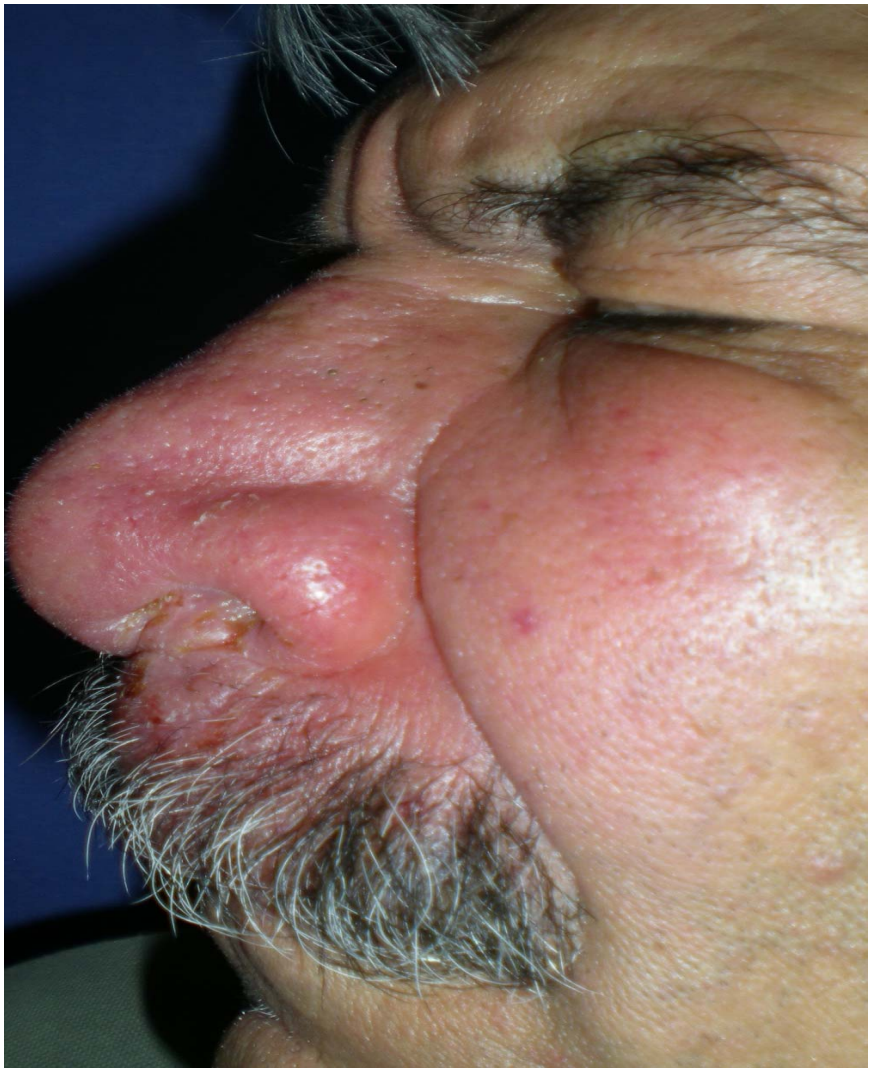


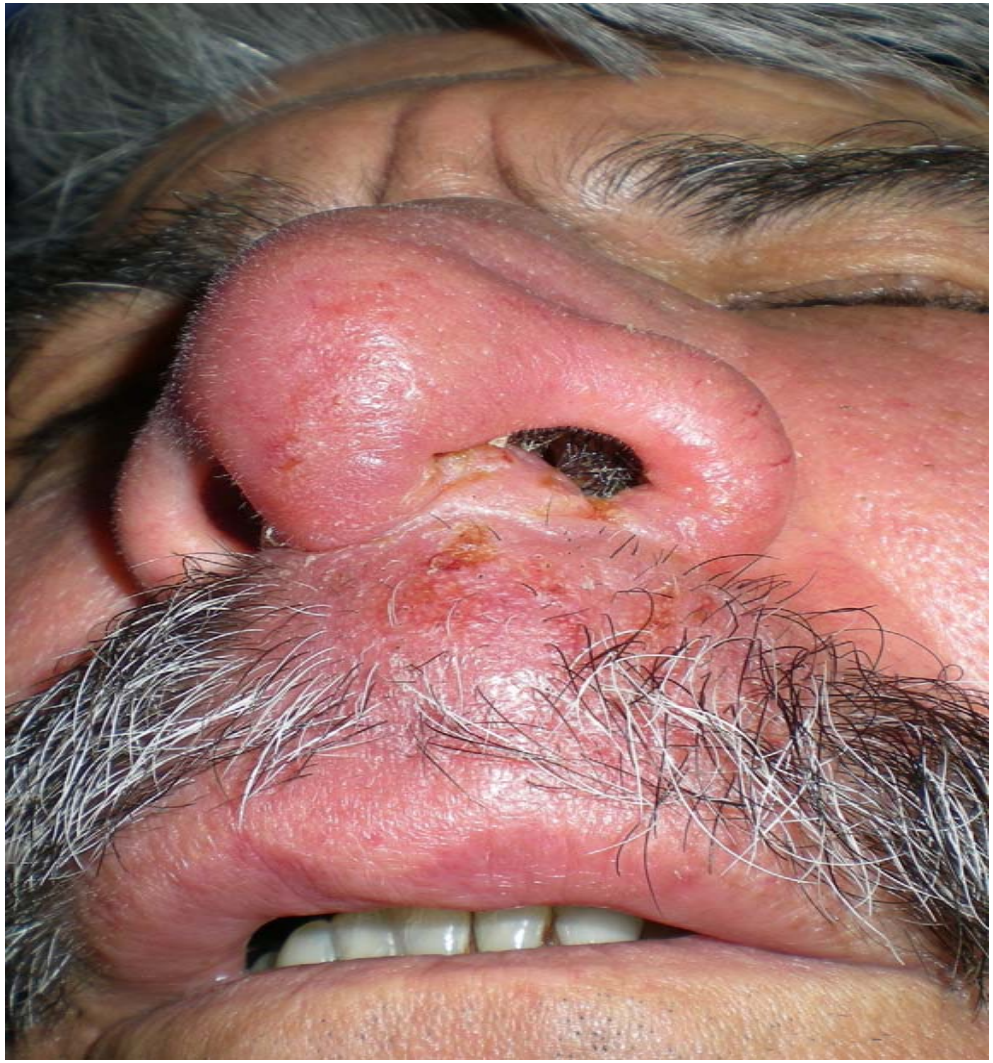
After treatment with
systemic antimony

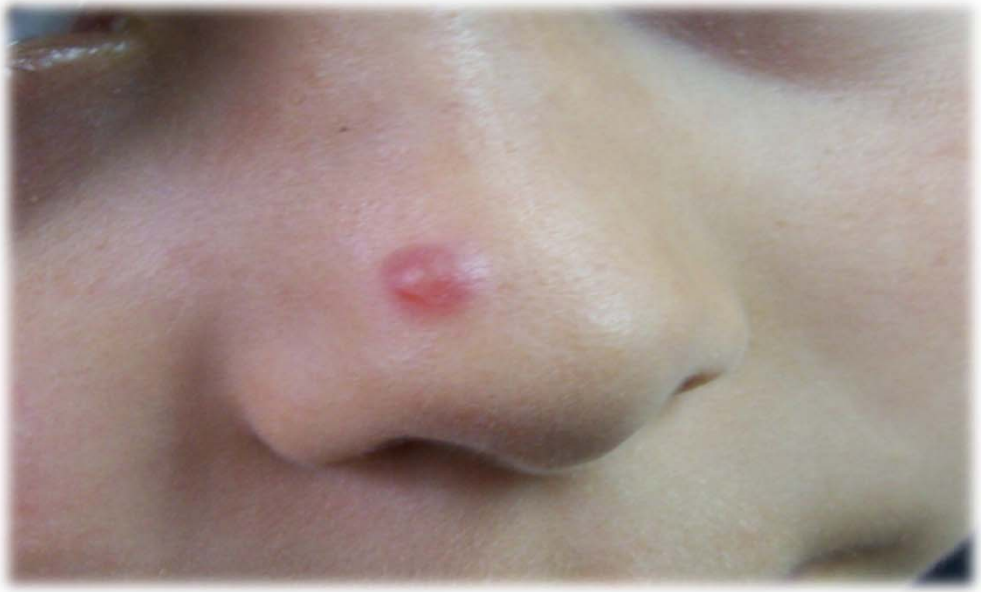
Nasal involvement

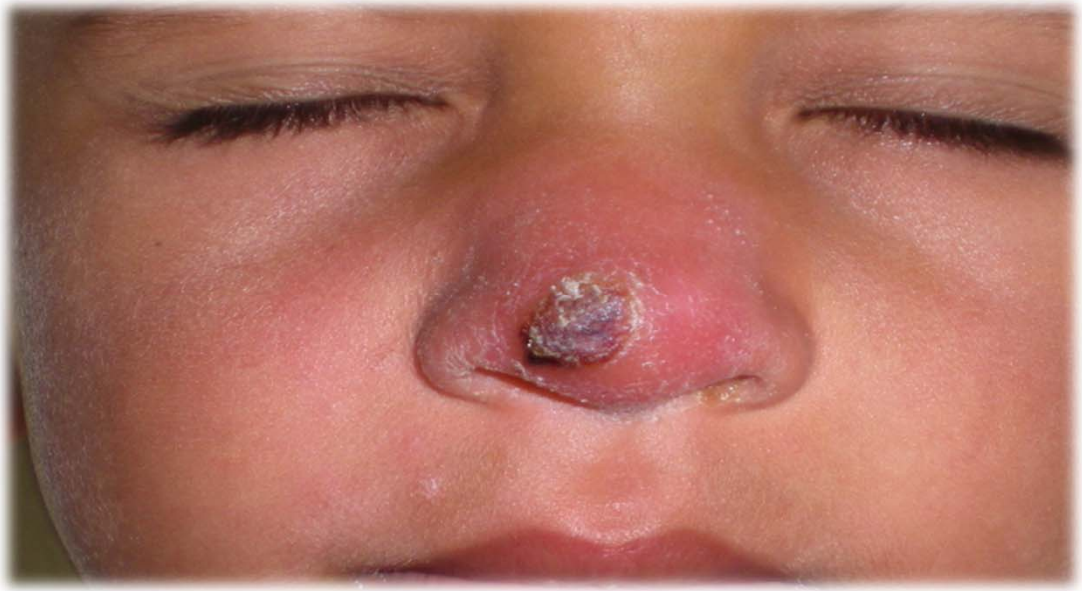


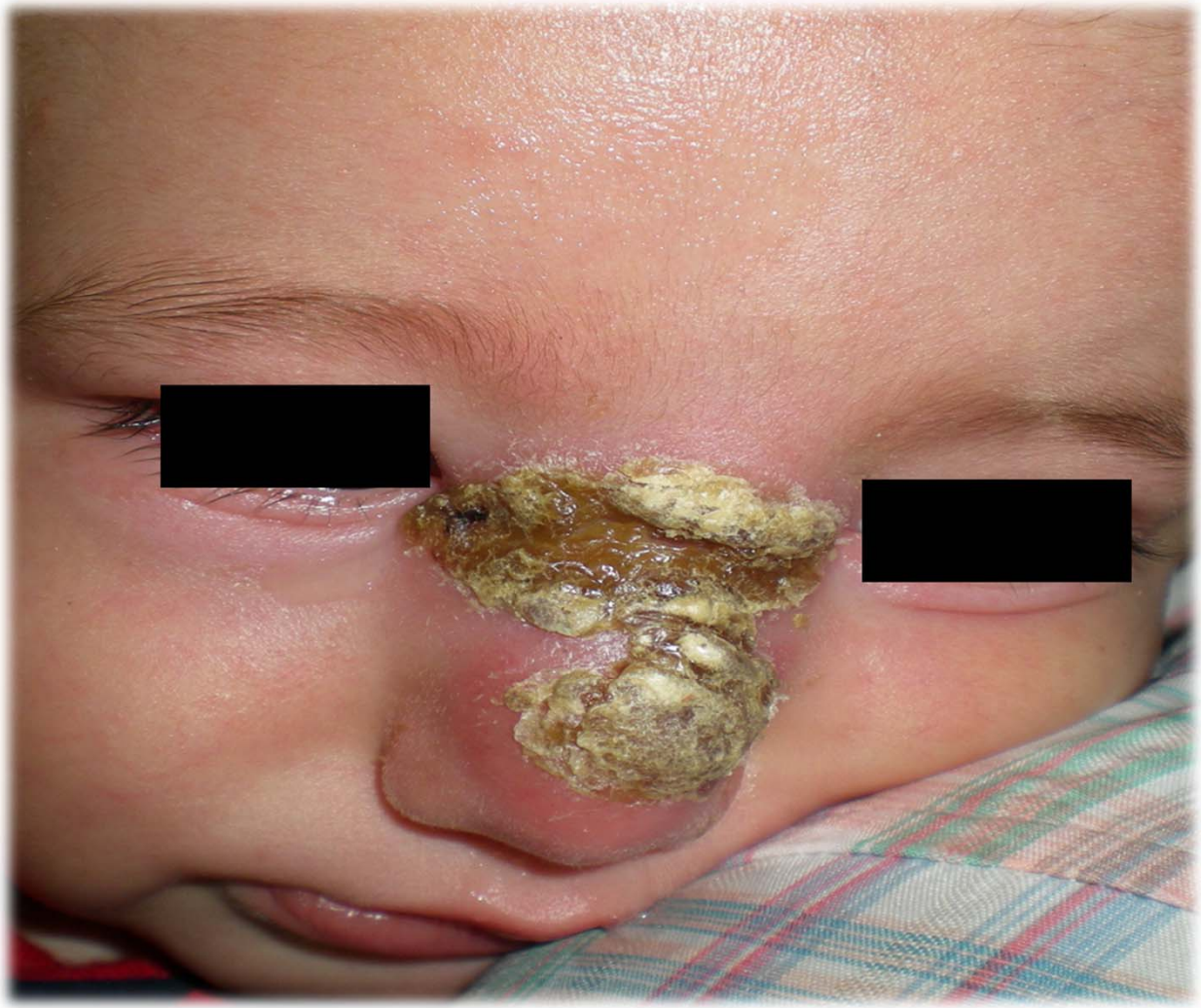
Rhinophymous leishmaniasis

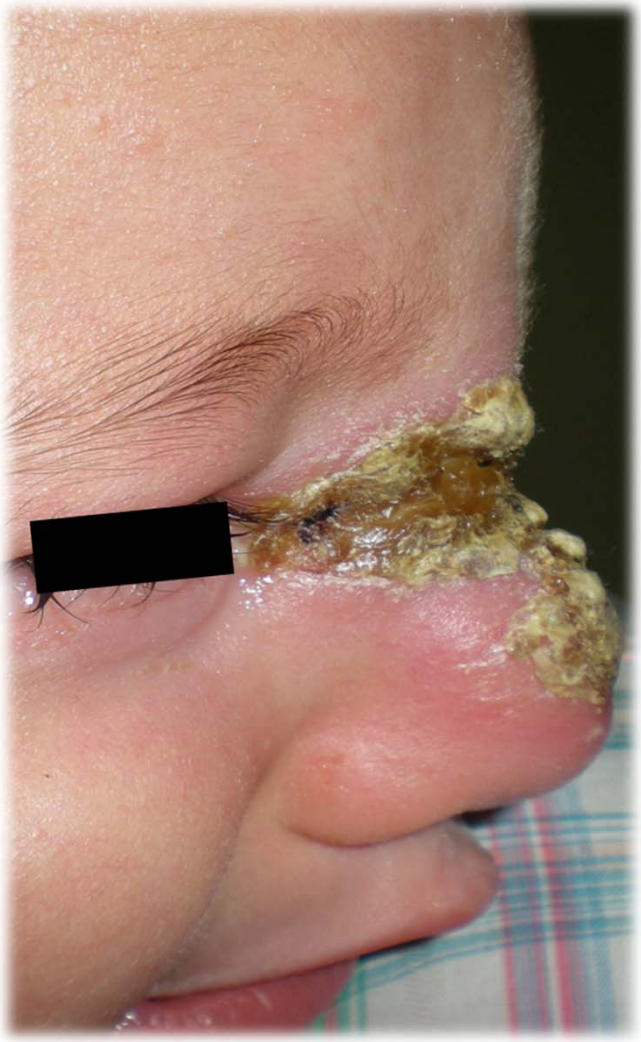




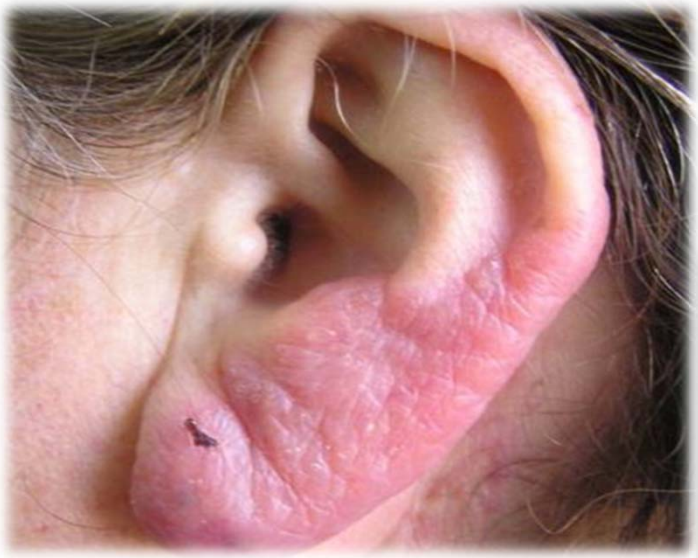


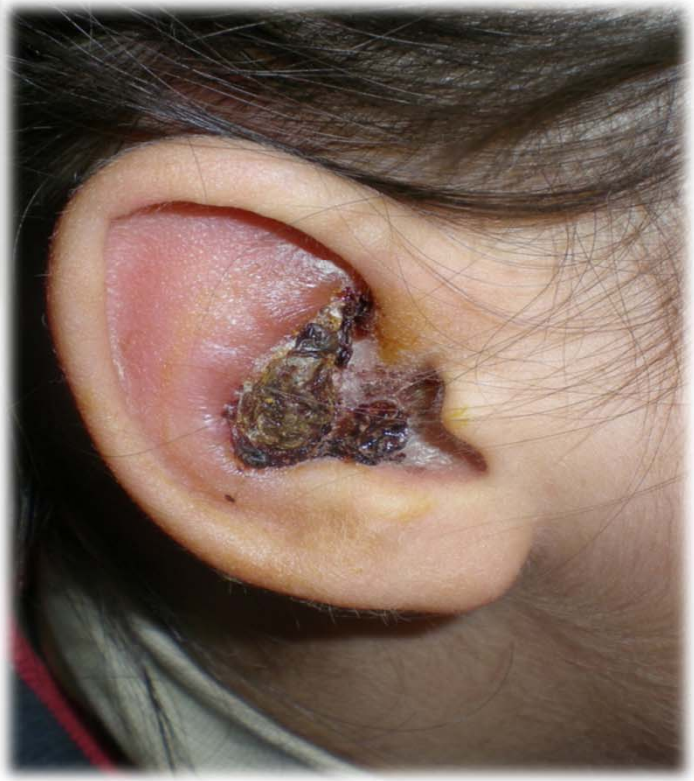


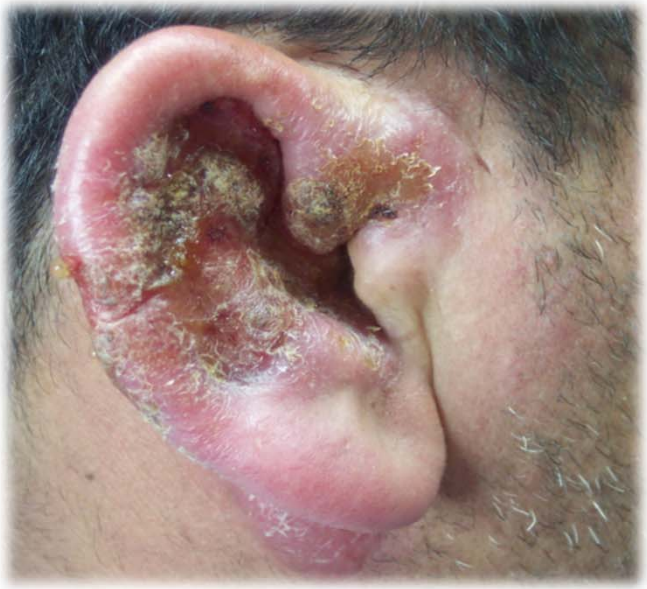


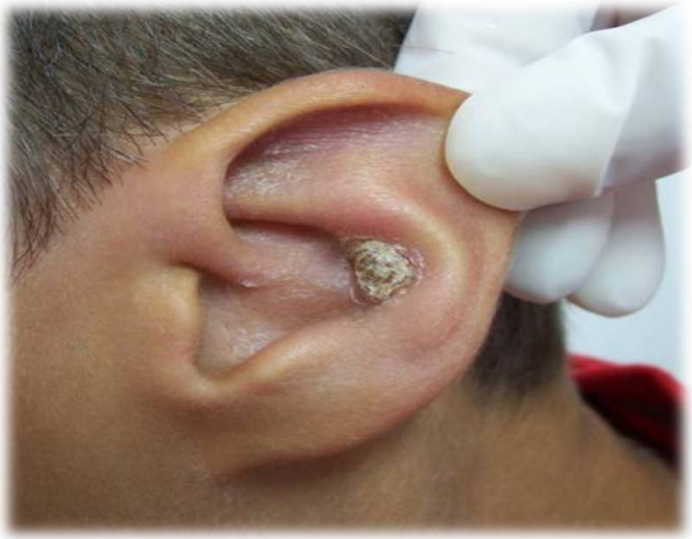


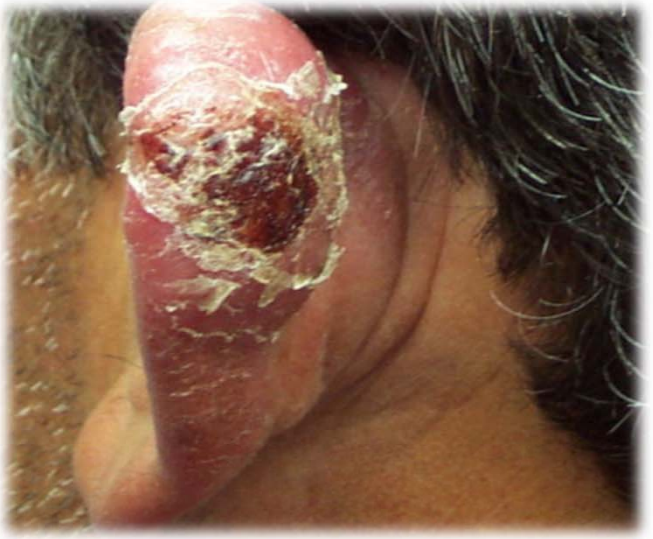
Auricular involvement

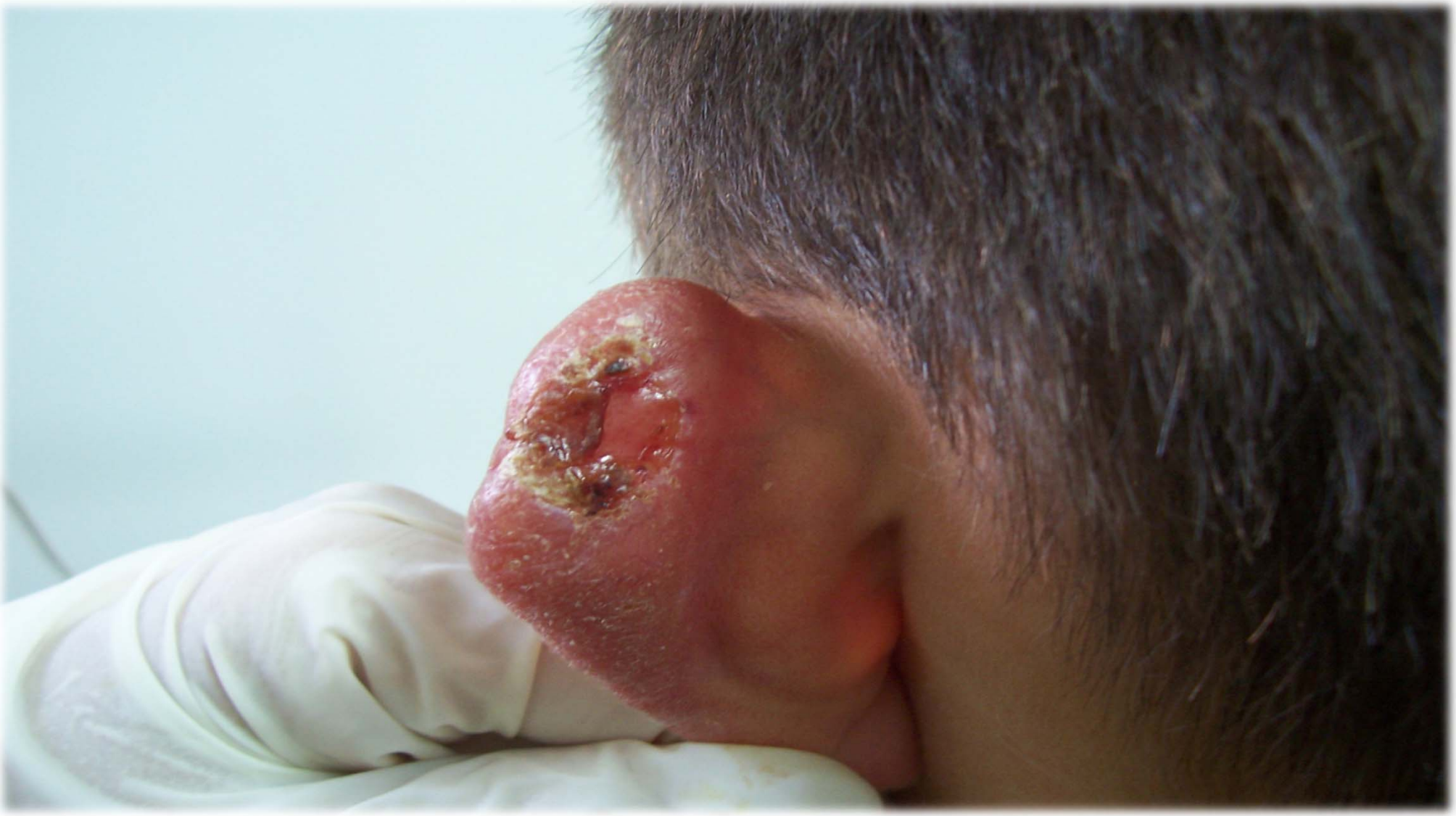


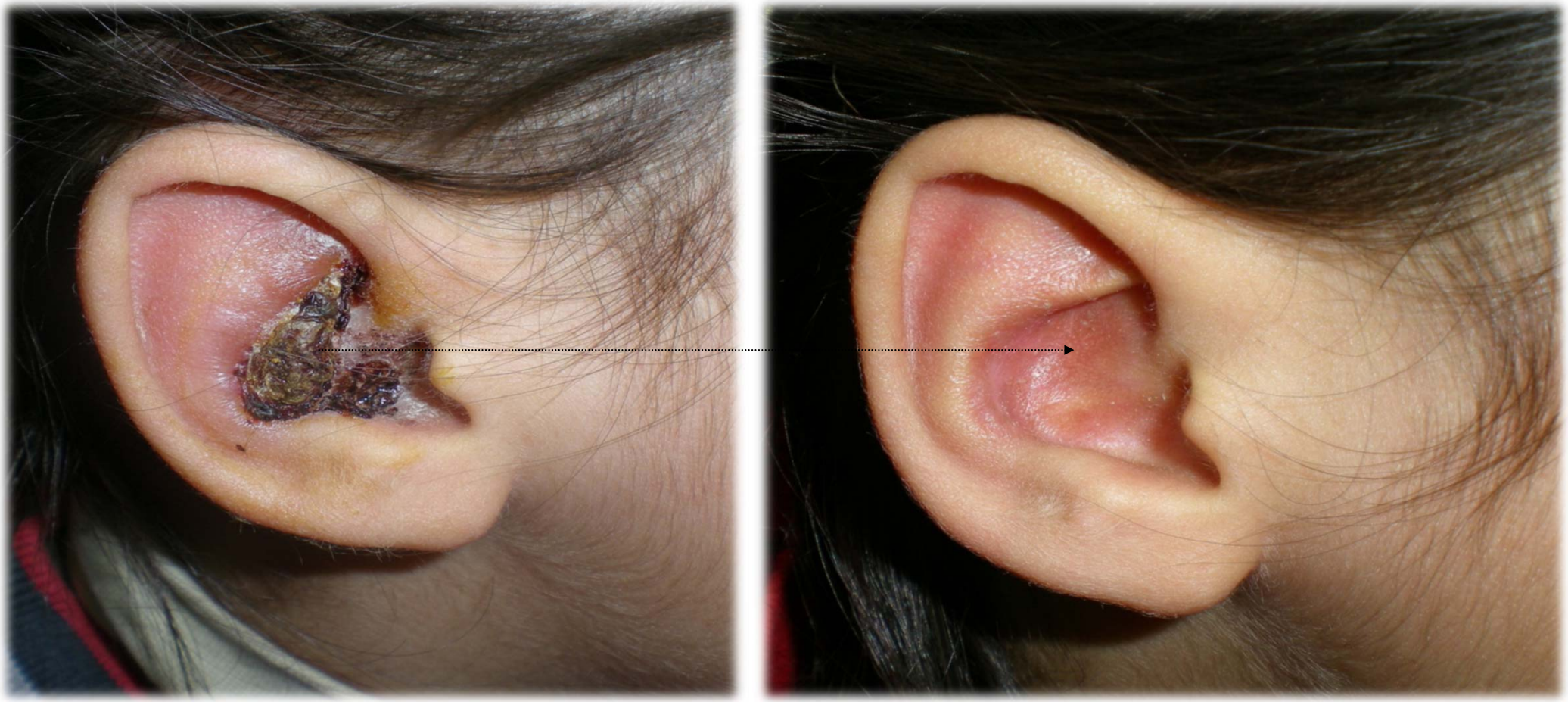




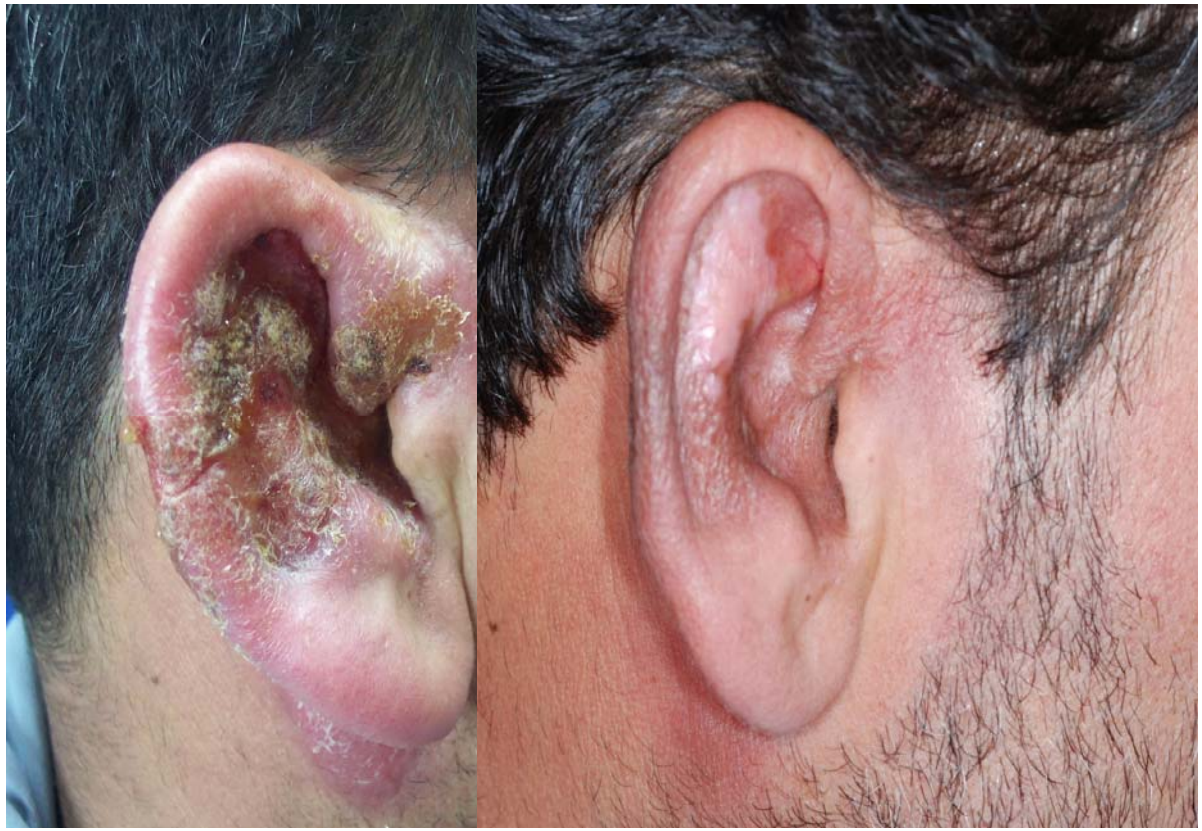


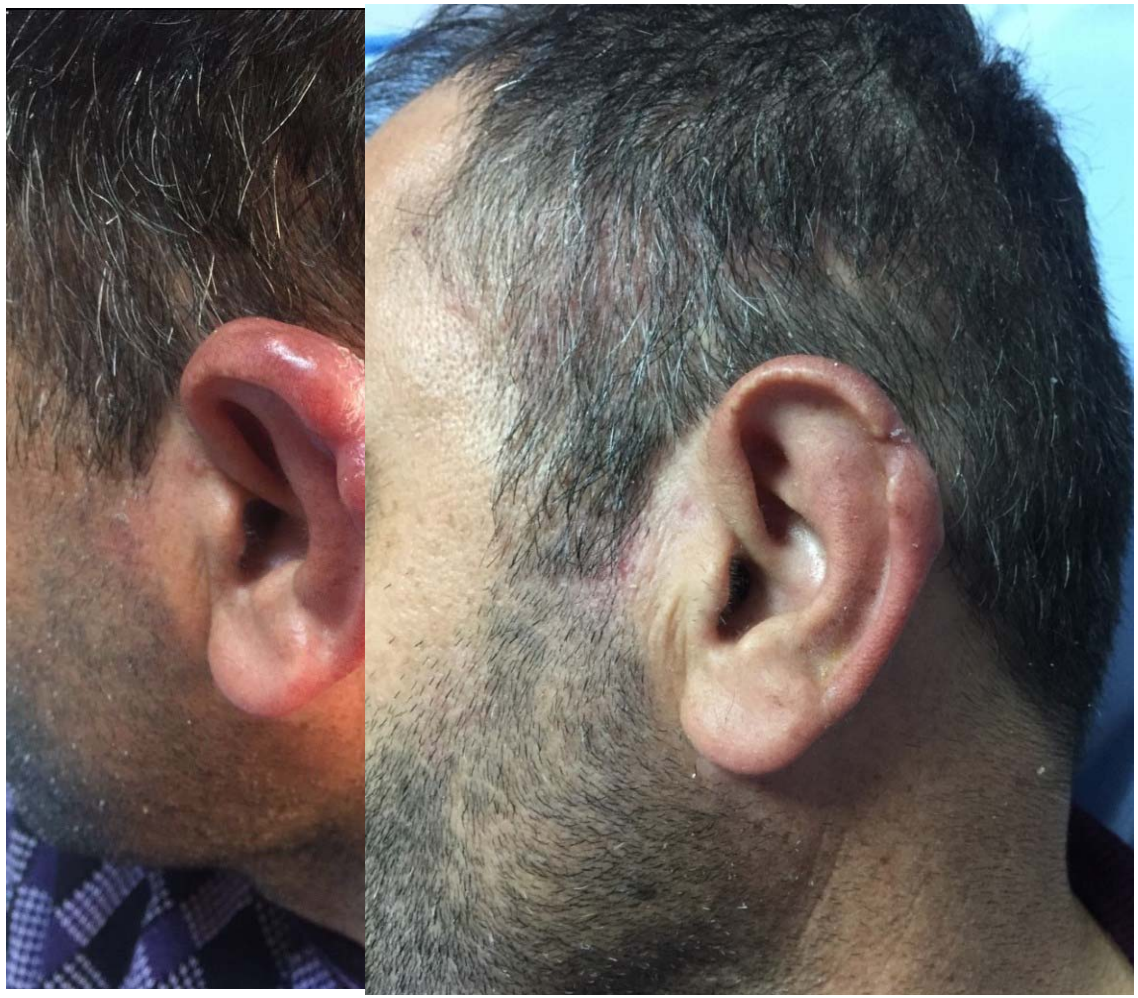


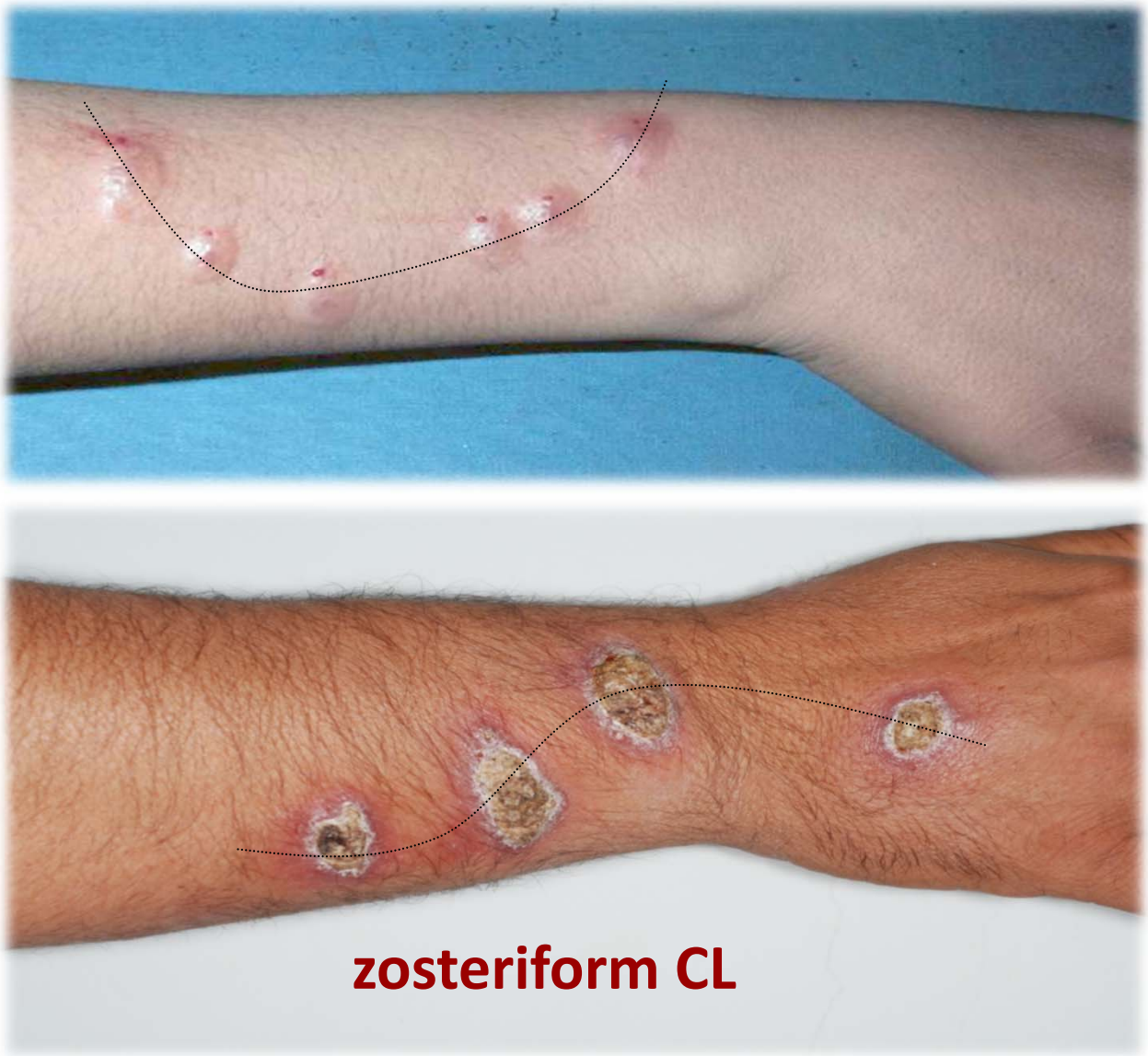




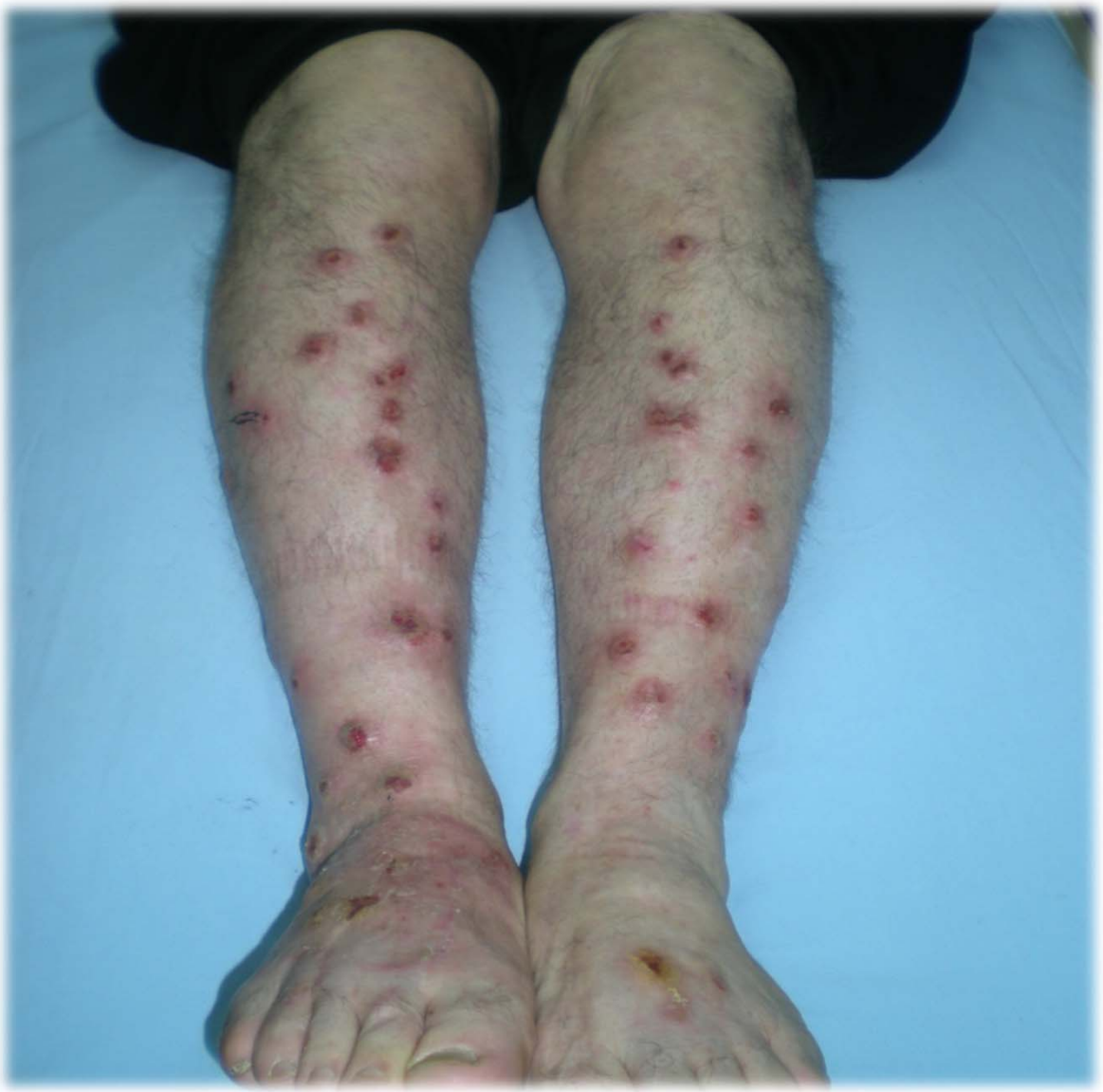
After treatment with PE antimony!



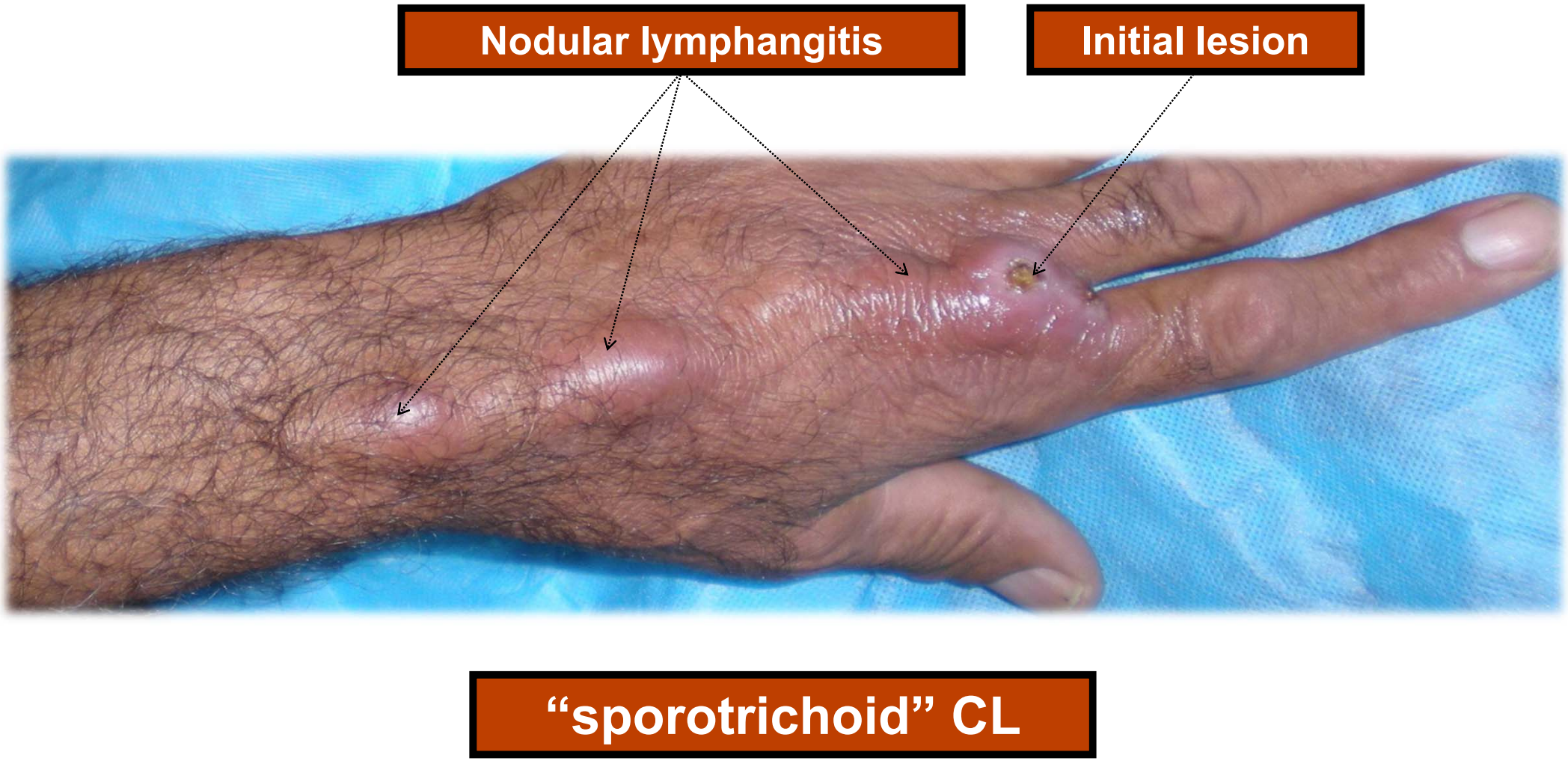


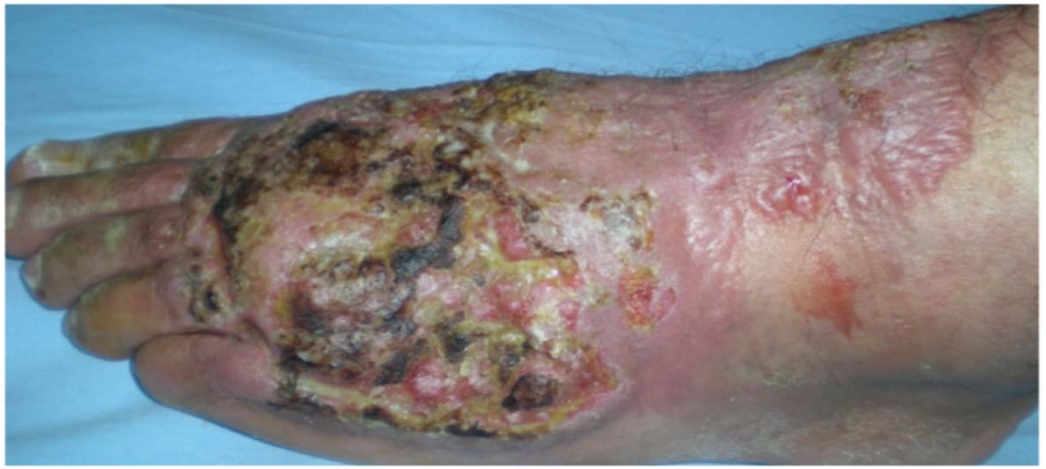


zosteriform CL

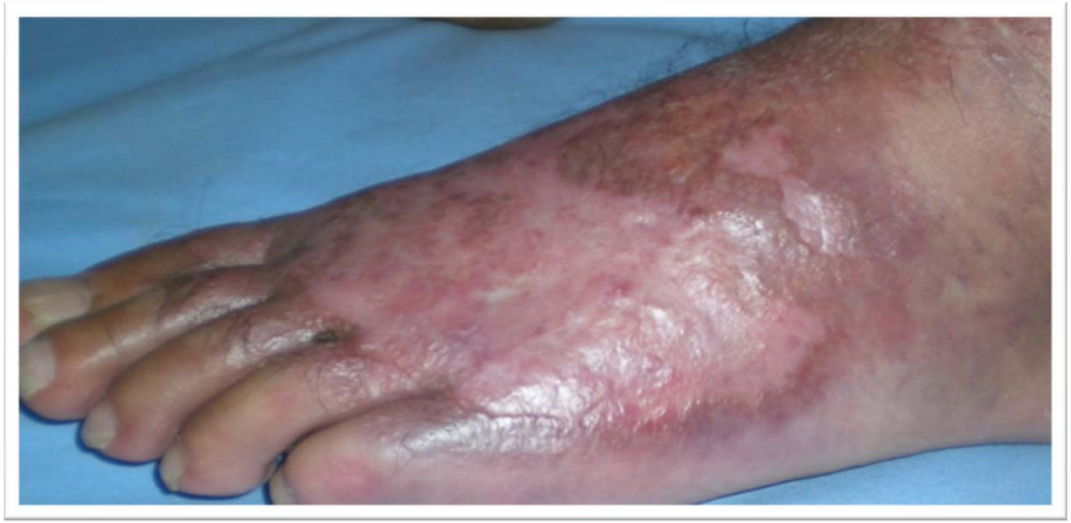


“Prurigo nodularis-like” CL

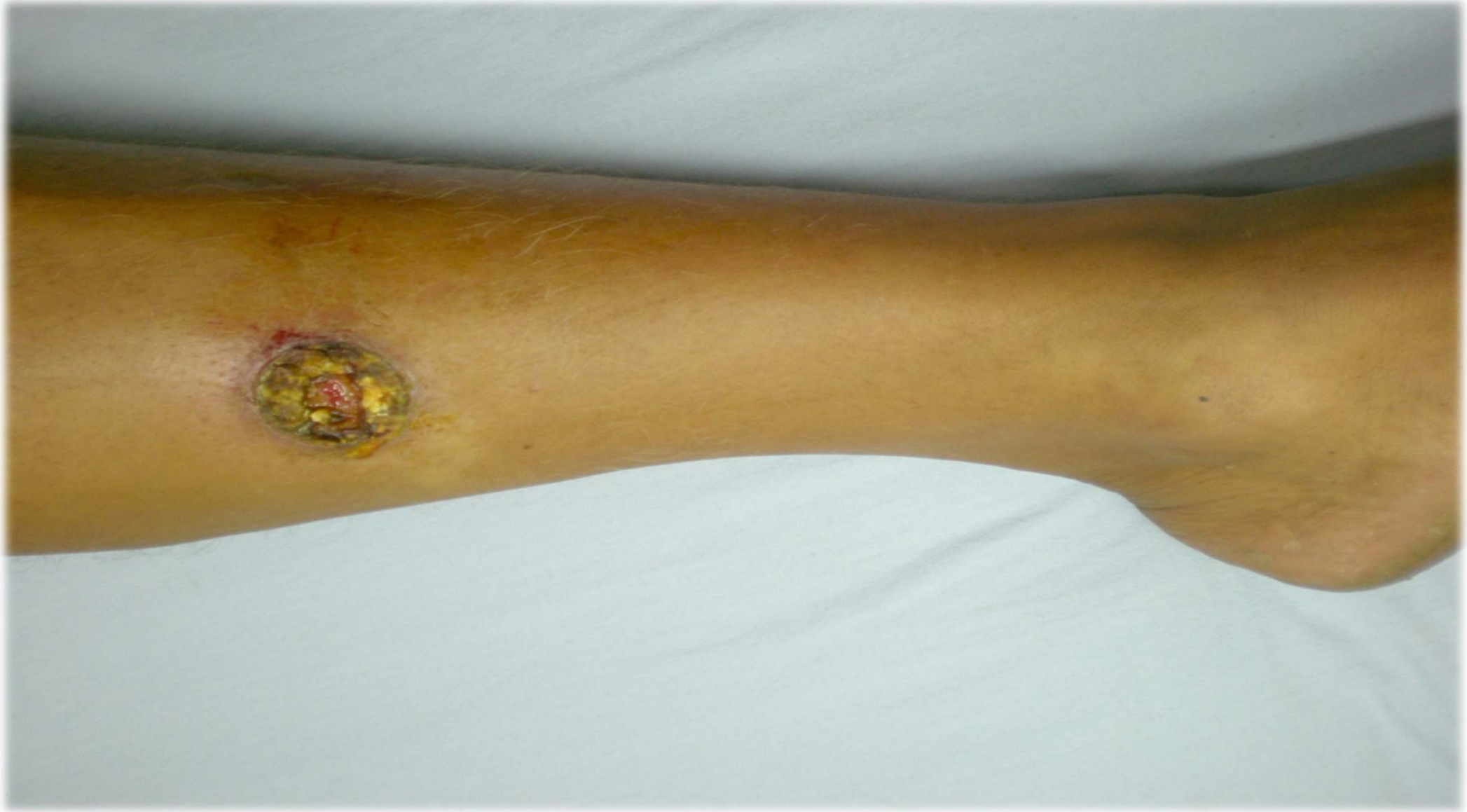

Nodular lymphangitis
Initial lesion
“sporotrichoid” CL



“Leg or foot ulcers” due to CL



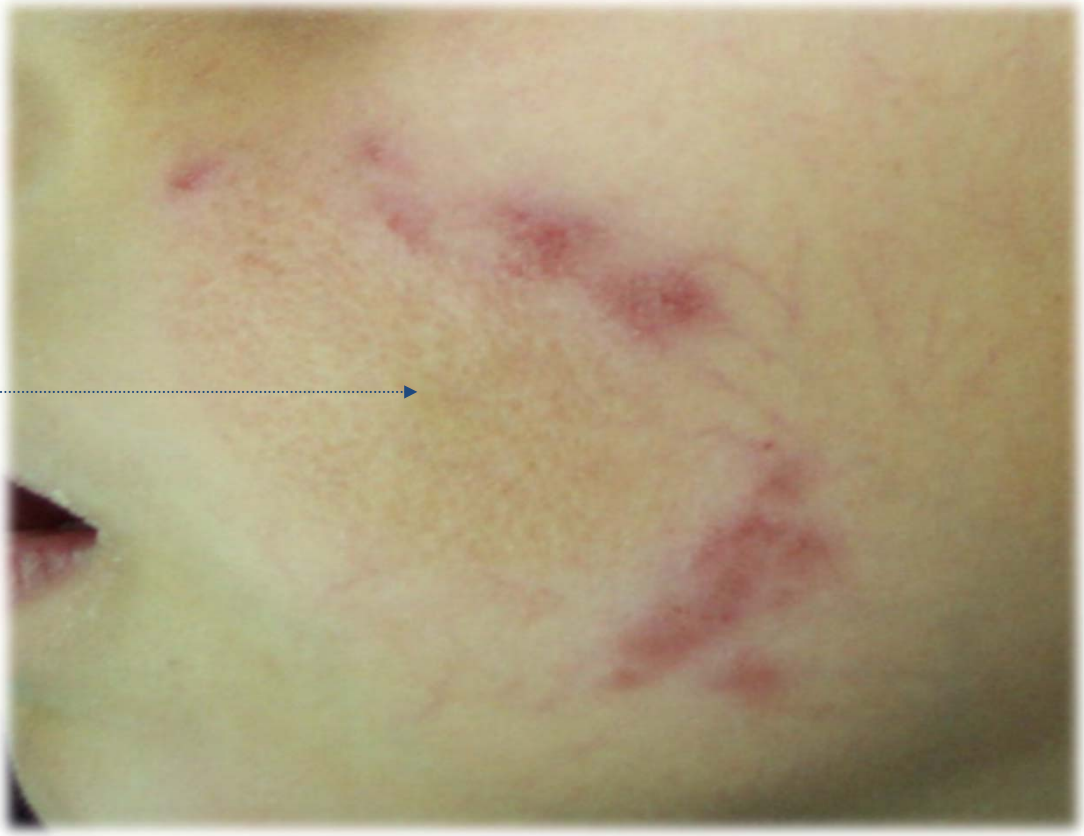
After treatment with systemic antimony!

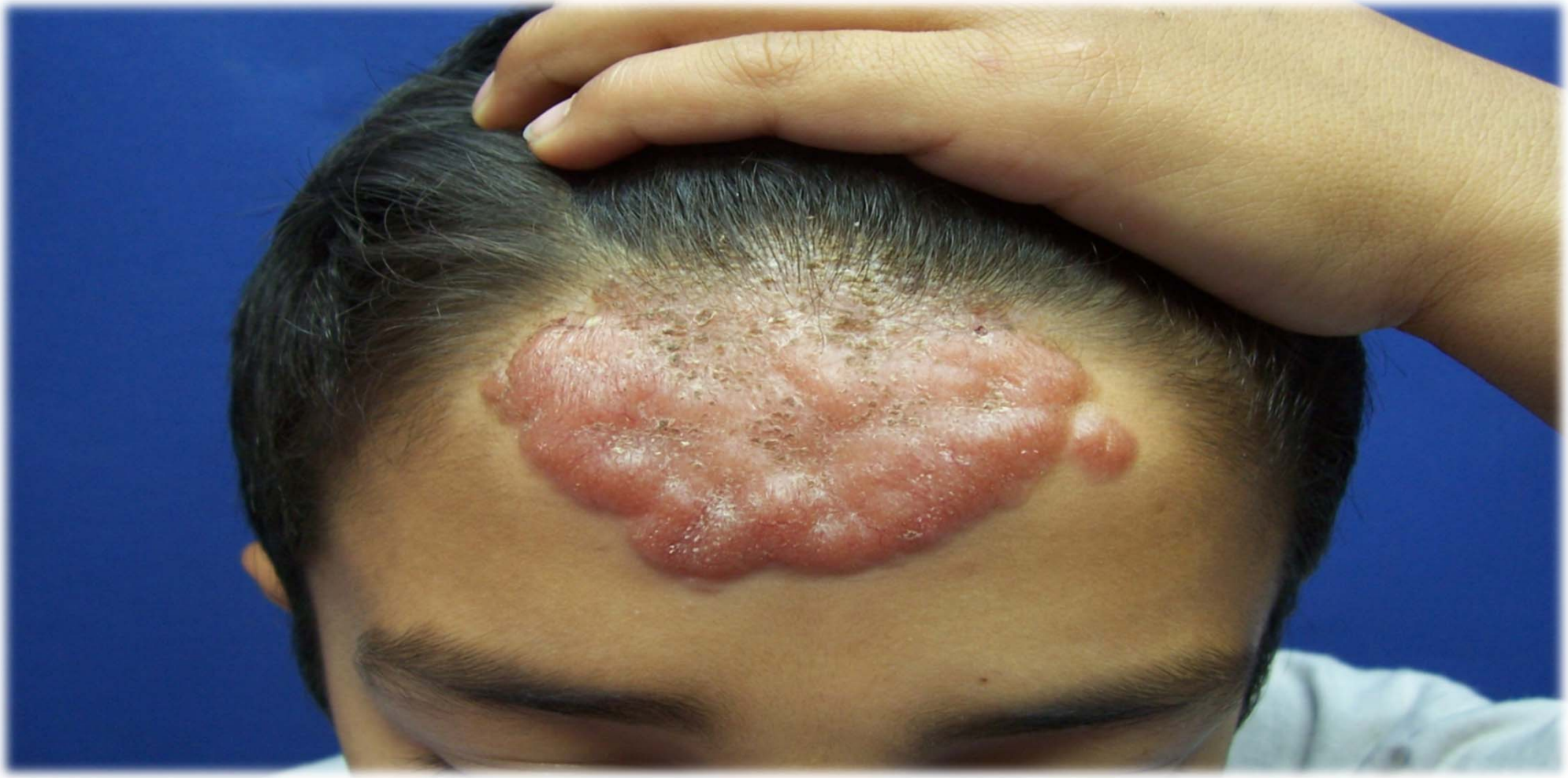


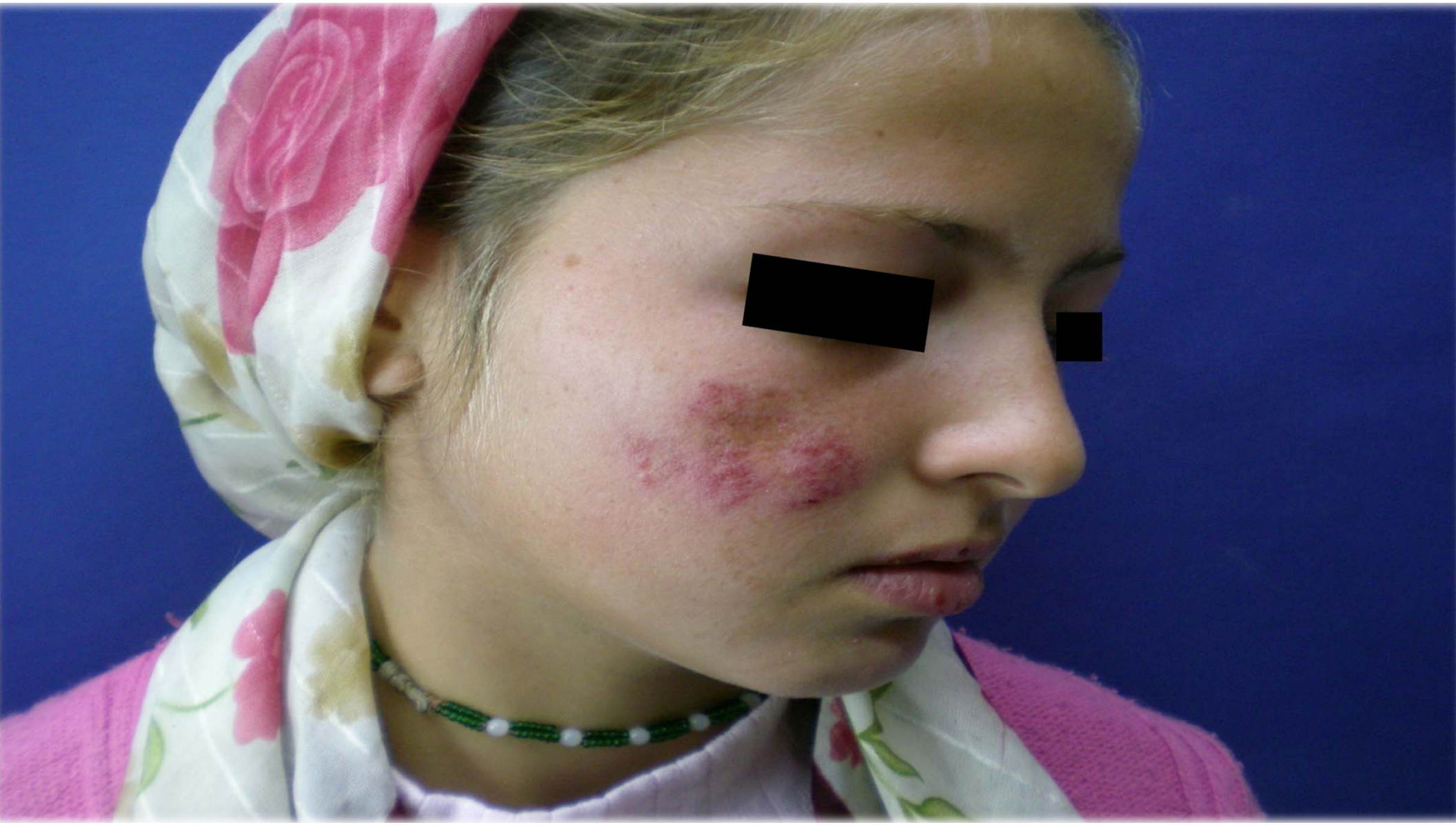
Lupoid leishmaniasis (1%)

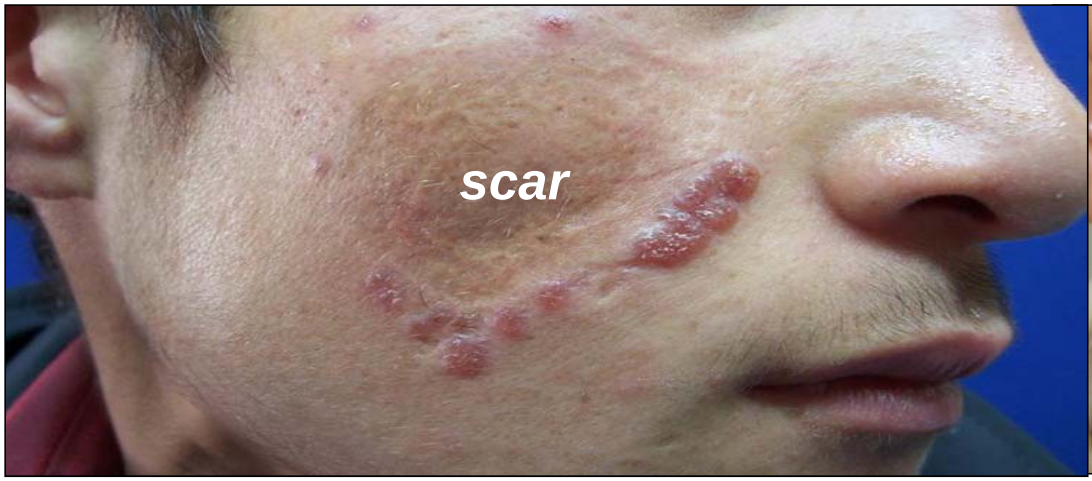
(Skin tuberculosis-like CL)

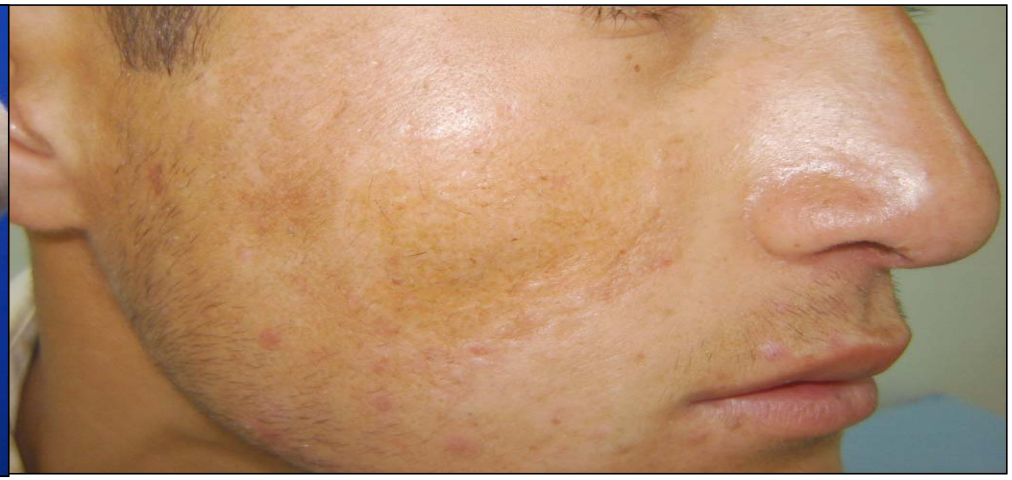
..occures as new fresh lesions around scar tissue after 1-2 years following the acute lesion











After systemic+IL antimony treatment

International Journal of Dermatology

Tropical medicine rounds

Clinical practice guidelines for the diagnosis and treatment of cutaneous leishmaniasis in Turkey

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Abstract

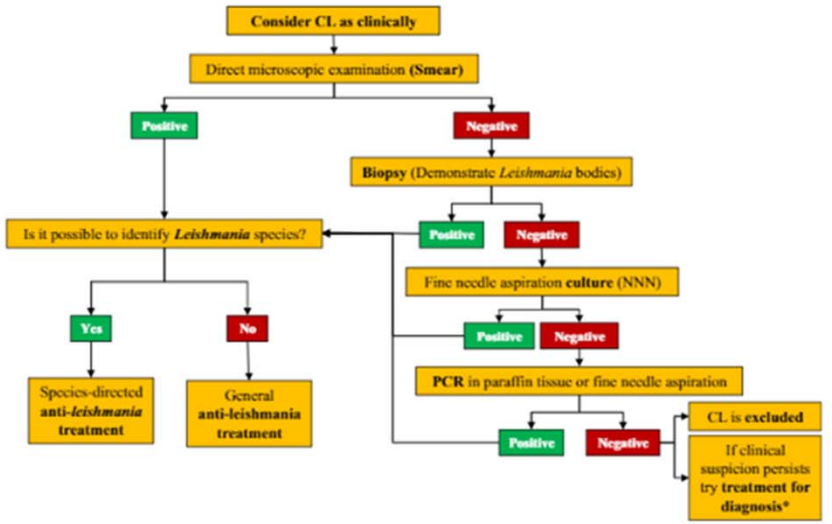
Background Cutaneous leishmaniasis (CL) is a vector-born parasitic disease characterized by various skin lesions that cause disfiguration if healed spontaneously. Although CL has been endemic for many years in the southern regions of Turkey, an increasing incidence in nonendemic regions is being observed due to returning travelers and, more recently, due to Syrian refugees. Thus far, a limited number of national guidelines have been proposed, but no common Turkish consensus has emerged.

Objectives The aim of this study was to develop diagnostic and therapeutic guidelines for the management of CL in Turkey.

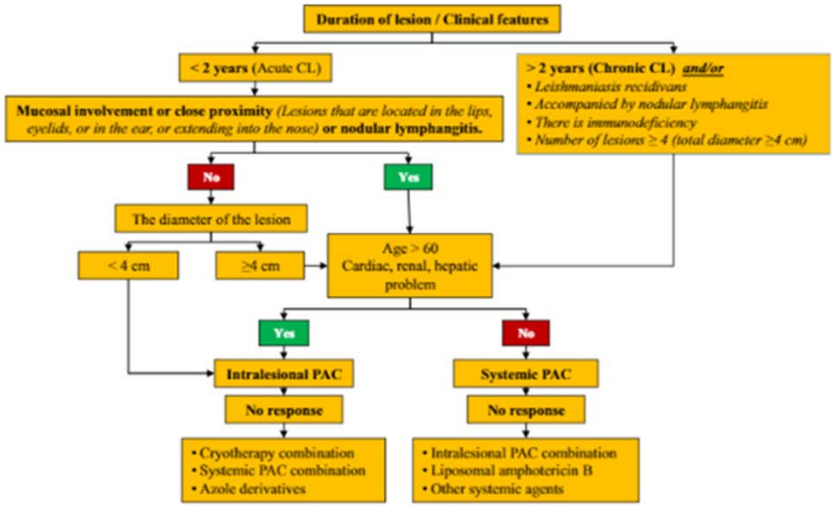
Methods This guideline is a consensus text prepared by 18 experienced CL specialists who have been working for many years in areas where the disease is endemic. The Delphi method was used to determine expert group consensus. Initially, a comprehensive list of items about CL was identified, and consensus was built from feedback provided by expert participants from the preceding rounds.

Results Evidence-based and expert-based recommendations through diagnostic and therapeutic algorithms according to local availability and conditions are outlined.

Conclusion Because CL can mimic many other skin diseases, early diagnosis and early treatment are very important to prevent complications and spread of the disease. The fastest and easiest diagnostic method is the leishmanial smear. The most common treatment is the use of local or systemic pentavalent antimony compounds.



Uzun et al. Clinical guidelines of cutaneous leishmaniasis in Turkey **Tropical medicine rounds**

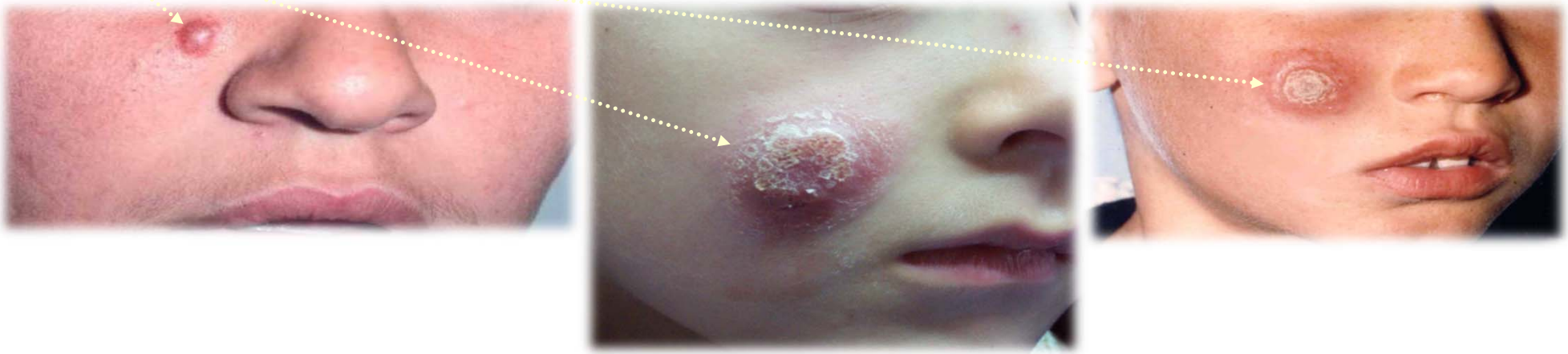


Clinical clues for CL

- **Erythematous elaveted or ulcerated lesion** (papule, plaque, nodule, ulcerated nodule, ulcerated plaque etc.*especially* **in children** *and young people!)*
- **Chronic course** (weeks, months or even years!)
- Lesions located **on exposed body sites**
- **Painless** lesion
- **Living in an endemic region**
- Before lesion appears to have **a travel history to an endemic region** (in summer!)
- **Presence of other individuals** with similar lesion in the same family

Clinical Diagnosis

..is often made on the basis of a clinically typical lesion in conjunction with an appropriate history of exposure!

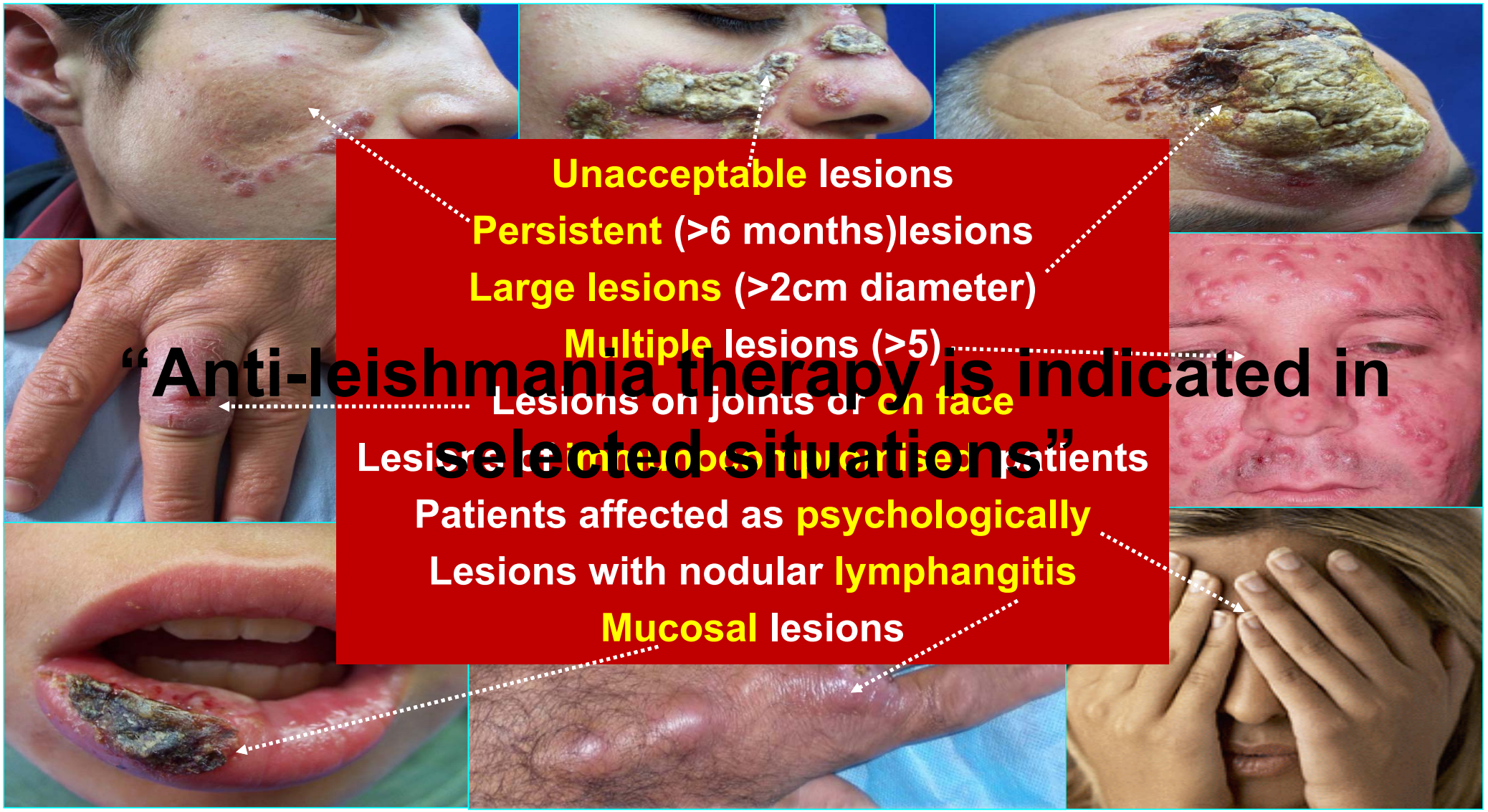


..broad clinical spectrum of CL makes clinical diagnosis of some cases difficult!!

Laboratory Diagnosis

"laboratory diagnosis is required to confirm clinical suspicion"

- **Smear**
- **Culture**
- **Histopathology**
- **PCR**



"Anti-leishmania therapy is indicated in selected situations"

There is no

single

optimal

treatment

for all forms

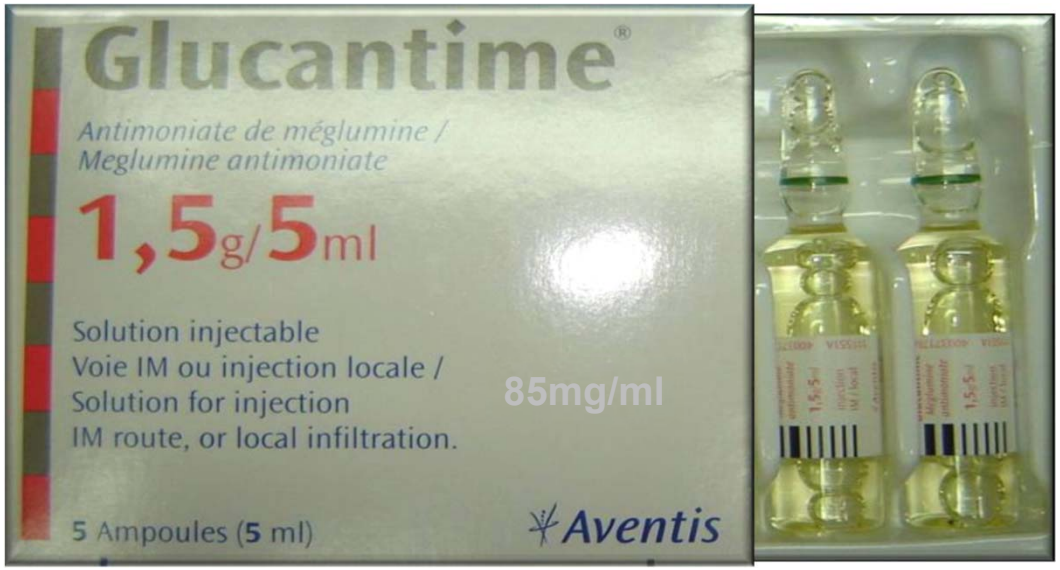
of CL!

Pentavalent antimonial drugs

(..given parenterally or intralesionally, remains <u>the first-line</u> treatment approach!)

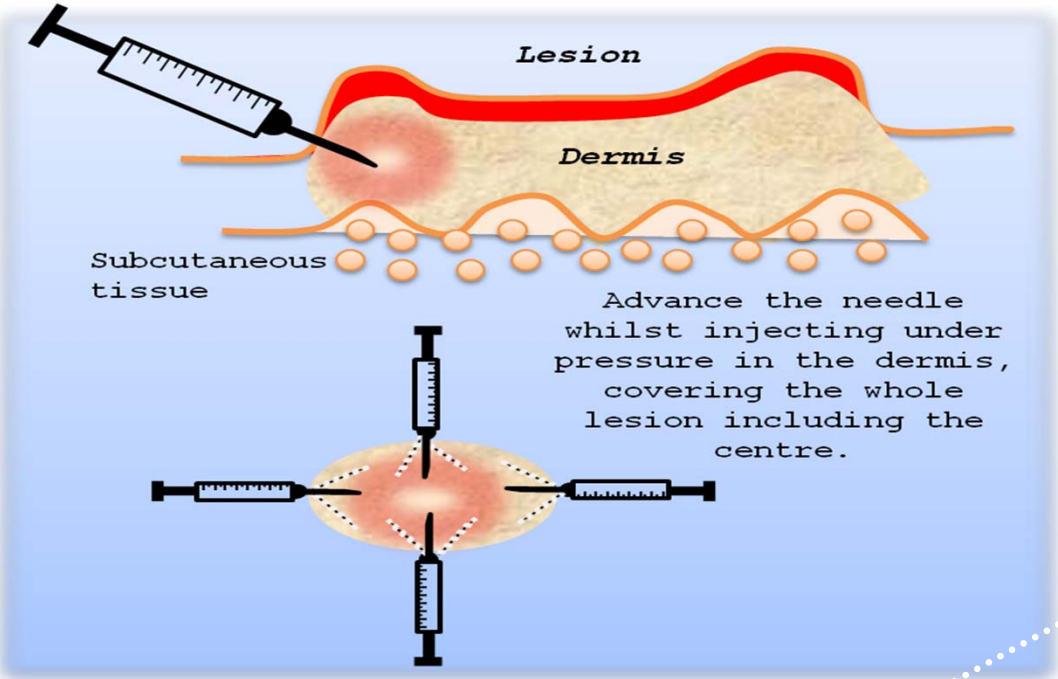
Sodium stibogluconate

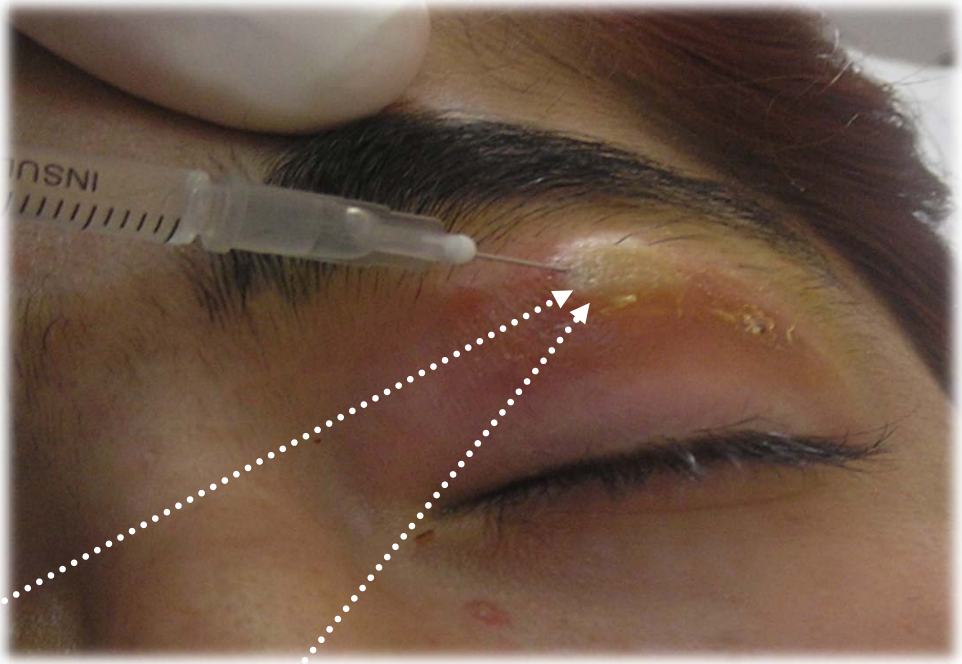
Meglumine antimoniate



Intralesional antimony treatment

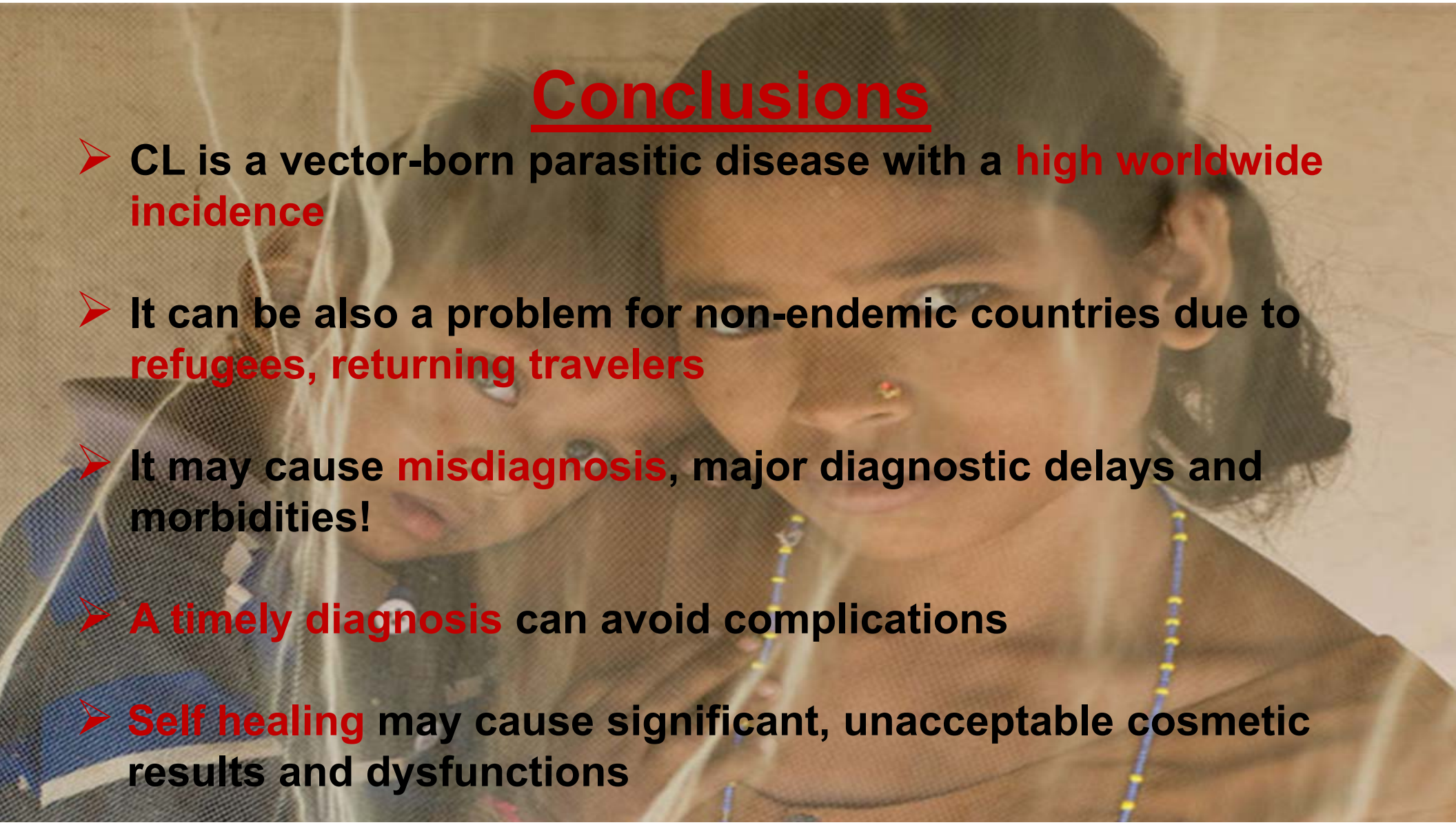
"Weekly or every other day until complete healing"





Optimal dose is the dose producing complete blanching at the base of the lesion..

..a higher drug concentration targets the site of infection, improving healing time



Conclusions

- CL is a vector-born parasitic disease with a high worldwide incidence
- It can be also a problem for non-endemic countries due to refugees, returning travelers
- It may cause misdiagnosis, major diagnostic delays and morbidities!
- A timely diagnosis can avoid complications
- Self healing may cause significant, unacceptable cosmetic results and dysfunctions