Lupus cutáneo

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ESPECTRO DEL LUPUS ERITEMATOSO (LE)

Clasificación

A. LE Discoide Crónico (LED)
   - Localizado
   - Hipertrófico
   - Generalizado

B. LE Cutáneo Subagudo (LECSA)
   - Papuloescamoso (psoriasiforme)
   - Anular policíclico

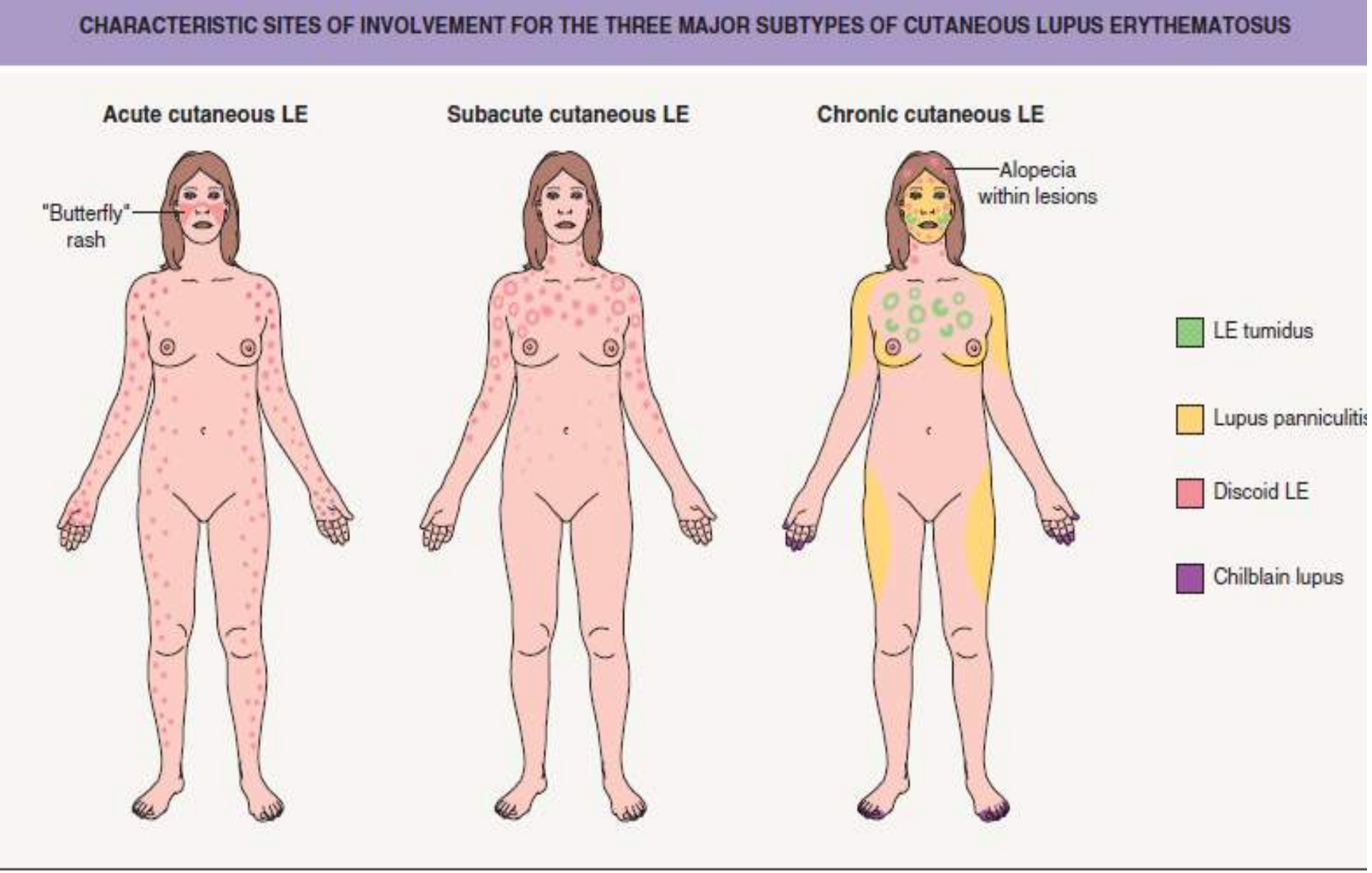
C. LE Sistémico (LES)

D. LE Profundo

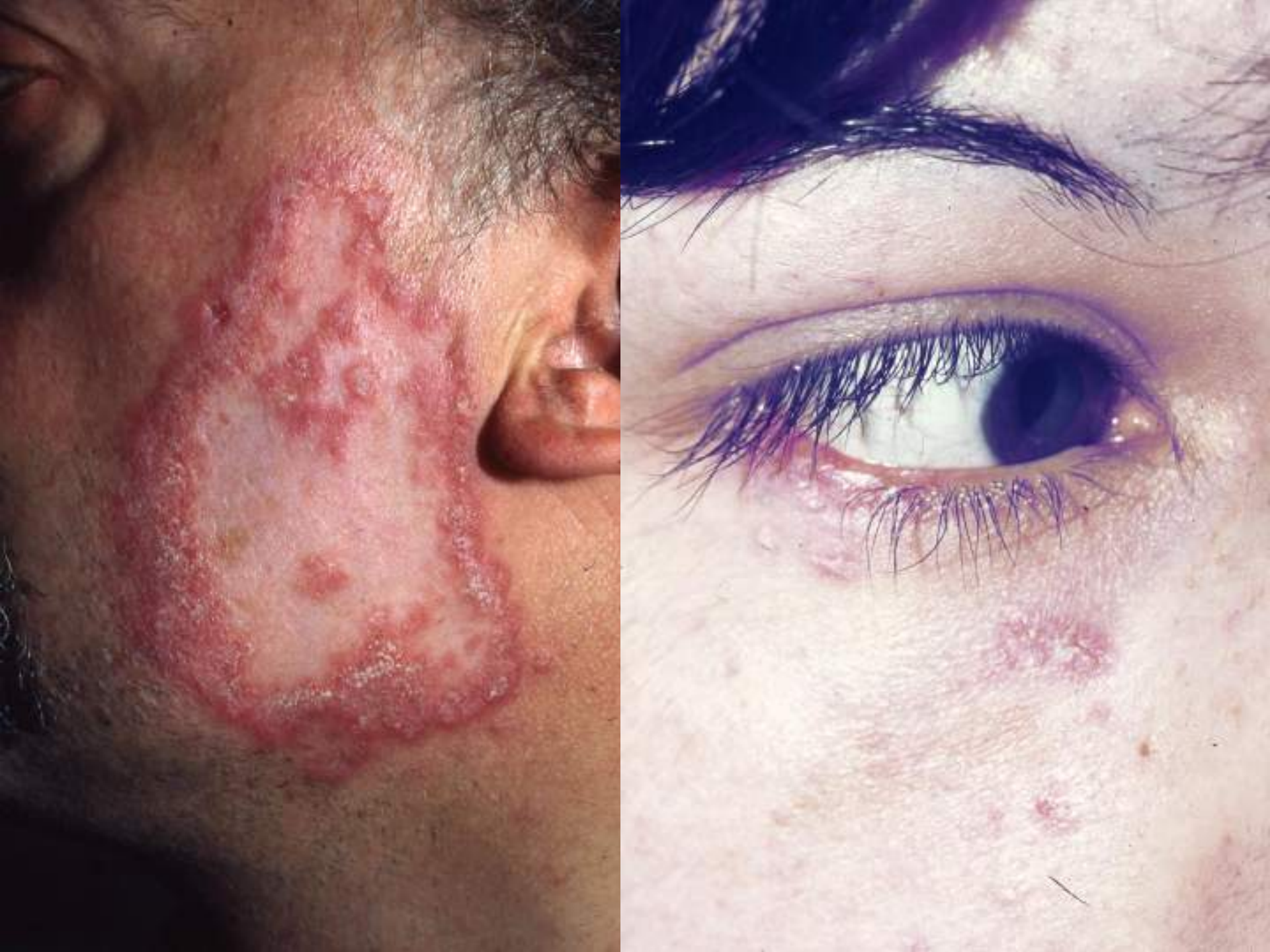
E. LE Neonatal

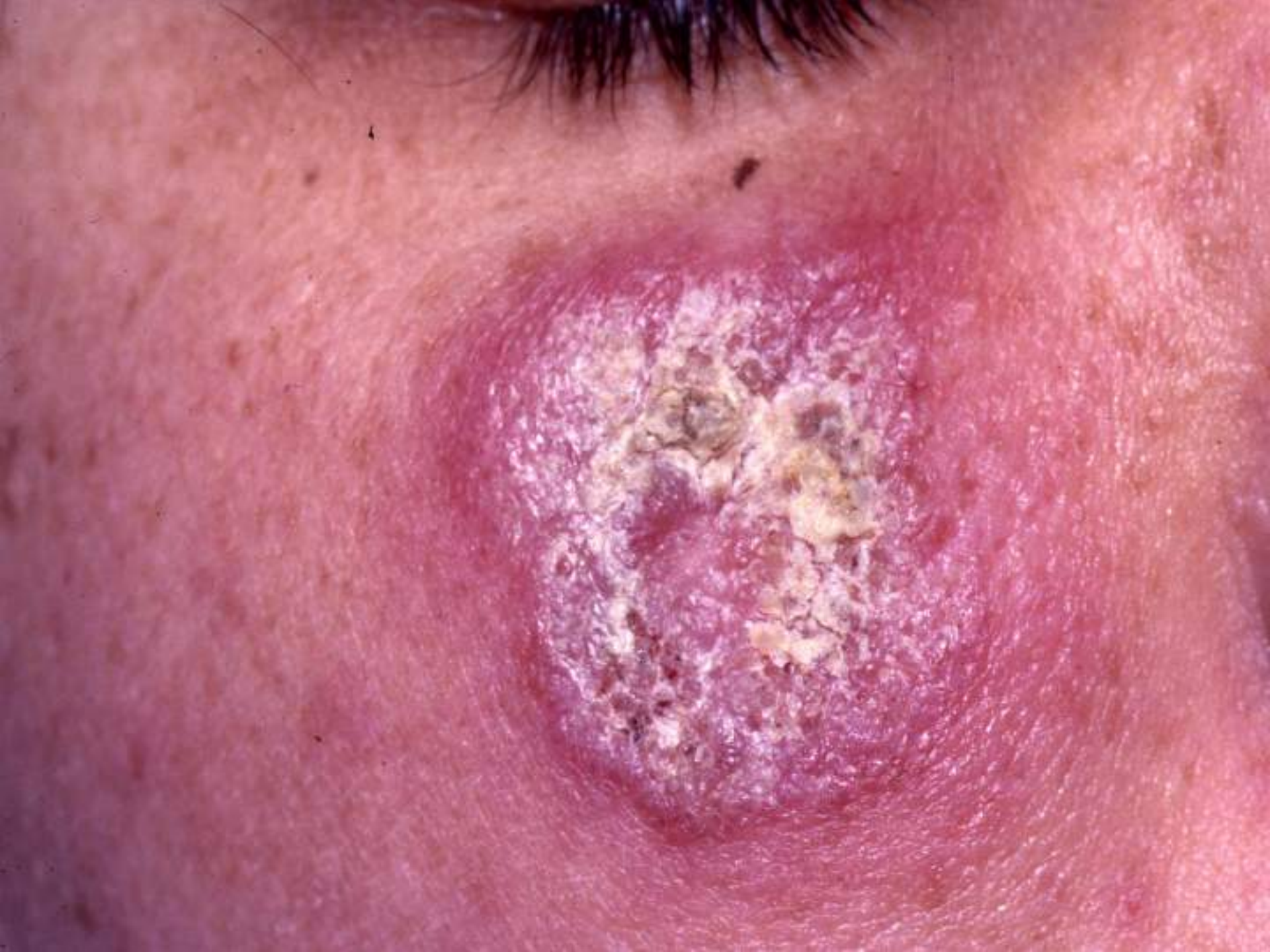
F. LE con Ac Antifosfolípidos

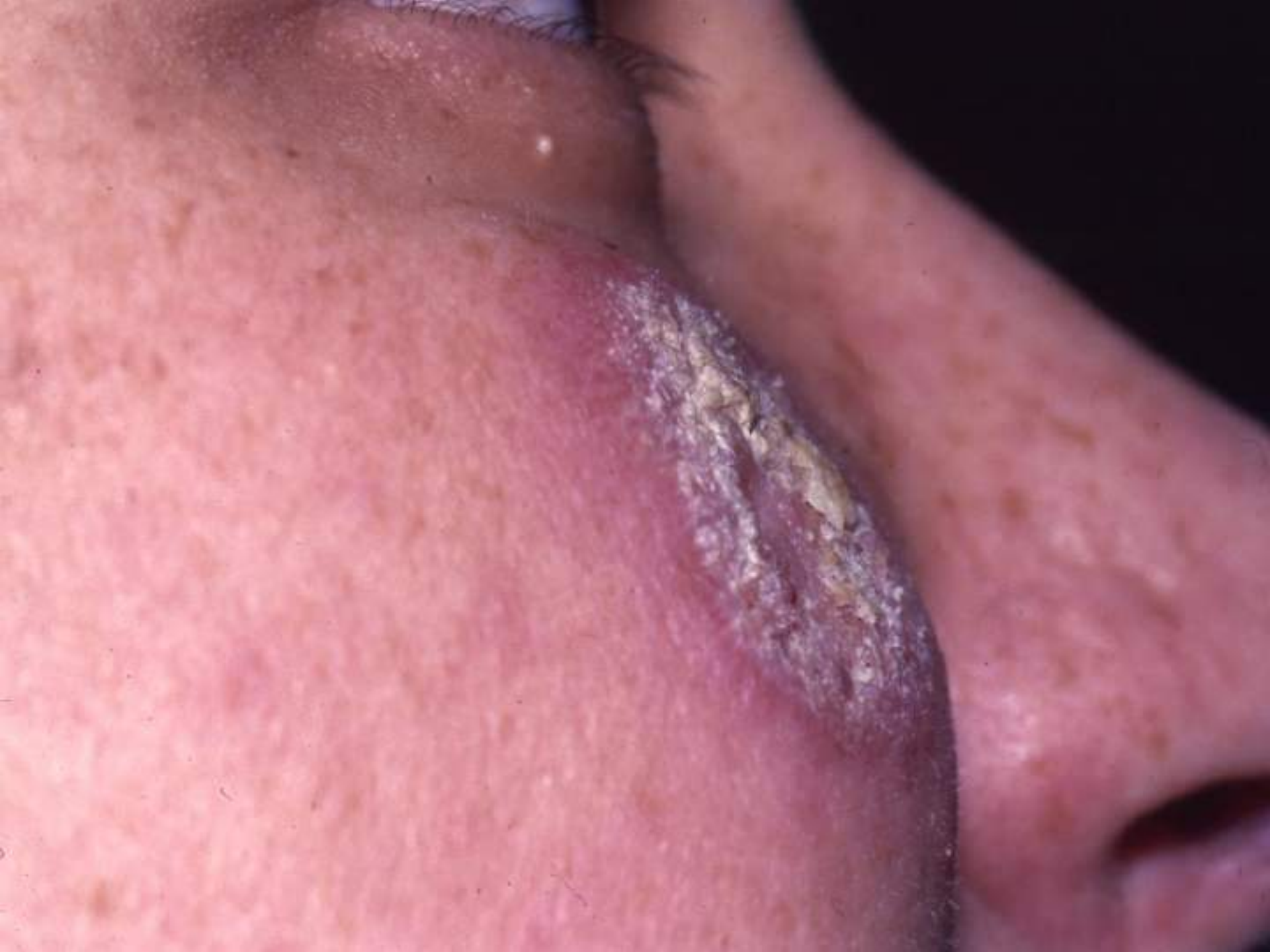
G. Deficiencia de C_2 y C_4

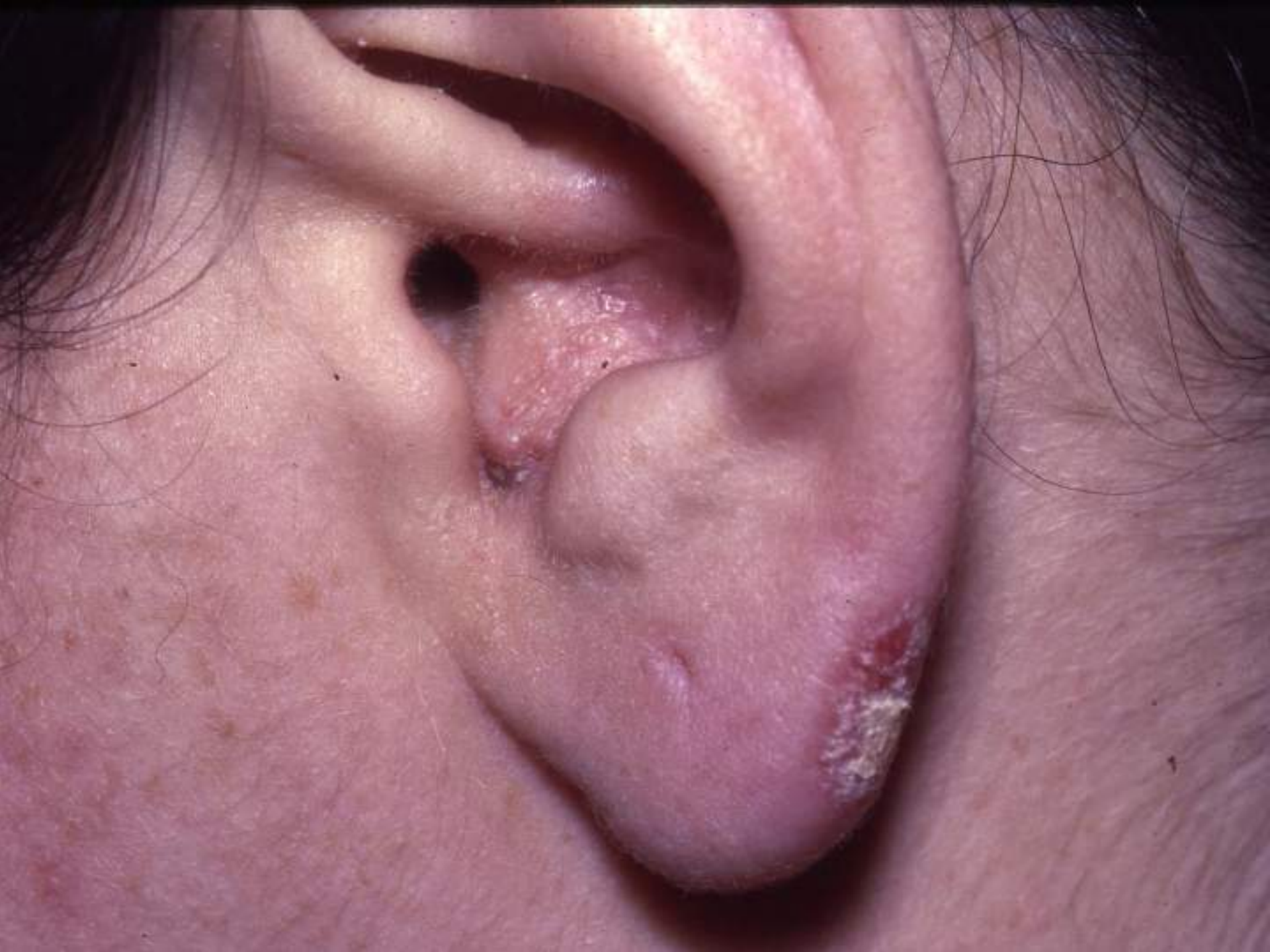


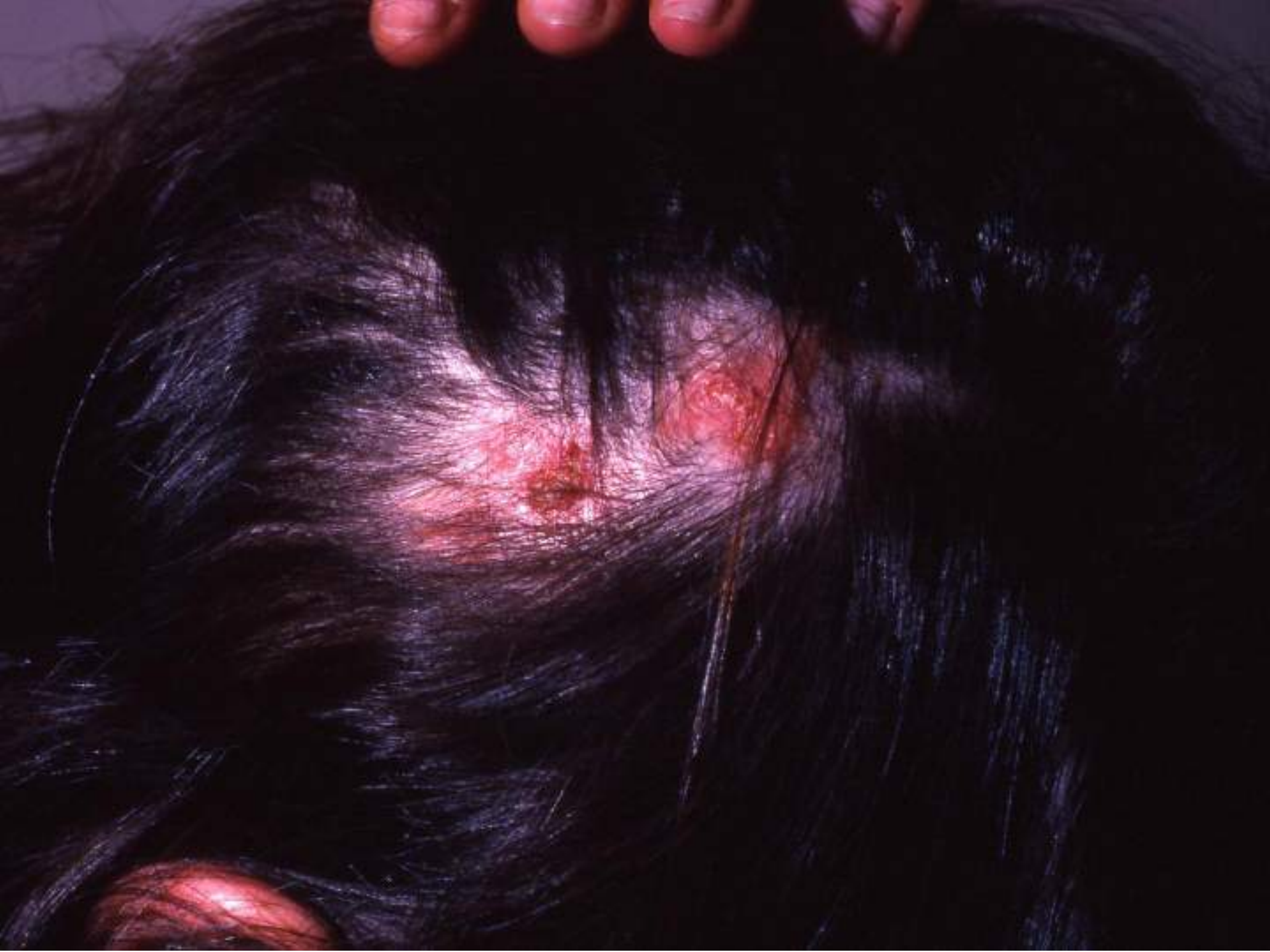
Characteristic sites of involvement for the three major forms of cutaneous lupus erythematosus (LE).

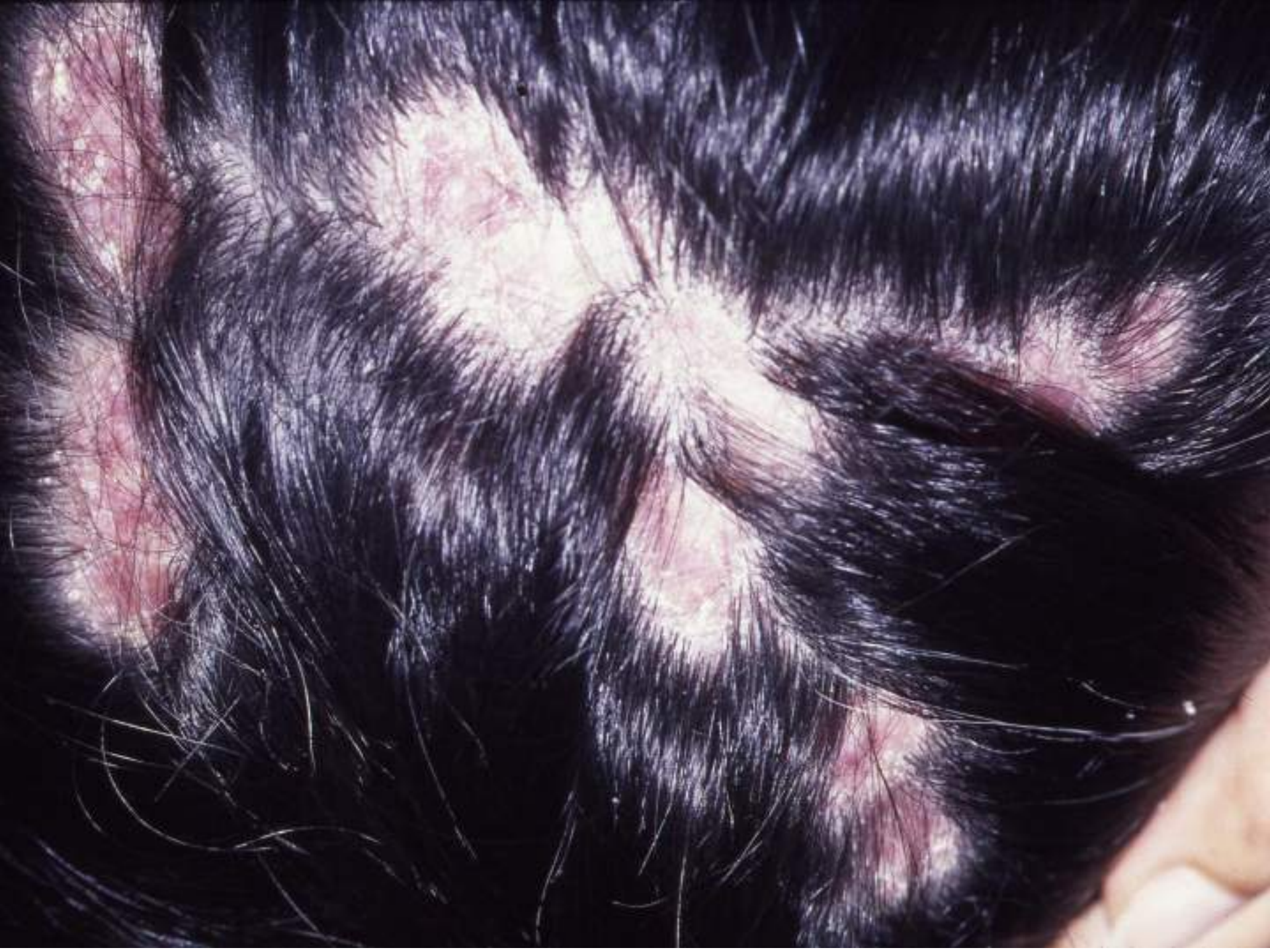


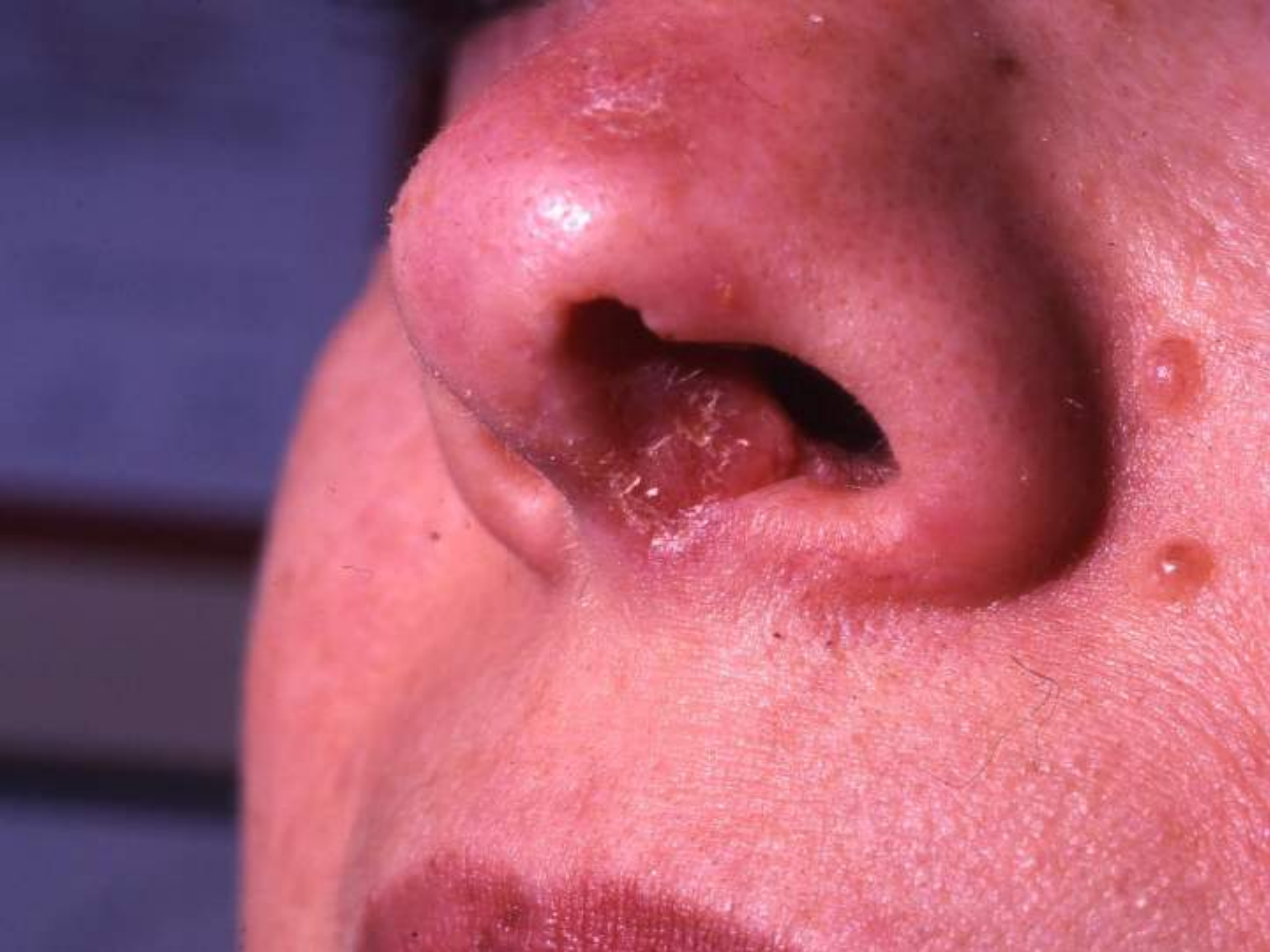


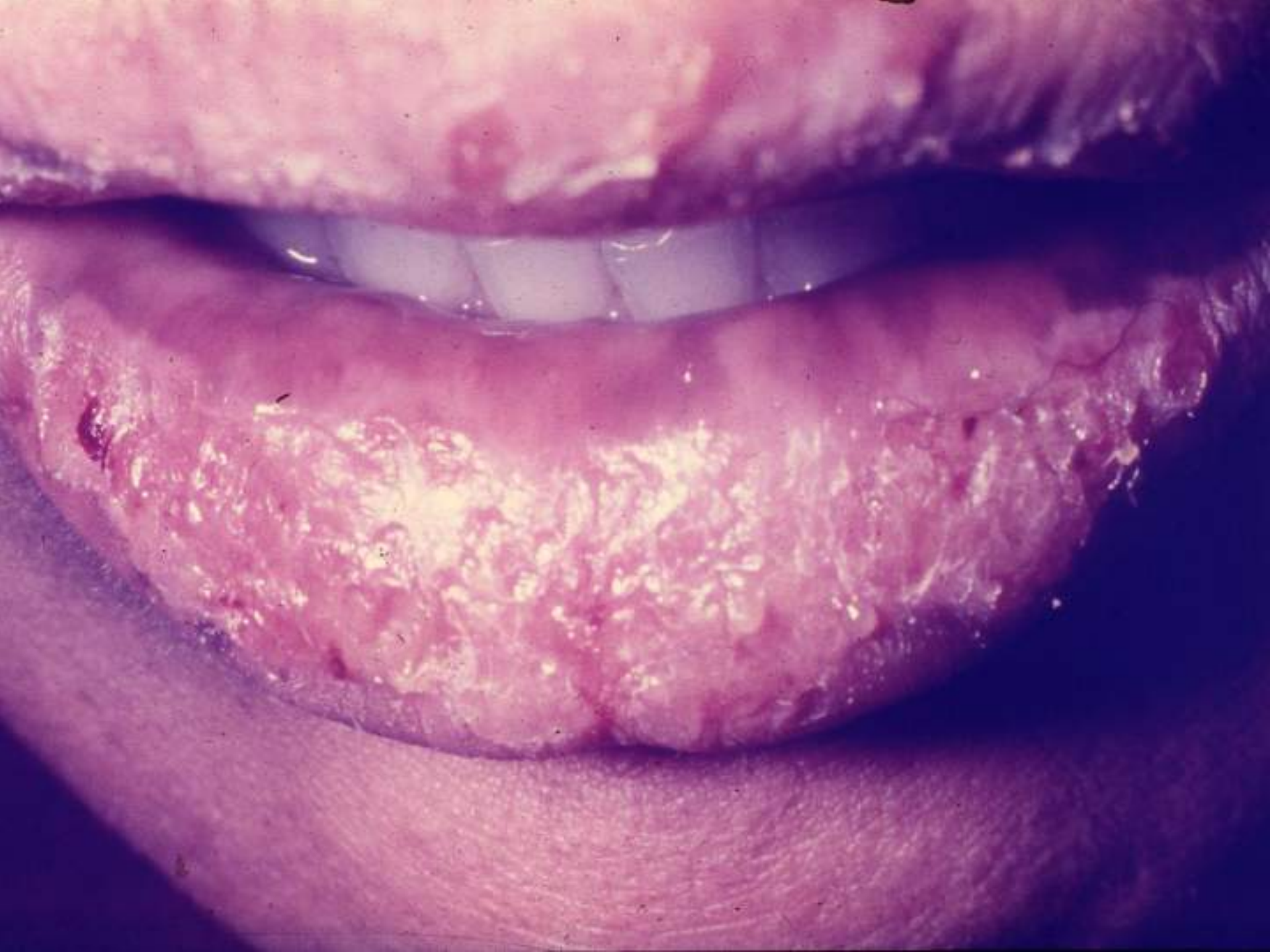


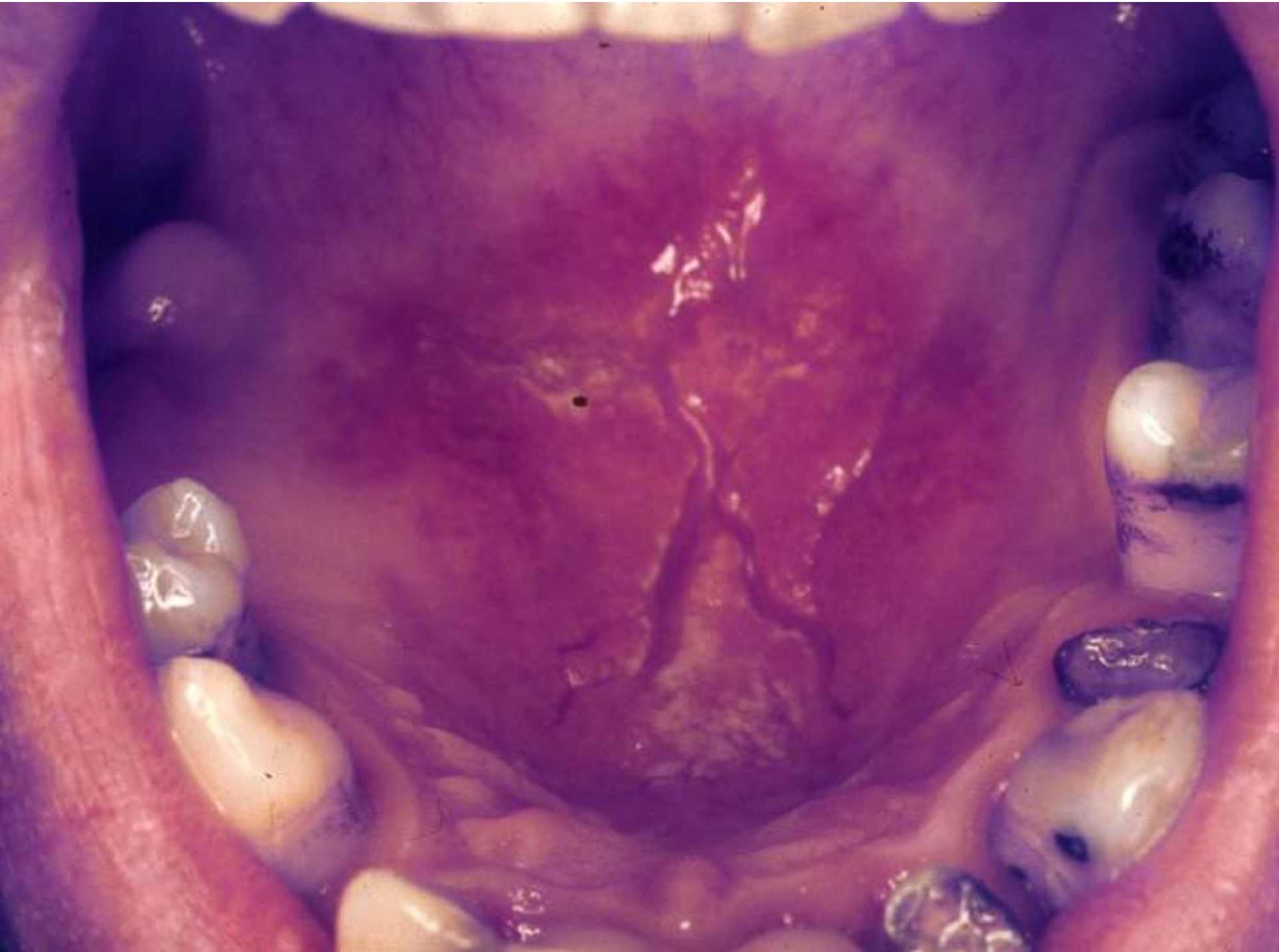


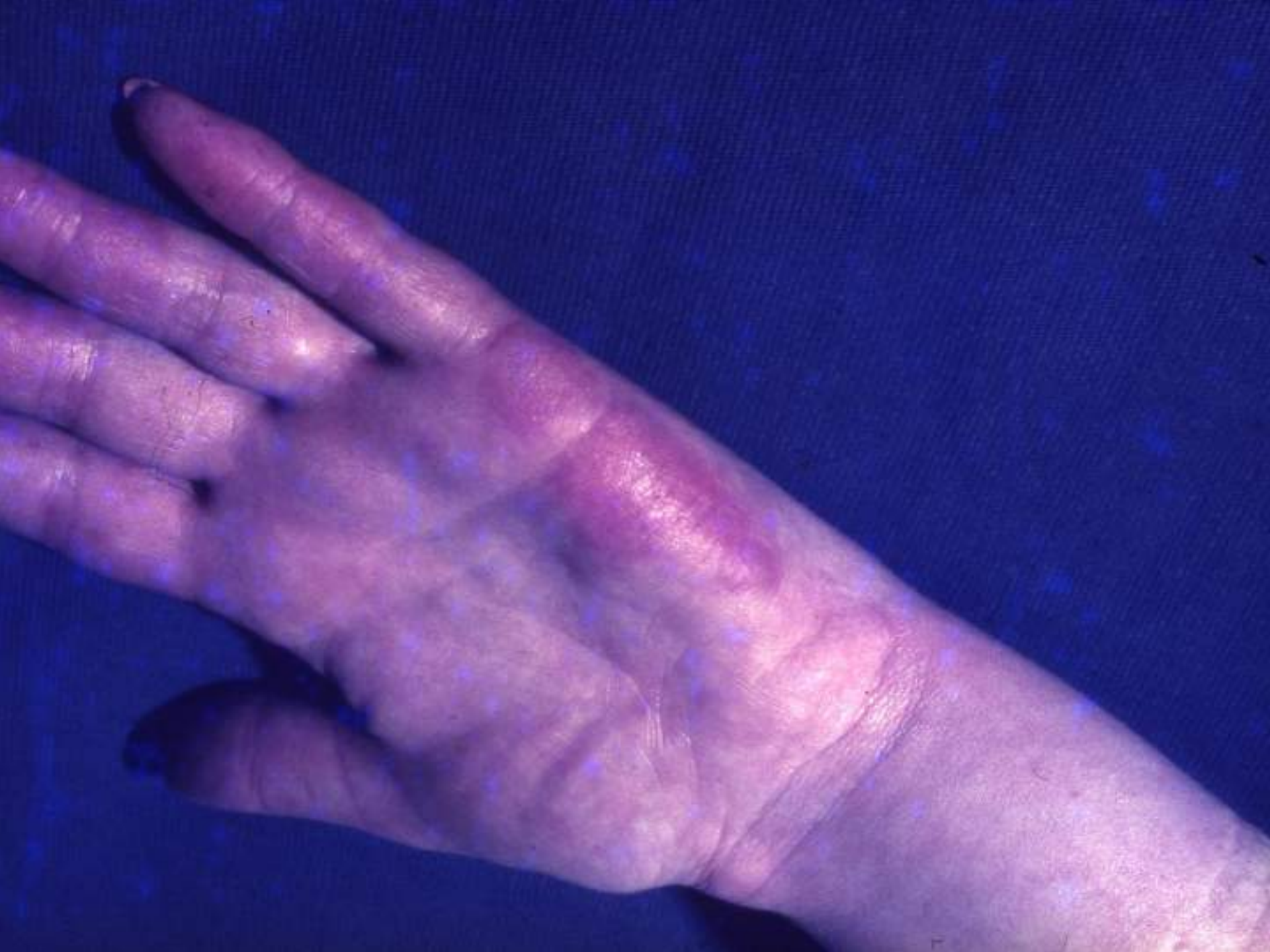


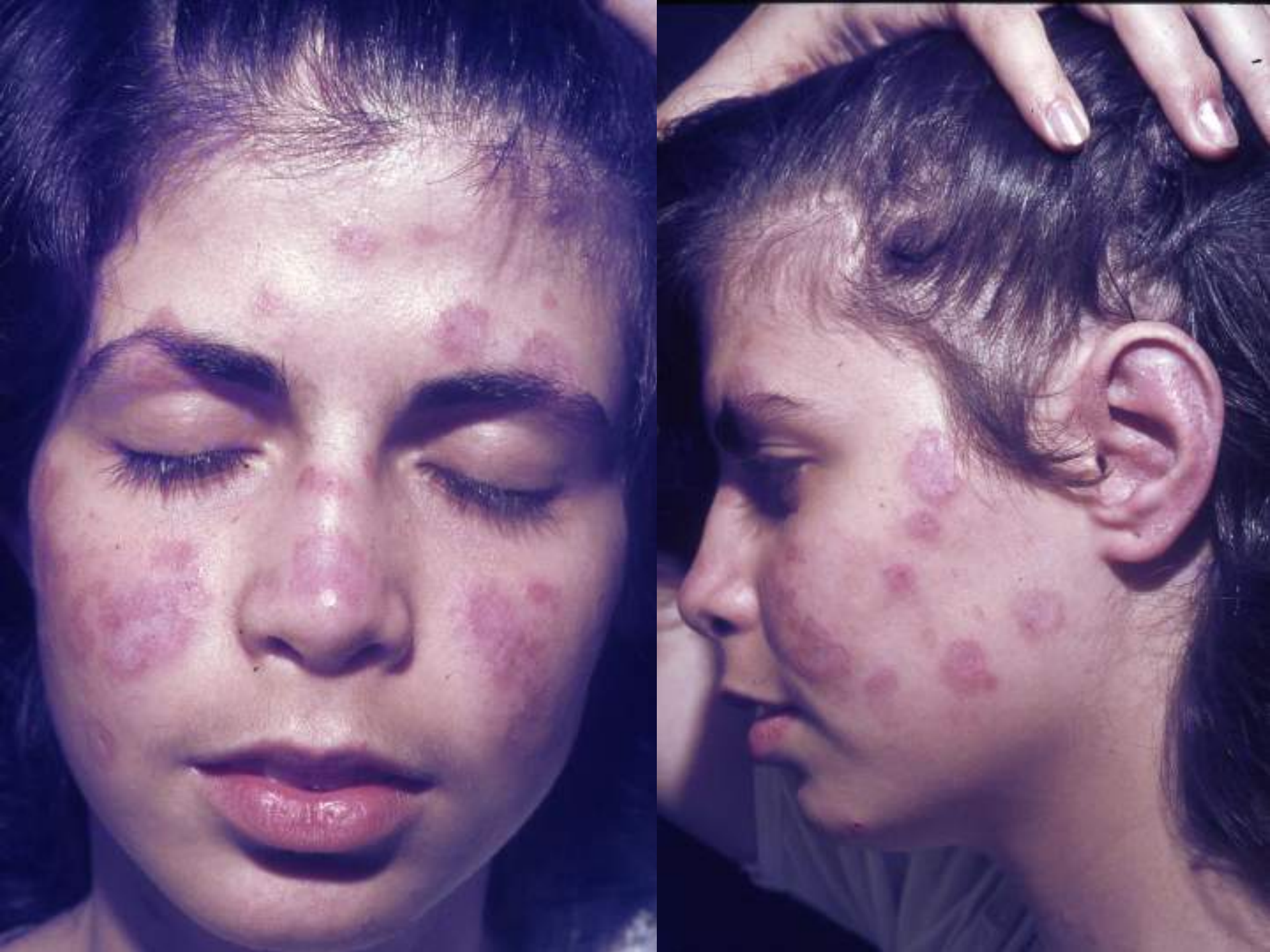


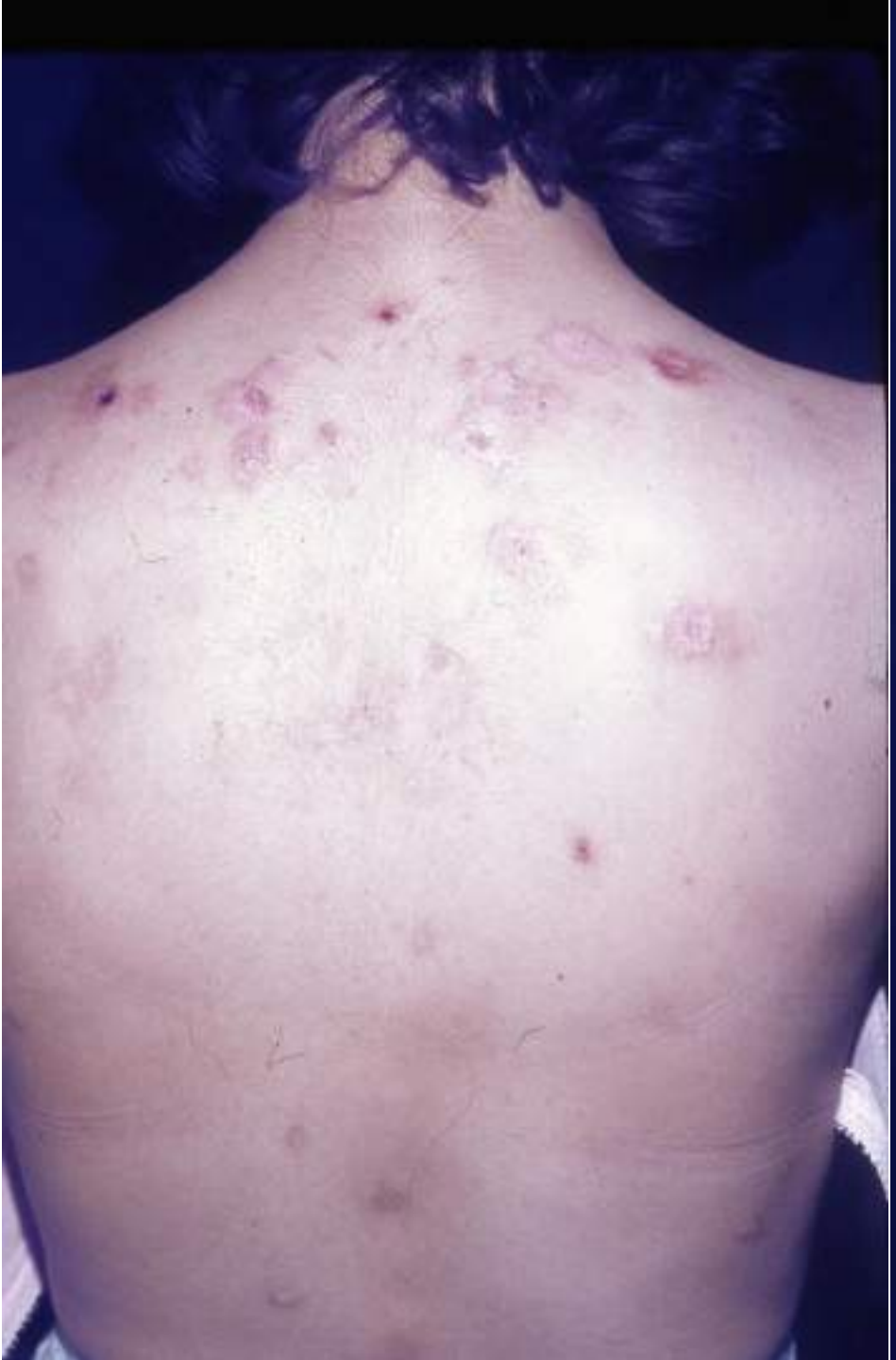
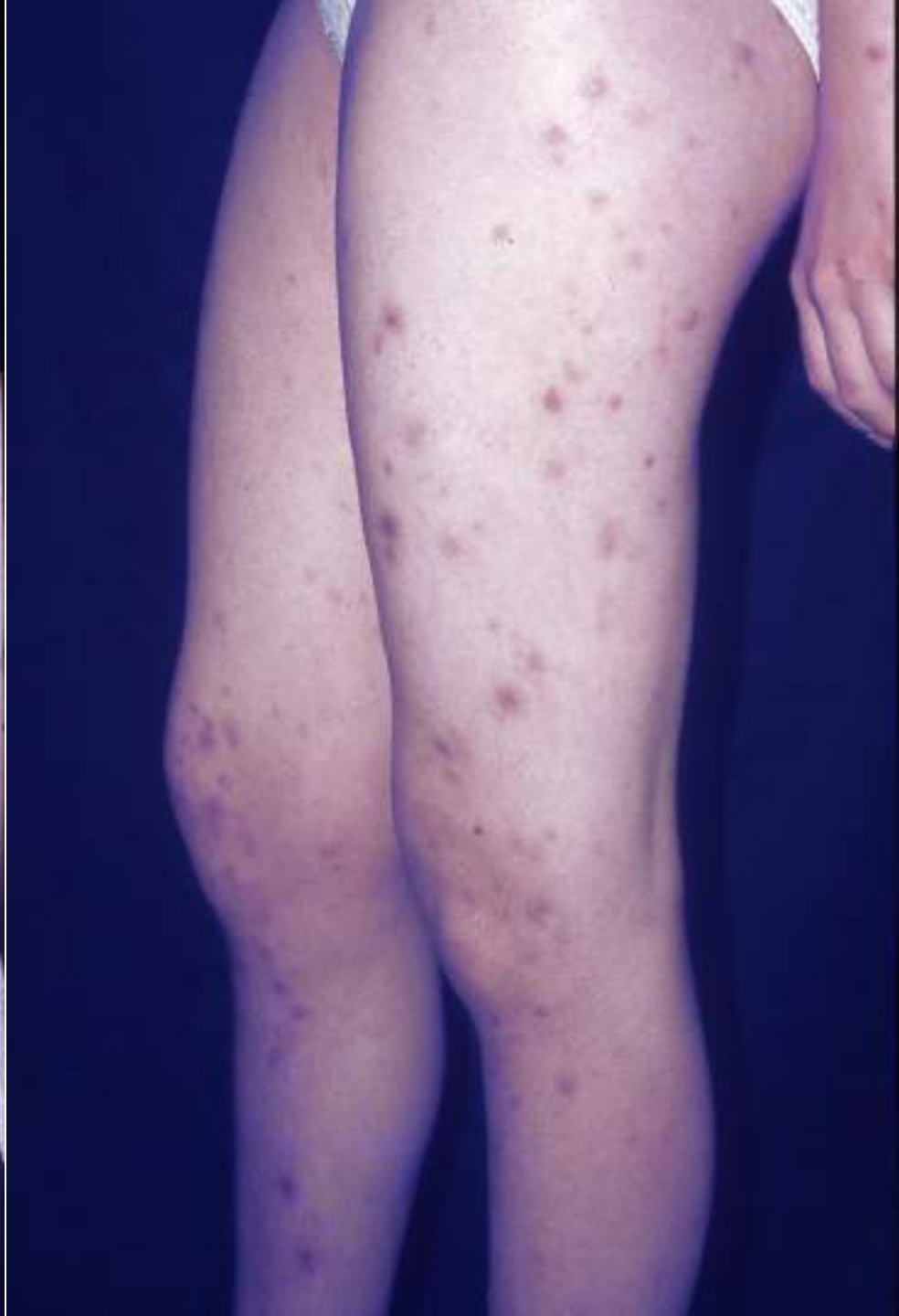


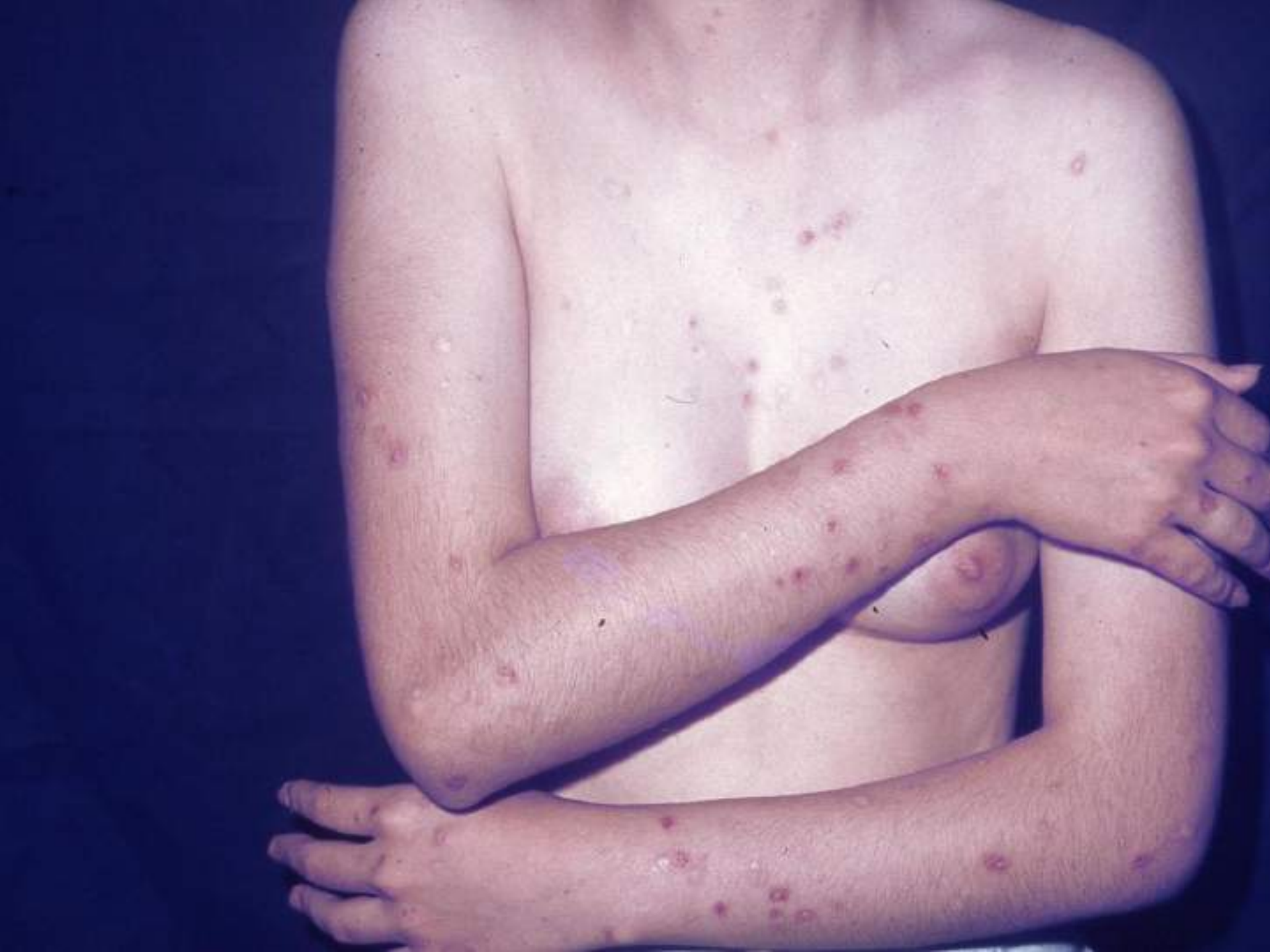


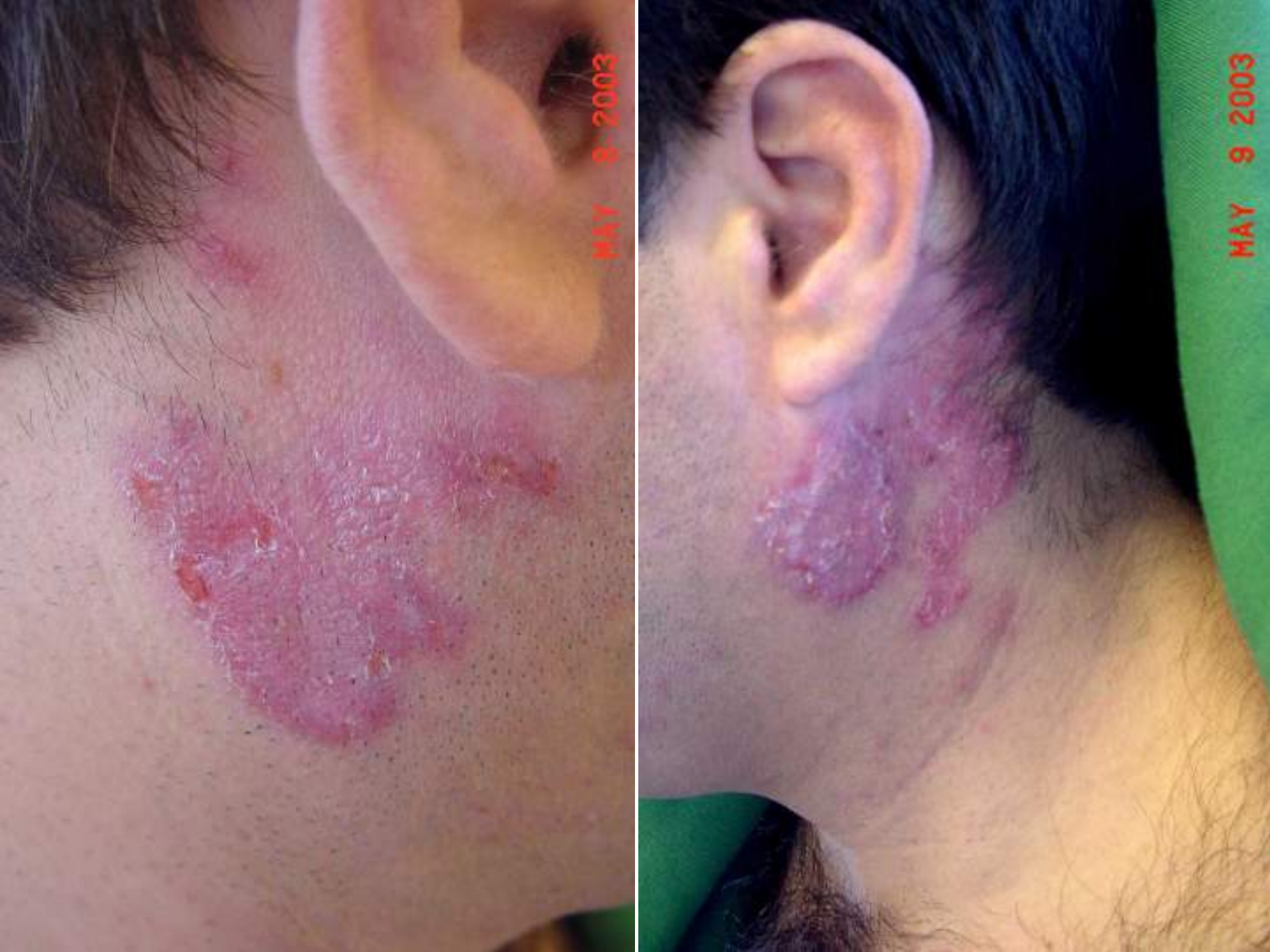






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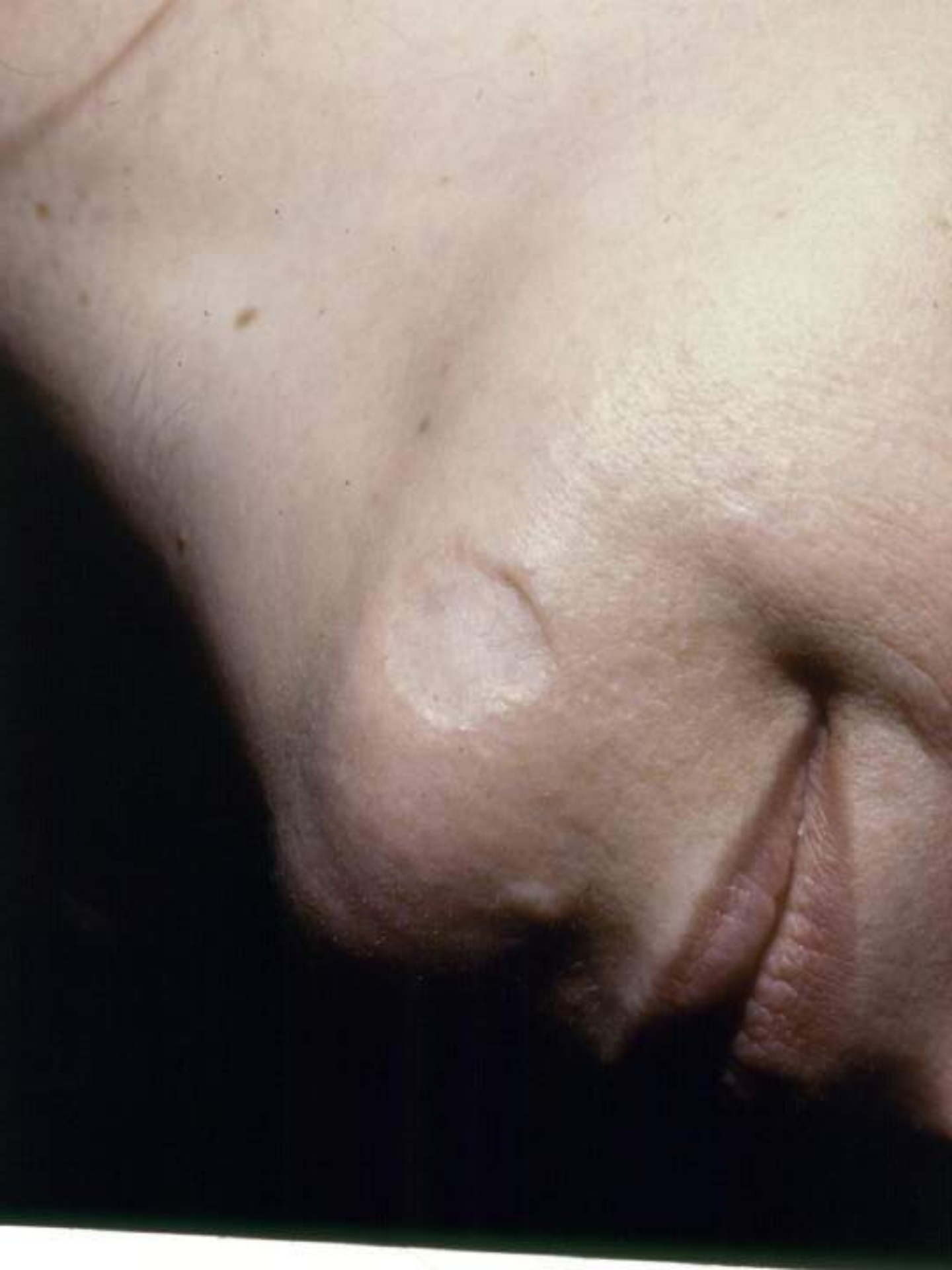

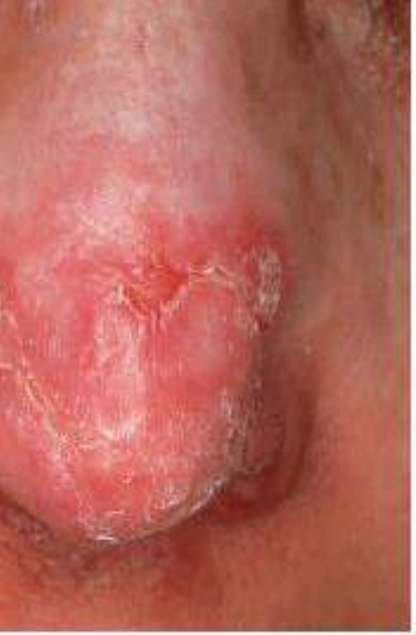

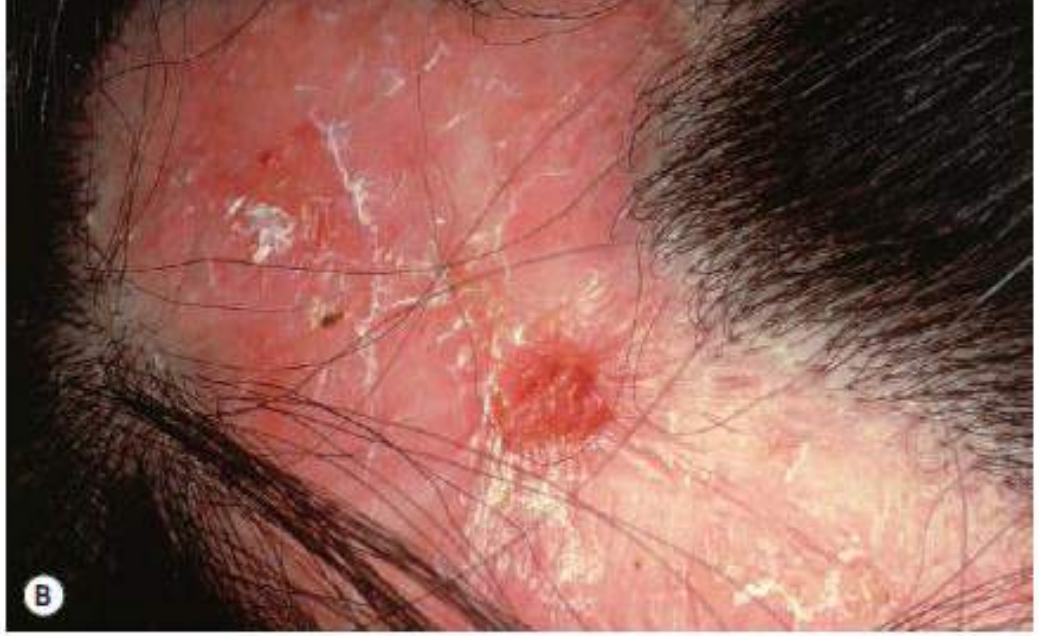
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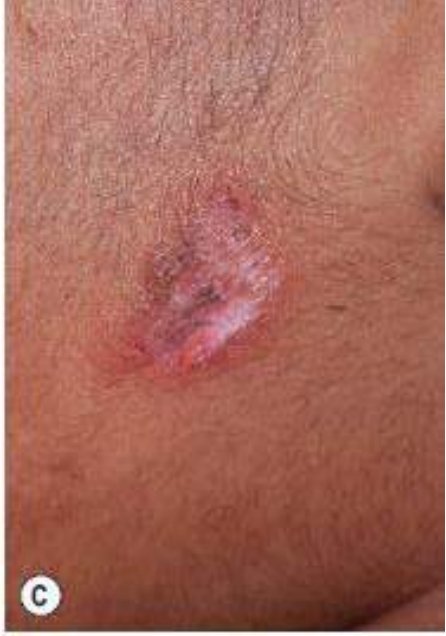
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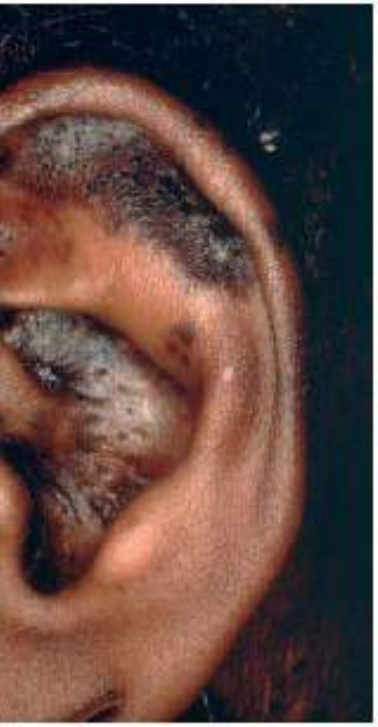

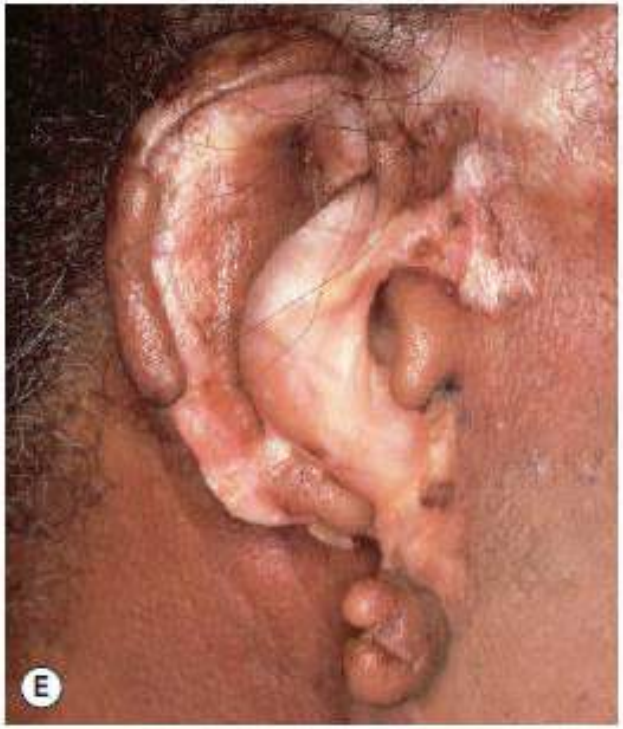
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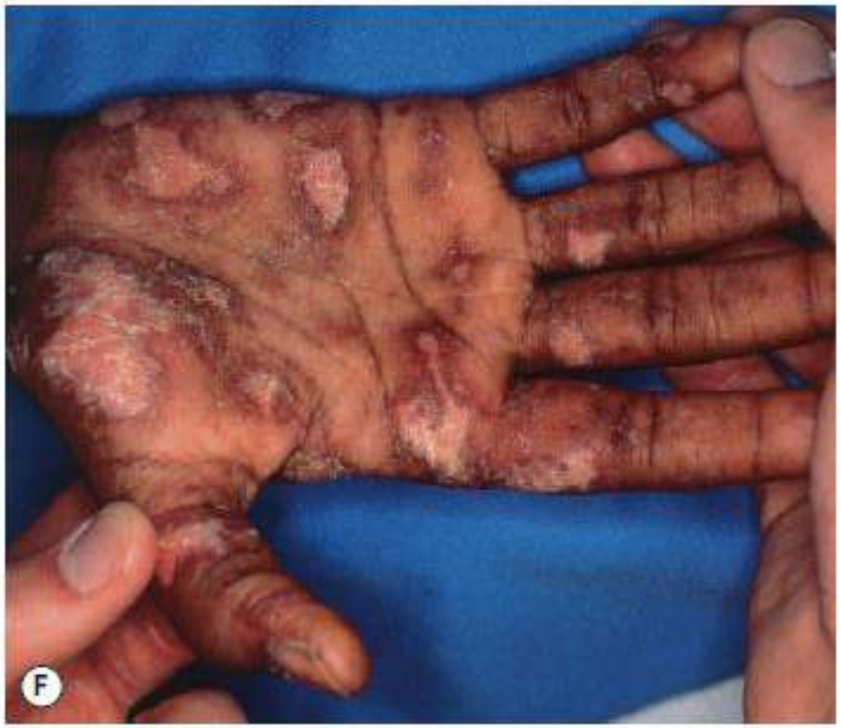
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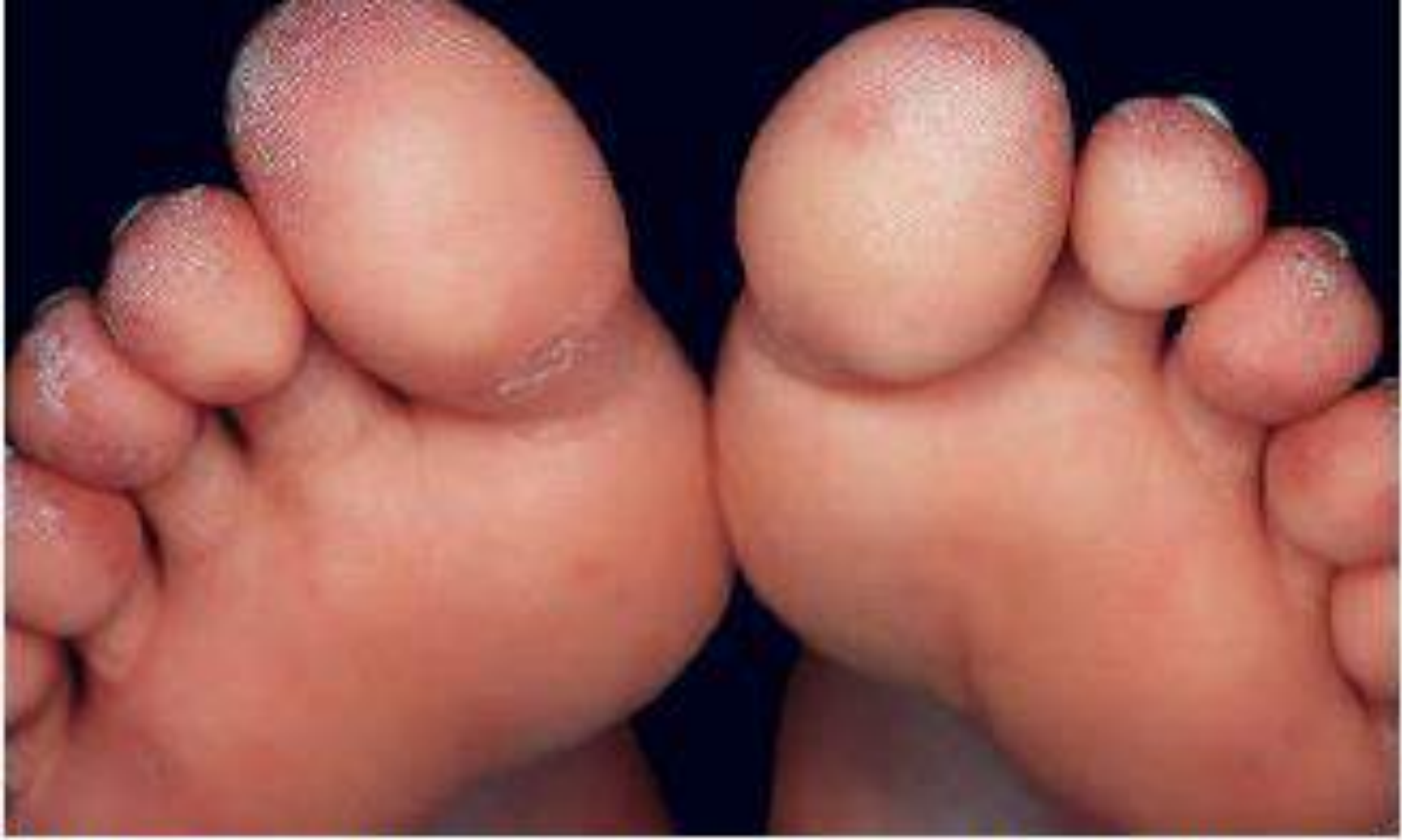
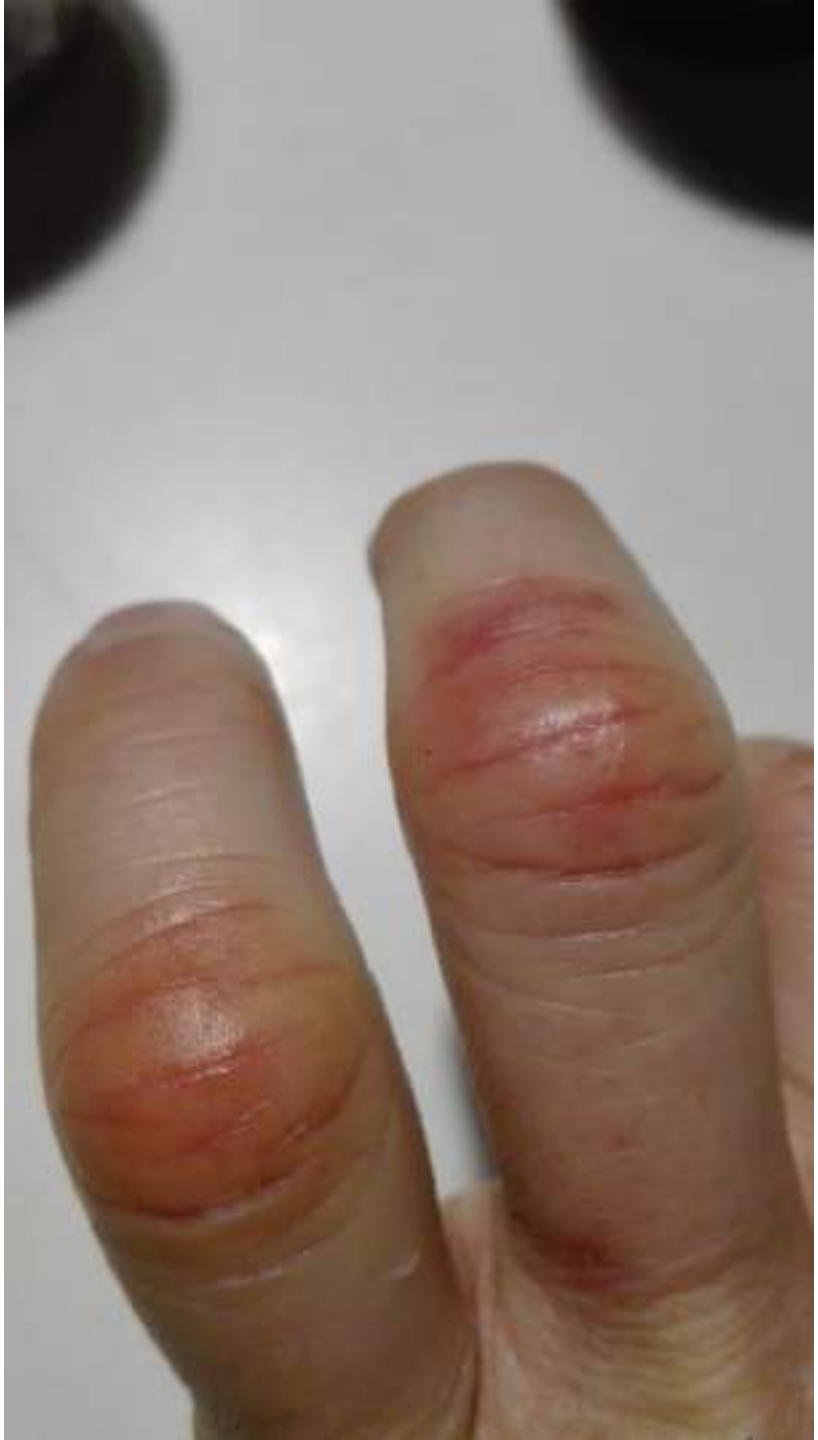
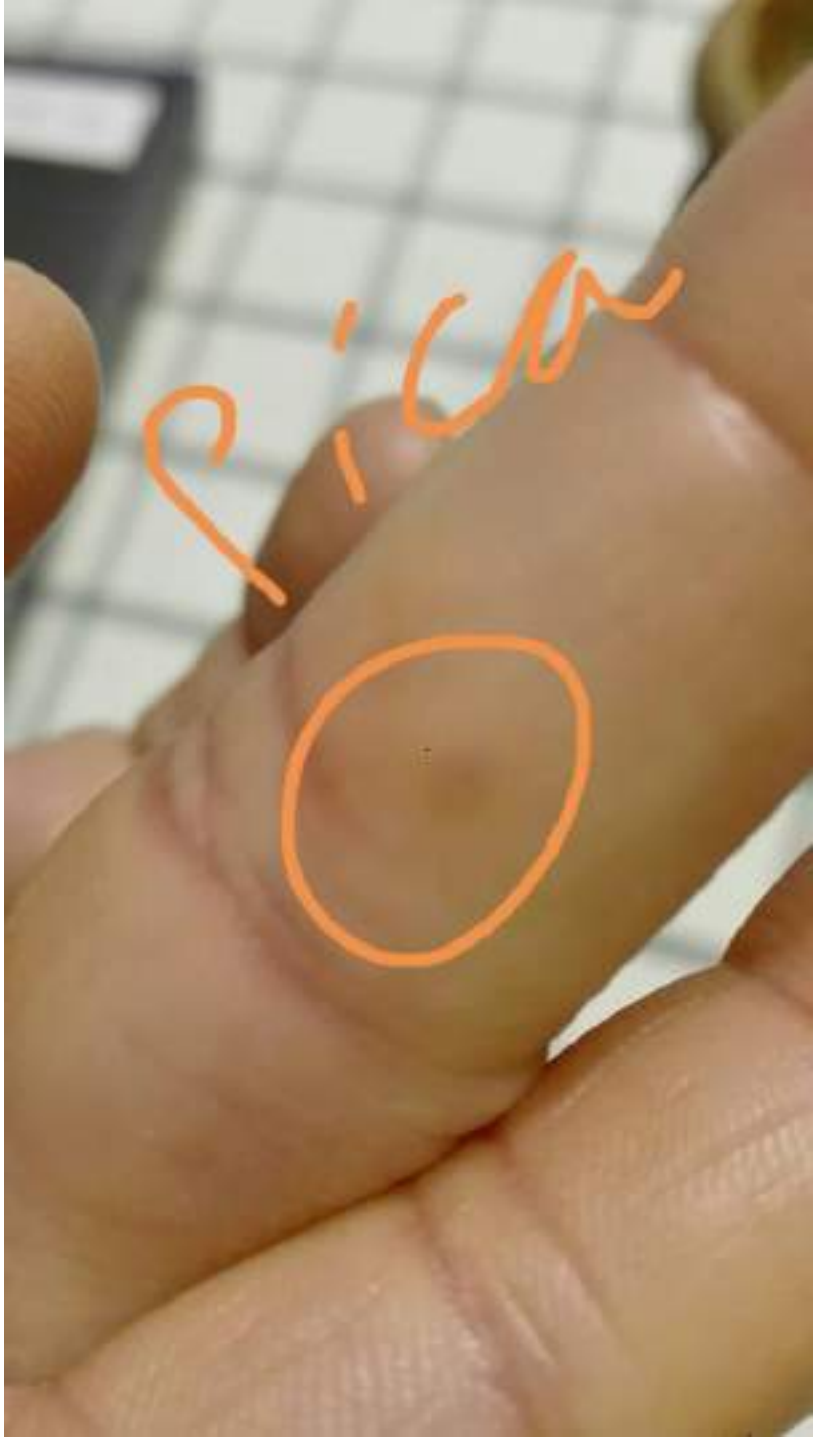
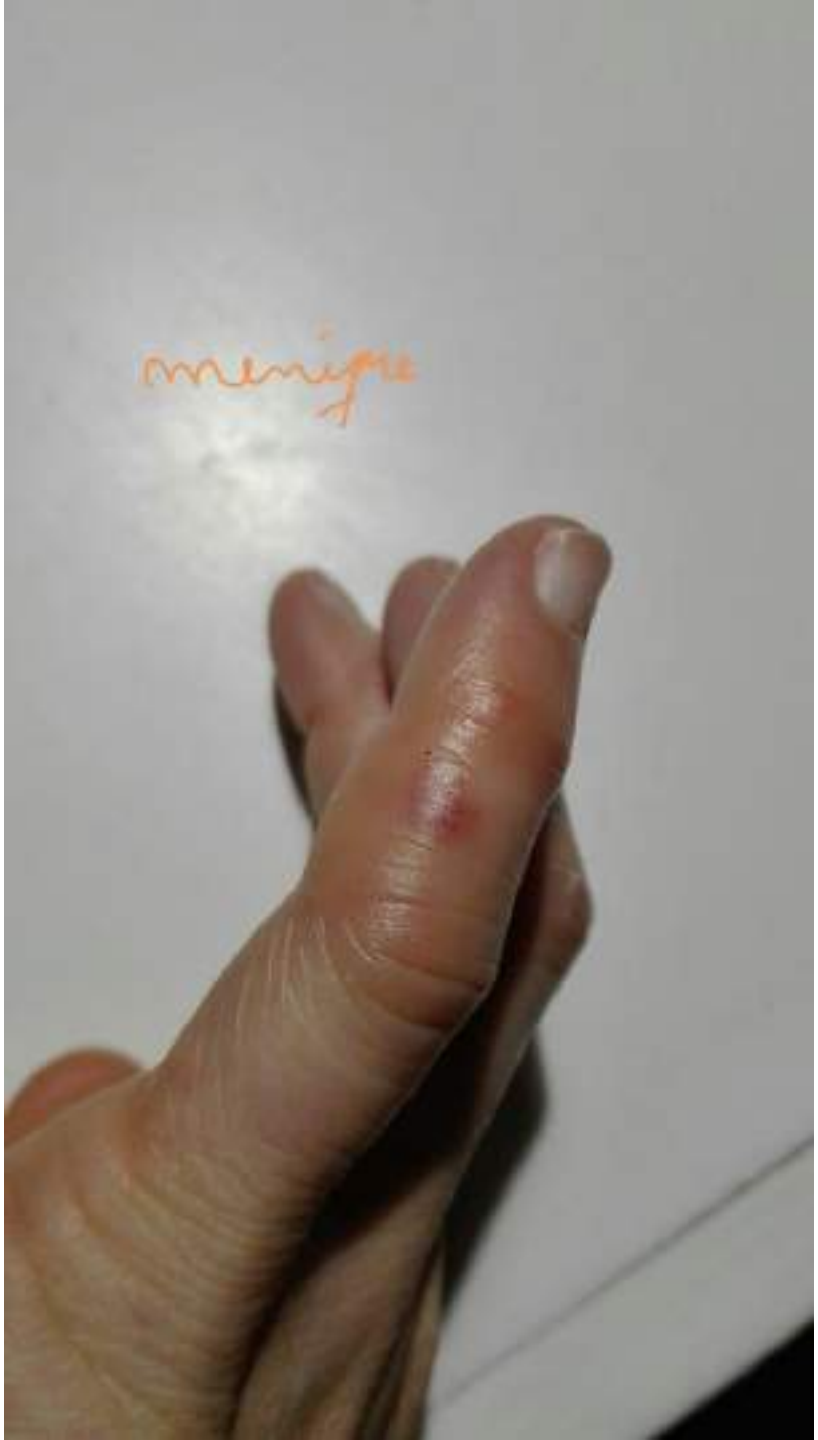
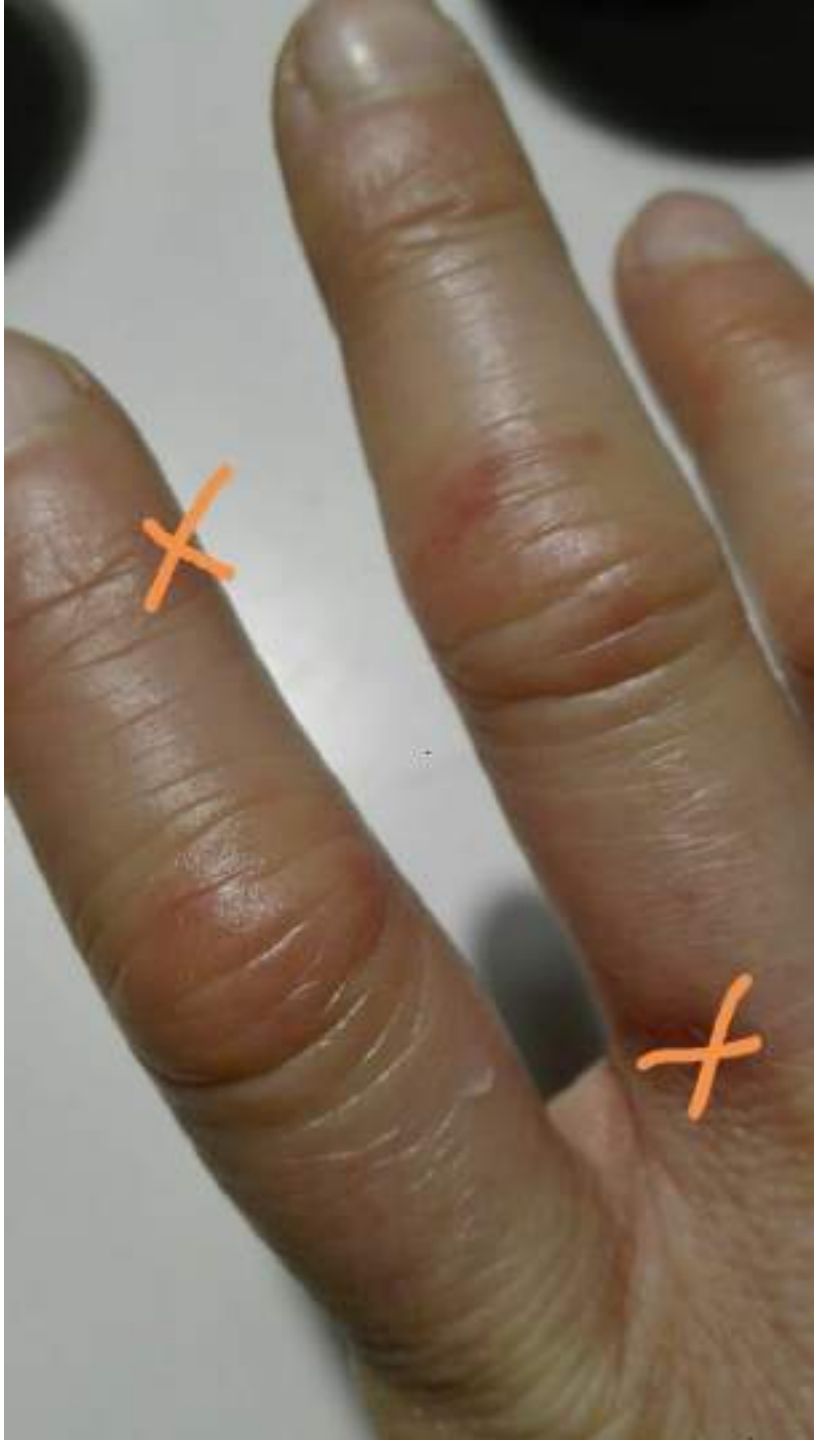


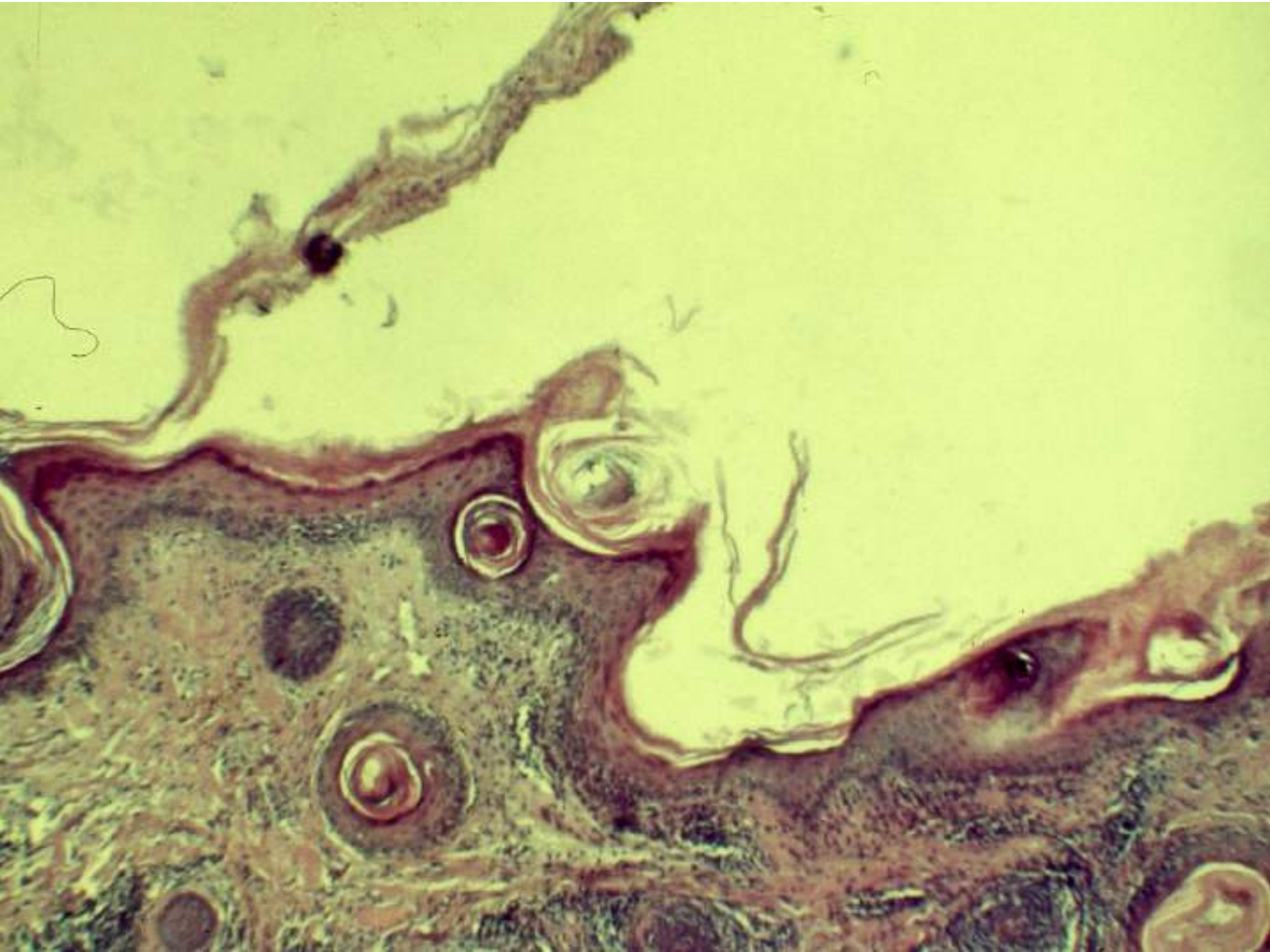
Fig. 41.13 Chilblain lupus. Violaceous plaques, some with scale, on toes. If there is a family history of this disorder, the possibility of mutations in *TREX1*, which encodes a DNA exonuclease, or *SAMHD1*, which encodes a host restriction nuclease that plays a role in the innate immune response, can be considered.

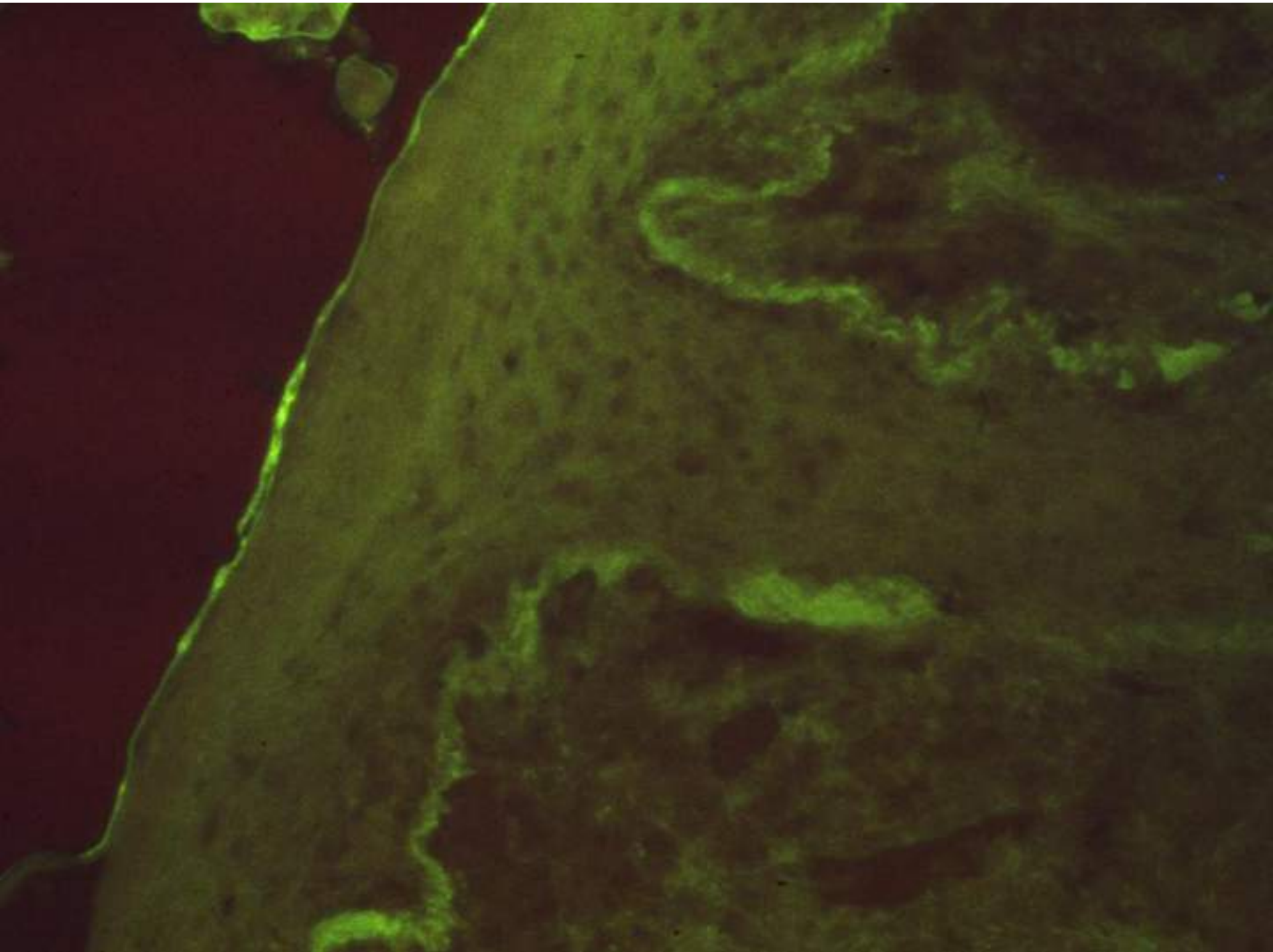












L.E. DISCOIDE CRONICO

FAN + -

ADN -

Ausencia de lesiones viscerales

+ Piel enferma (50%)

Band Test

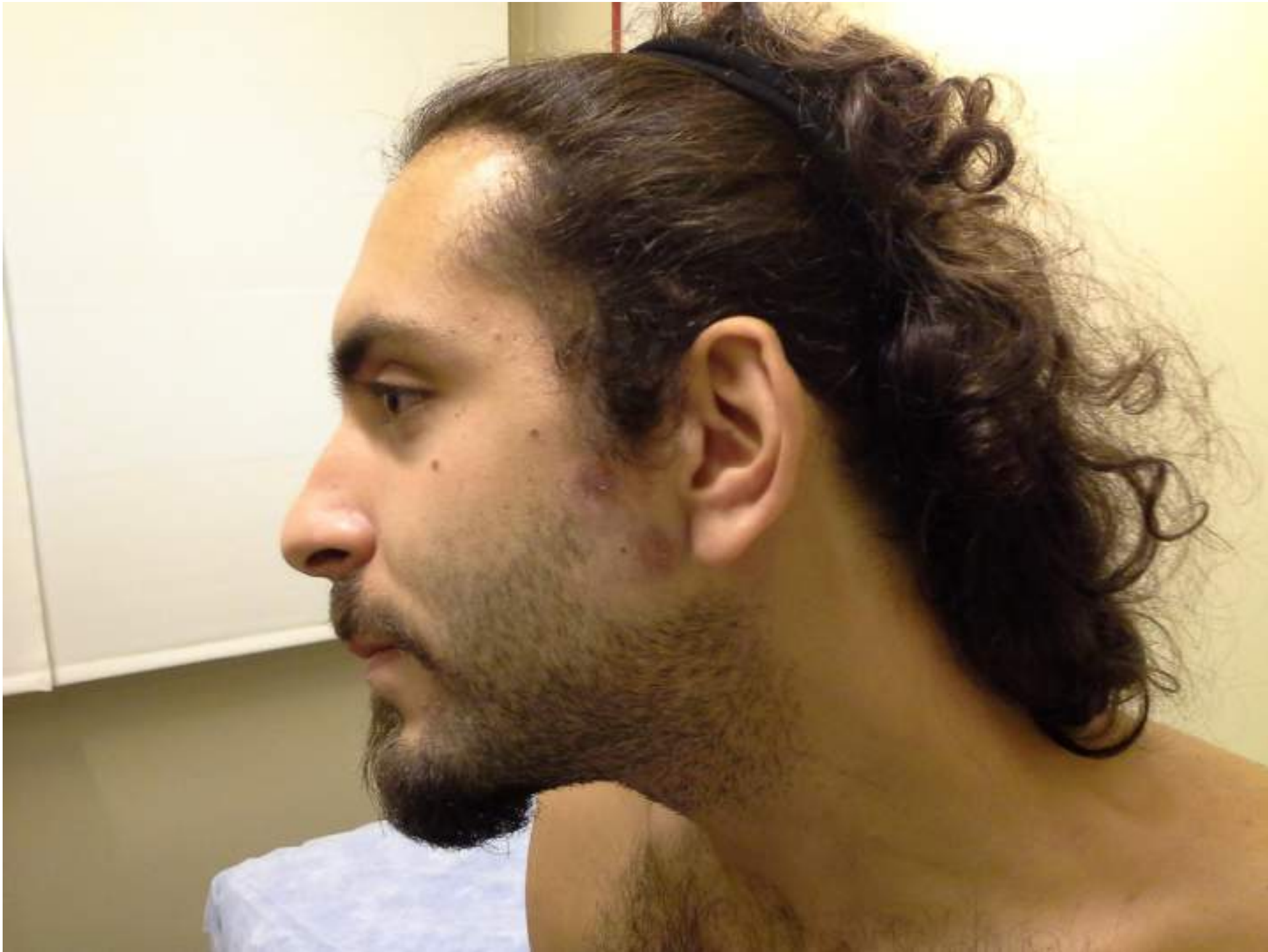
- Piel sana

Buen pronóstico

Entendiendo cuando el lupus cutáneo progresa al sistémico (B Chong. JAMA Dermatol 2014;150: 296 comentario)

Dice que el 23% de los lupus cutáneos progresan a LES en varios años.

- ✓ La progresión es lenta y debe ser monitoreada por los dermatólogos.
- ✓ El estudio enseña que 18% (13 pacientes) van a LES y solo el 7% tiene una forma moderada o severa. El resto tiene lesiones mucocutáneas o de lab.



- Tratamiento:

✓ Fotoprotección.

✓ Tópico.

✓ Antimaláricos. (efectividad del 75%)

✓ Talidomida (DAPS, clofazimine, oro)

✓ Inmunosupresión.

✓ Otros.

Antimaláricos: Retinopatía ocular

- <6.5mg/kg/día HCQ 3mg/kg/día CLQ
- Guía Americana de oftalmología 2002.
  - Pacientes de alto riesgo
    - >de 60 años, con índices de grasa corporal aumentado, enf renal, hepática o trastornos de retina, dosis mayores a las recomendadas. Necesitan control anual.
  - Pacientes de bajo riesgo
    - Dosis recomendadas menos de 5 años y examen basal normal. No necesita control x 5 años.

Terapia antimalárica actúa en LE sobre:

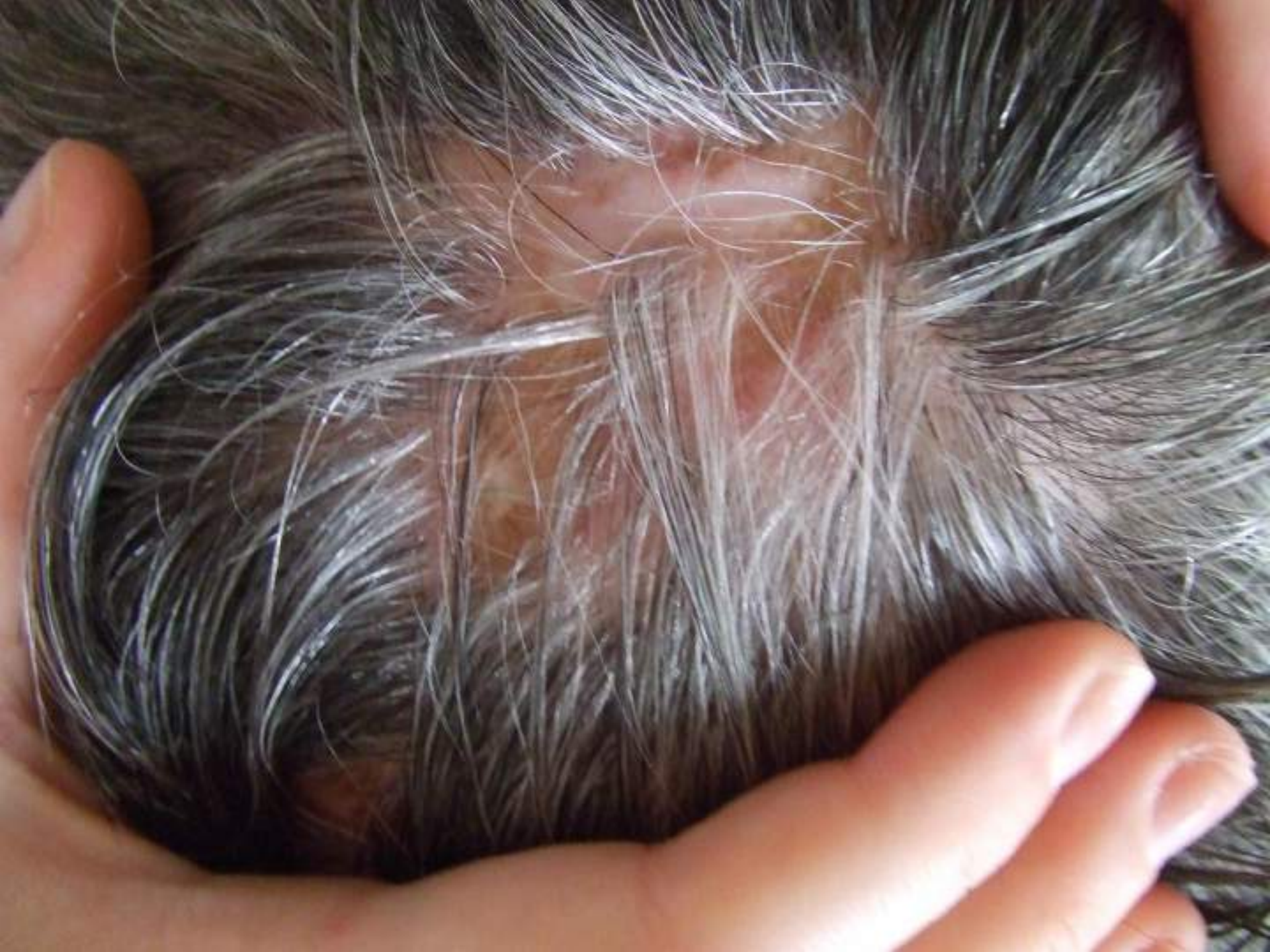
- LE: LECA, LECSA, LED, menos sobre formas verrugosas e hipertróficas, tumidus, paniculitis
- Eritema malar
- Alopecía
- Fotosensibilidad
- Ulceras orales
- Atralgia, mialgias, artritis y serositis

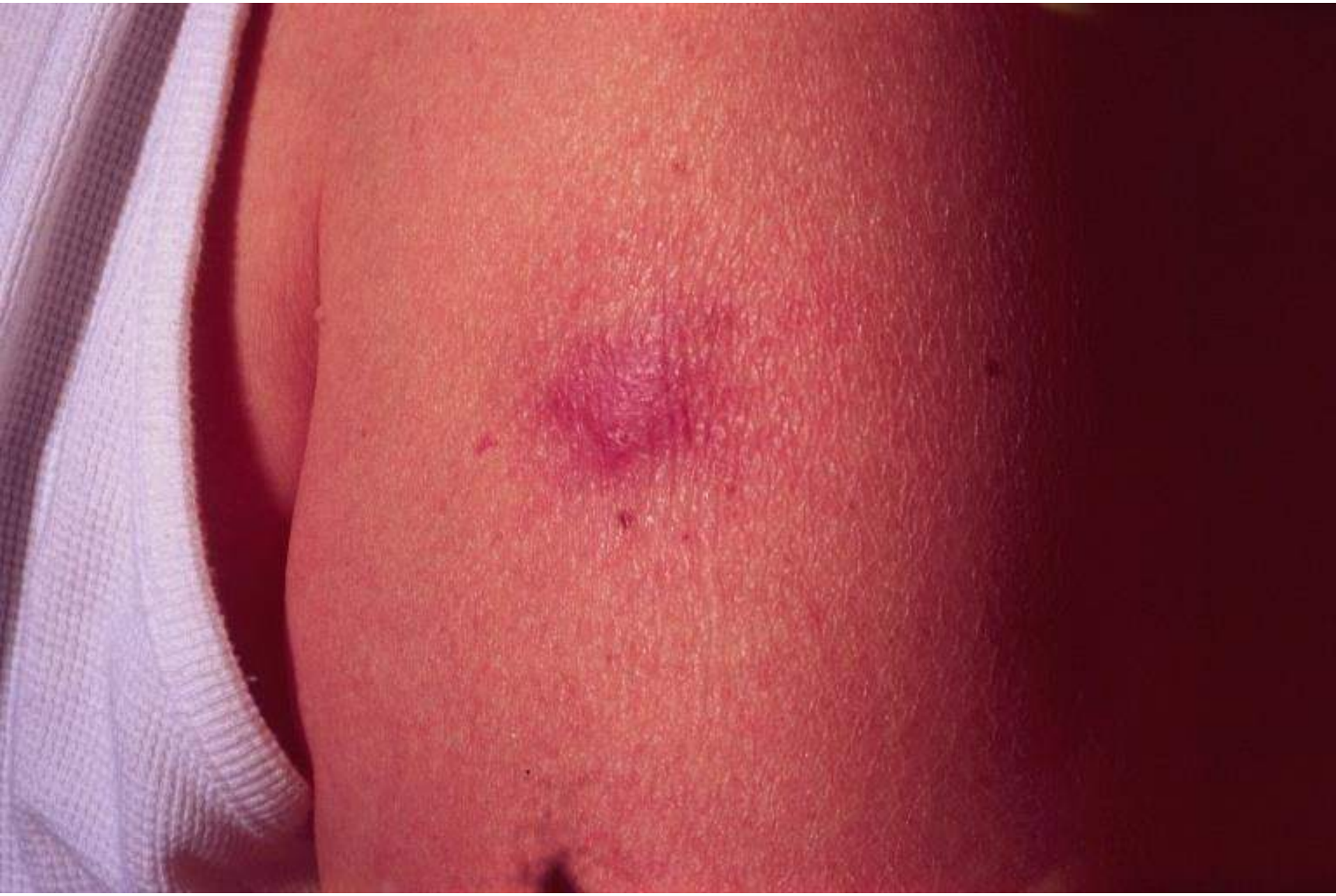
Antimaláricos manejos actuales

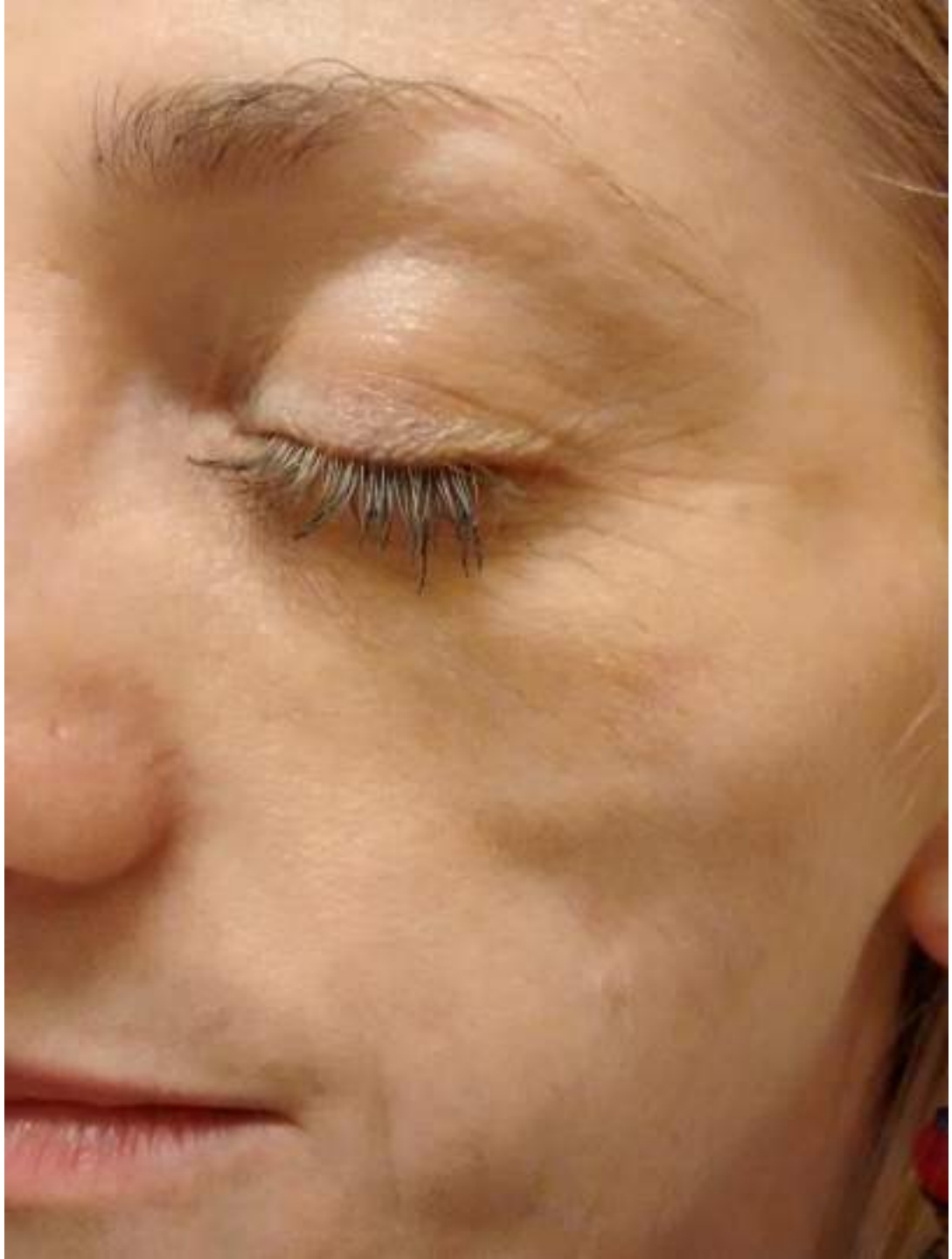
- Esperar 6 semanas
- Tomar después de una comida
- Embarazo clase C, seguro en lactancia
- Combinada con otras drogas
- Efectos colaterales
  - Reacciones x hipersensibilidad, hematol, hepáticos (def G6PD, PCT subclínica). Miopatía, cardiomiopatía, pigmentaciones cutáneas, trastornos oculares.

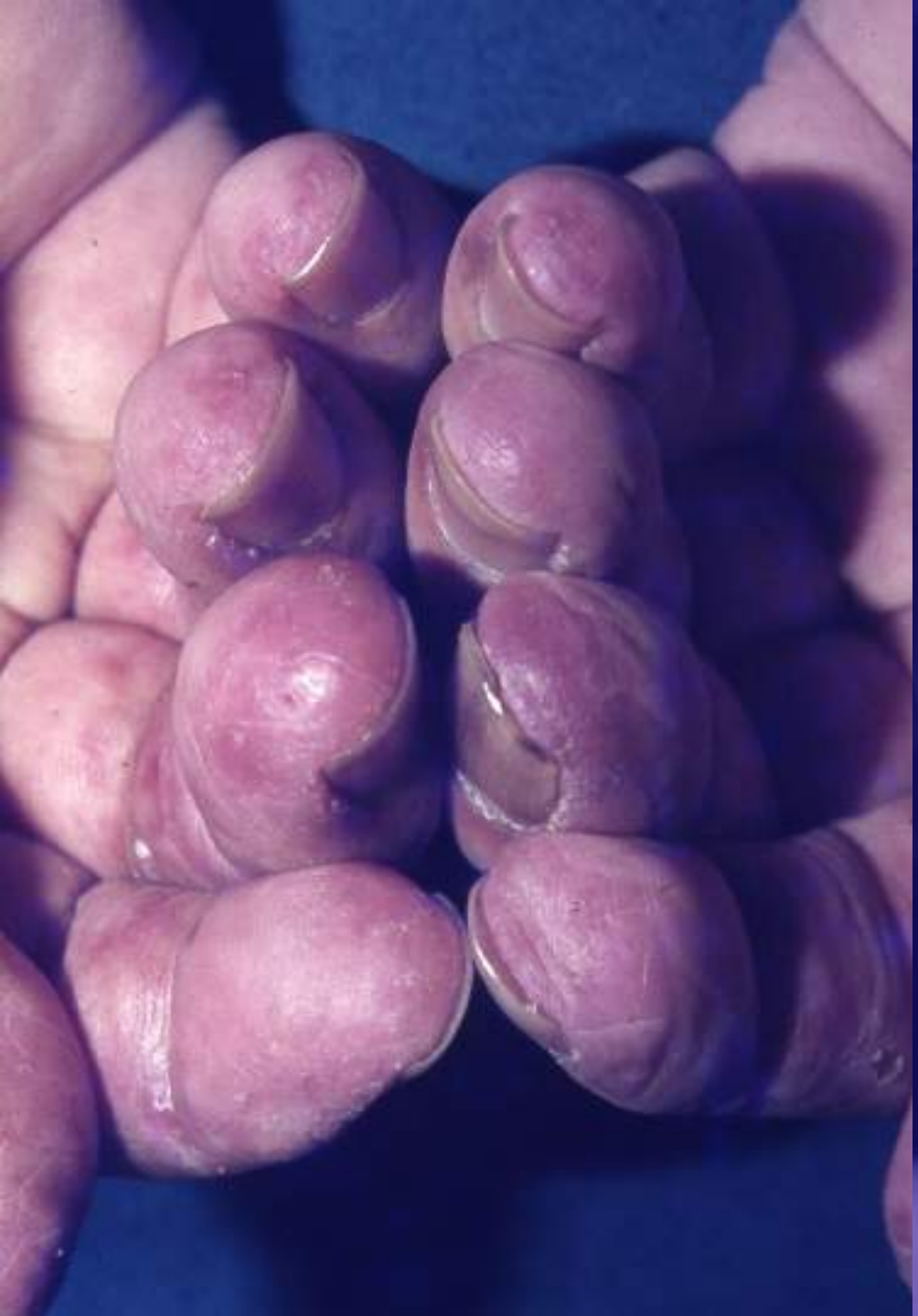
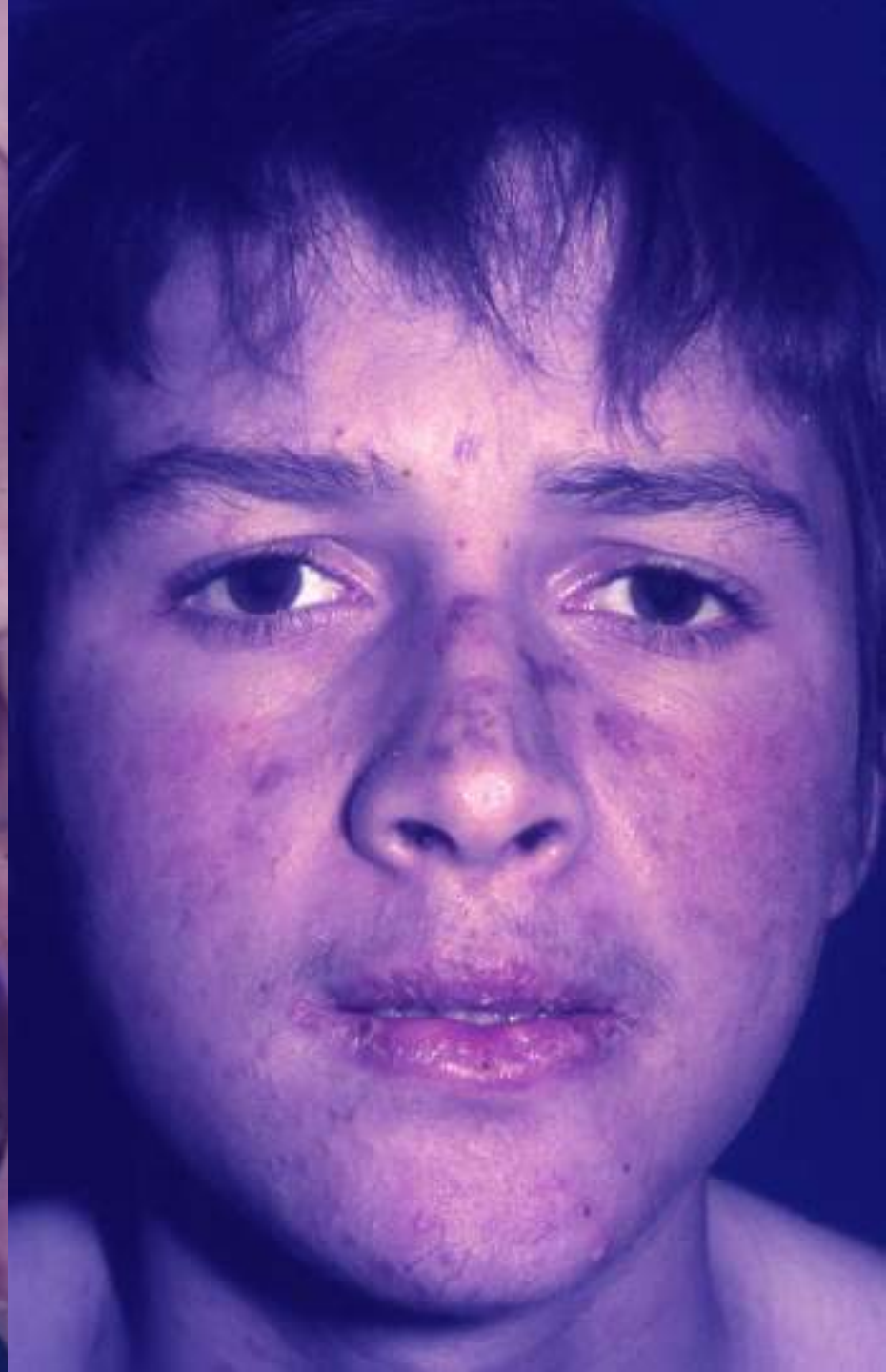
Hidroxicloroquina

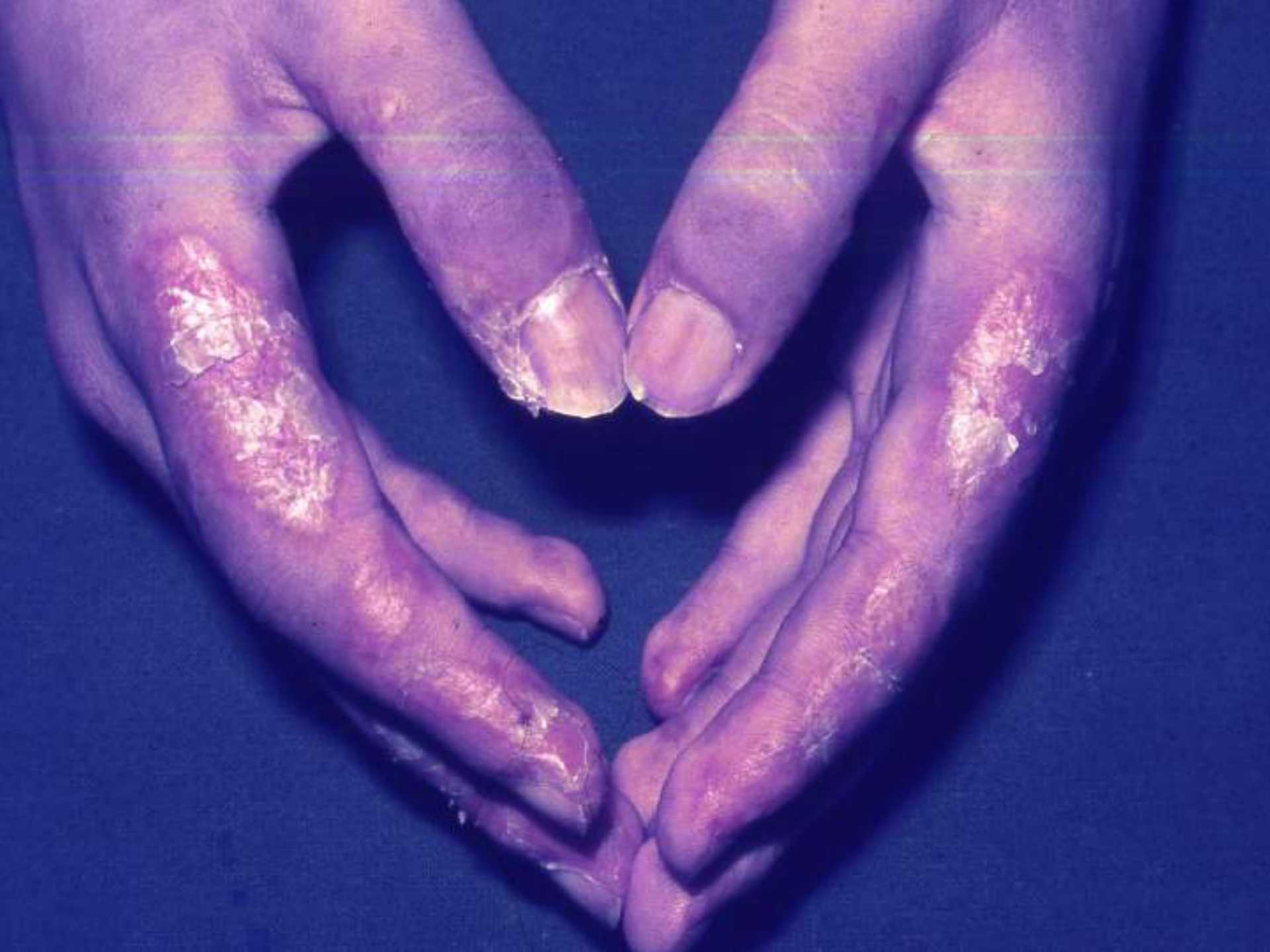
- Se absorbe mal en fumadores
- Tiene menos efectos adversos que la CQ
- Se combina con atabrine
- Se elimina después de dos meses
- Su suspensión en el embarazo favorece brote
- Pasa 2% a leche materna



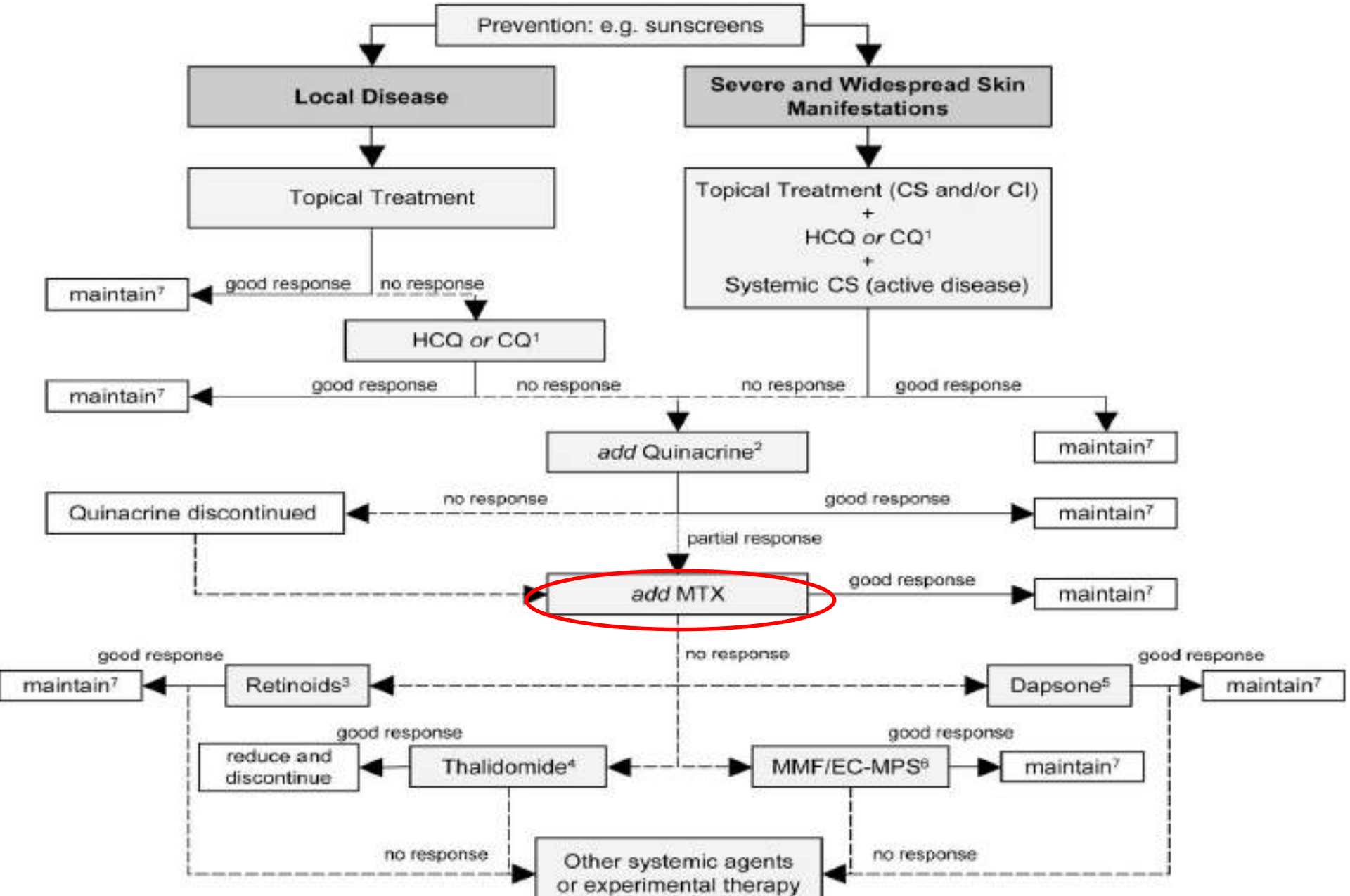






Cutaneous lupus erythematosus: Update of therapeutic options. Kuhn A et al. J Am Acad Dermatol 2011:65e; 179-193



Talidomida

- Actúa más rápido que los antimaláricos
- Dosis habitual 200mg/día (mantenimiento 25mg/día)
- 90% responde, 65% remite totalmente, 71% recidiva
- En el LES ahorra corticoides

Talidomida: efectos adversos

- Teratogenicidad
- Neuropatía periférica (hormigueos, disminución de la sensibilidad y calambres en manos y pies)
- Hipercoagulabilidad
- Somnolencia, constipación

Lenalidomida for the Treatment of Resistant Discoid Lupus Erithematosus

Shah A, Albrecht J,Bonilla –Martinez et al
Arch Dermatol 2009;145(3)303-306

- Es un análogo de la Talidomida.
- Se tratan dos pacientes con LED crónico refractarios
- Dosis de 5-10 mg día.
- Mejora uno de los dos casos (controlar neutropenia)
- Los cambios se deben medir según el índice de severidad actividad, de daño y de área de enfermedad .

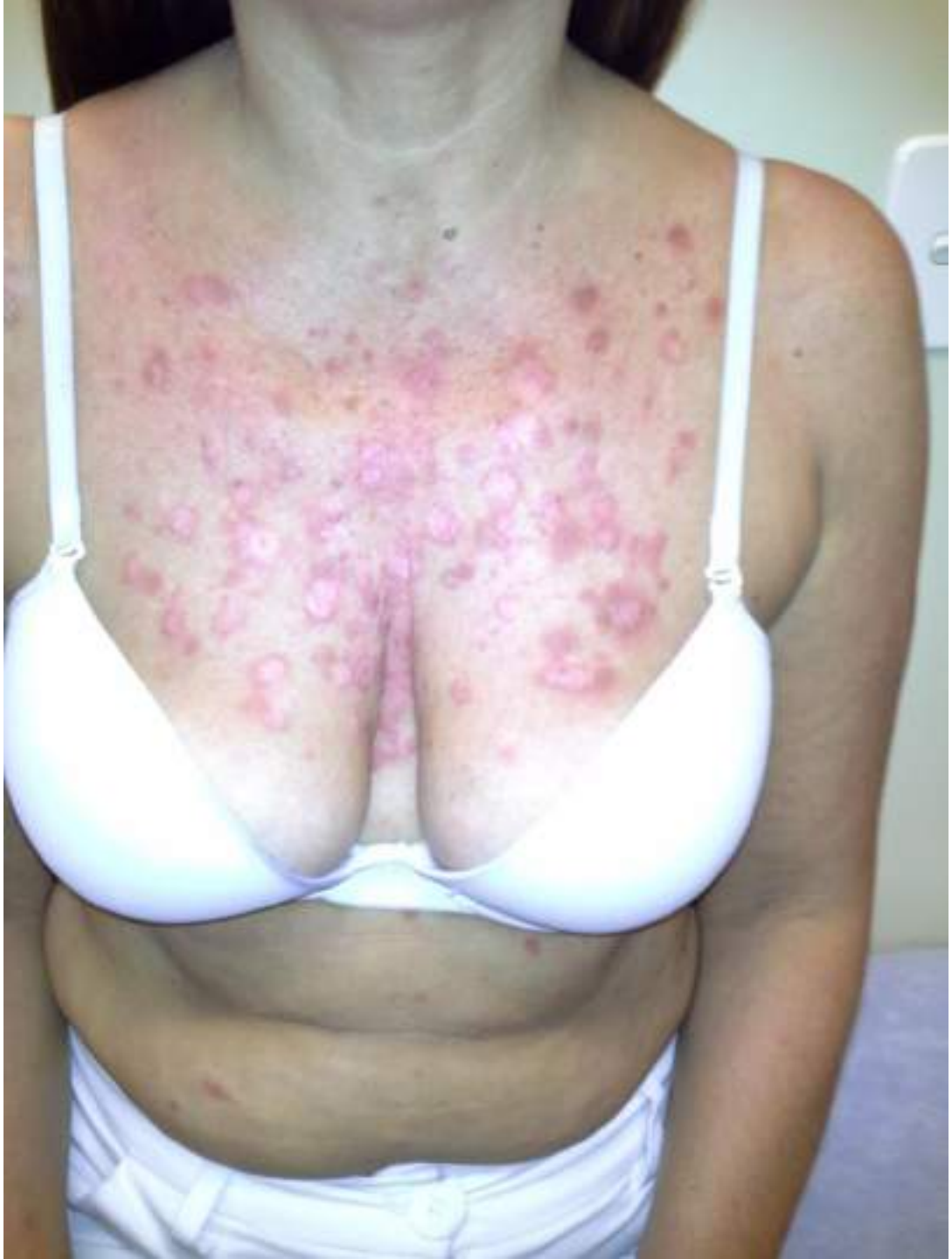
LECSA (Lupus eritematoso cutáneo subagudo)

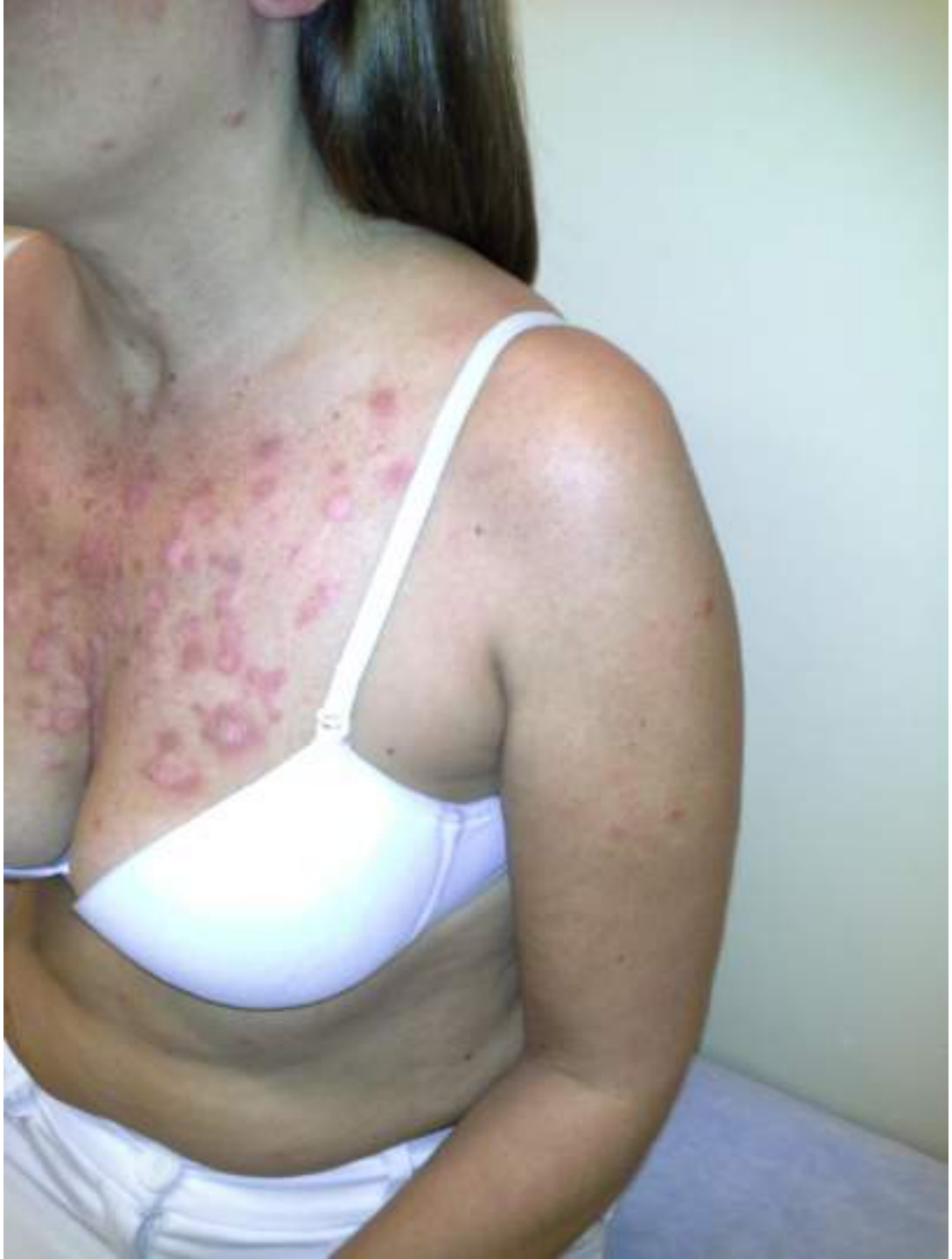
- ✓ Descripta por Guillian y Sontheimer en 1979, la forma inducida por drogas fue descripta por Reed en 1985.

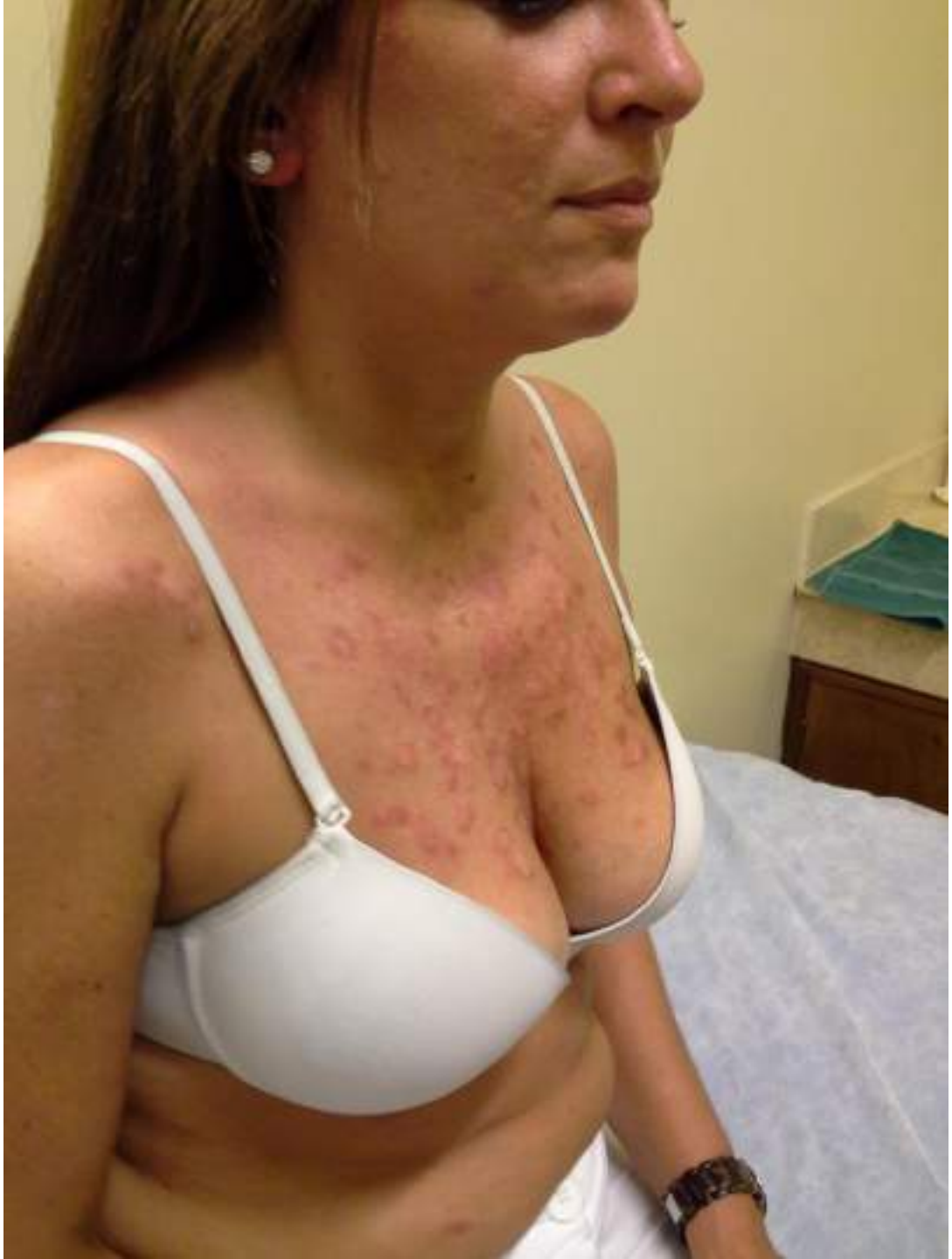
- ✓ Forma intermedia entre el LES y el LED

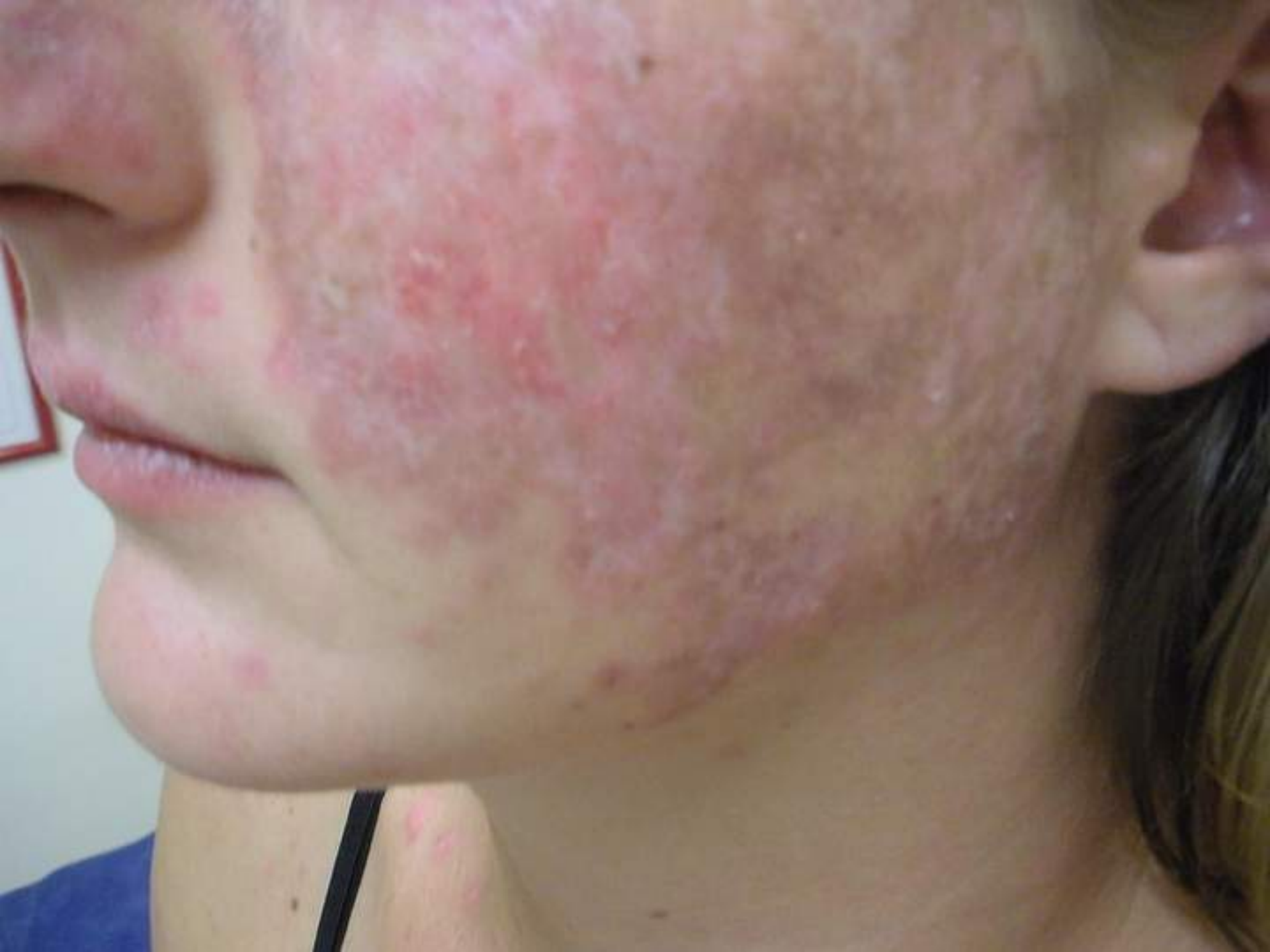
Lupus eritematoso cutáneo subagudo (LECSA)

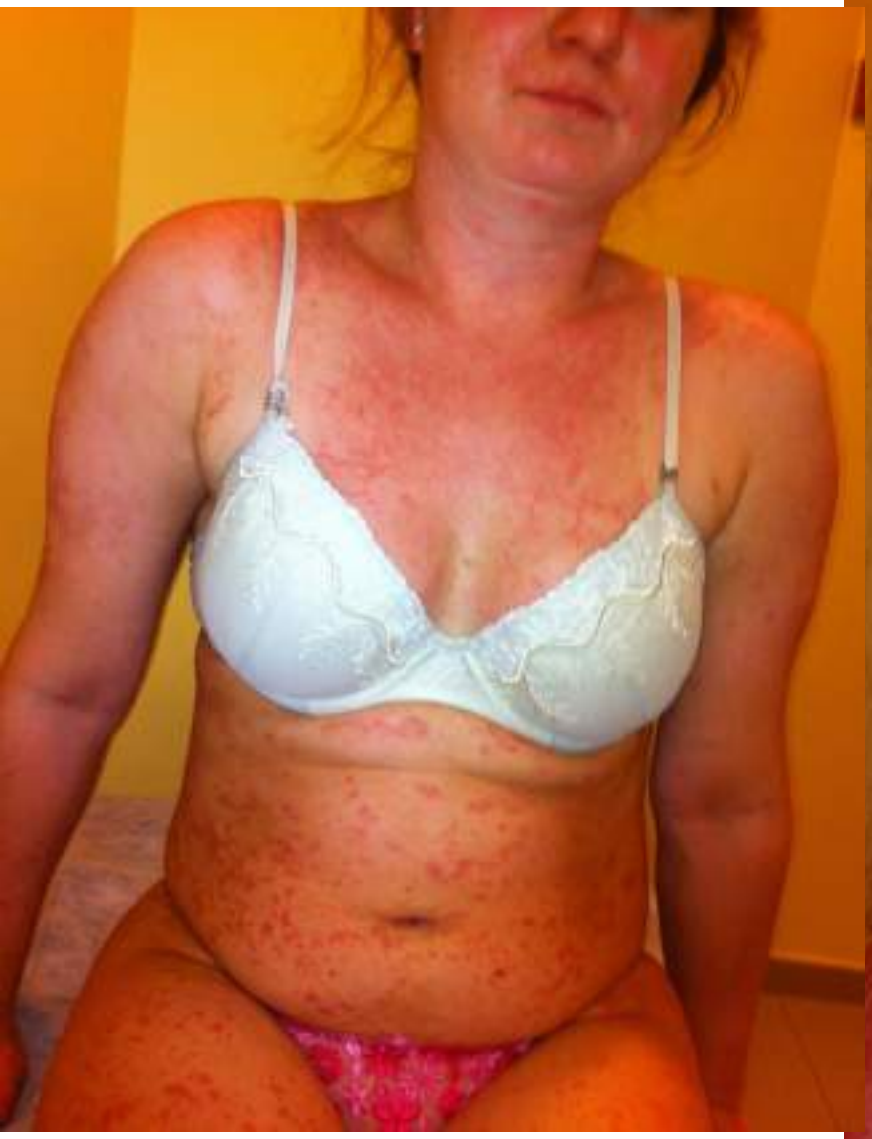
- ✓ Forma (subtipo) específica de lupus recurrente y superficial
- ✓ Lesiones generalizadas en la piel. Anulares y psoriasiformes, con exacerbaciones (primavera verano) y remisiones.
- ✓ **Sin induración ni cicatriz**, con hipopigmentación residual.
- ✓ Áreas expuestas al sol. **Fotosensibilidad.**
- ✓ Artralgias 50%, riñón y SNC 10-15%. Buen pronóstico.

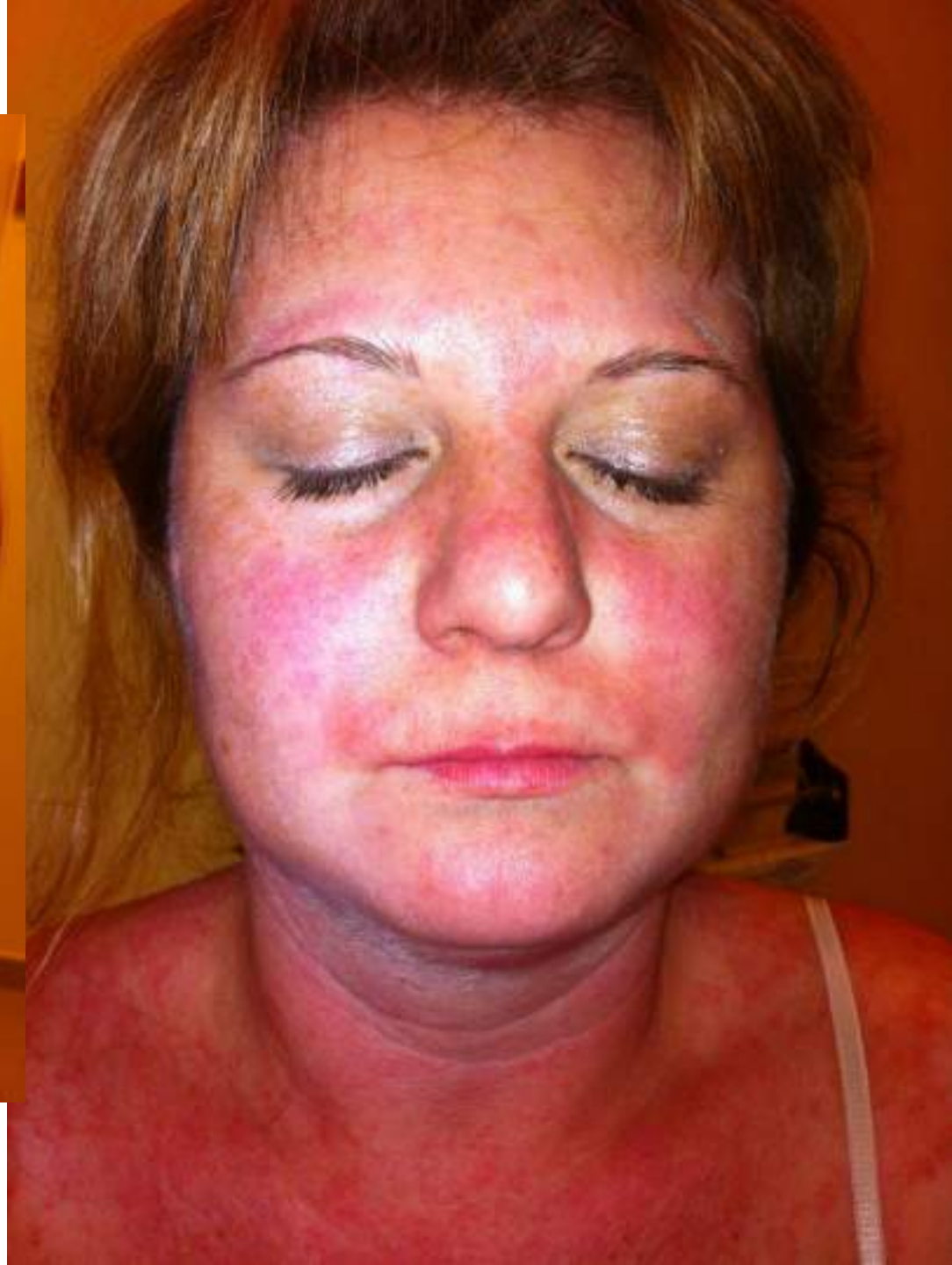


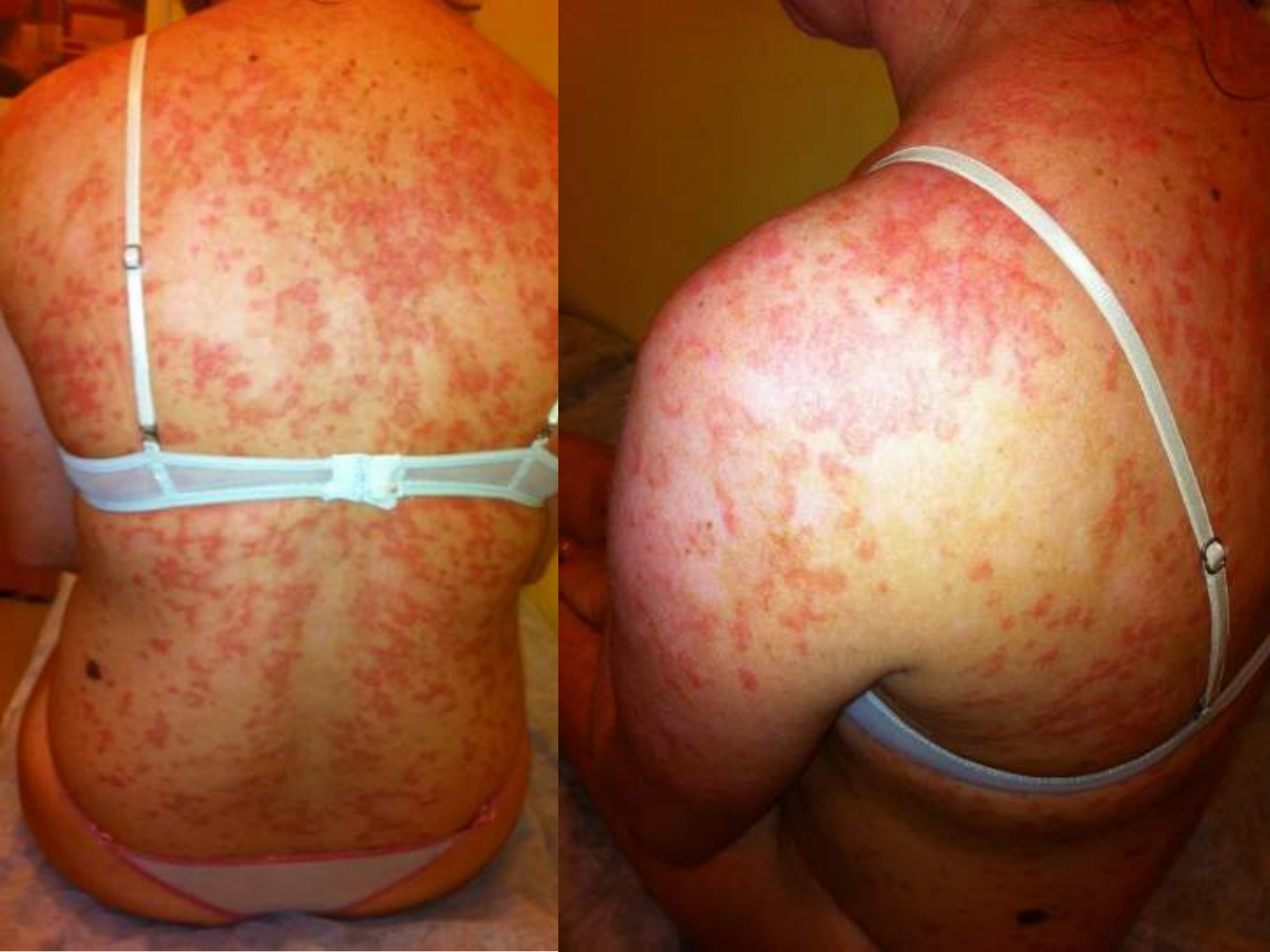


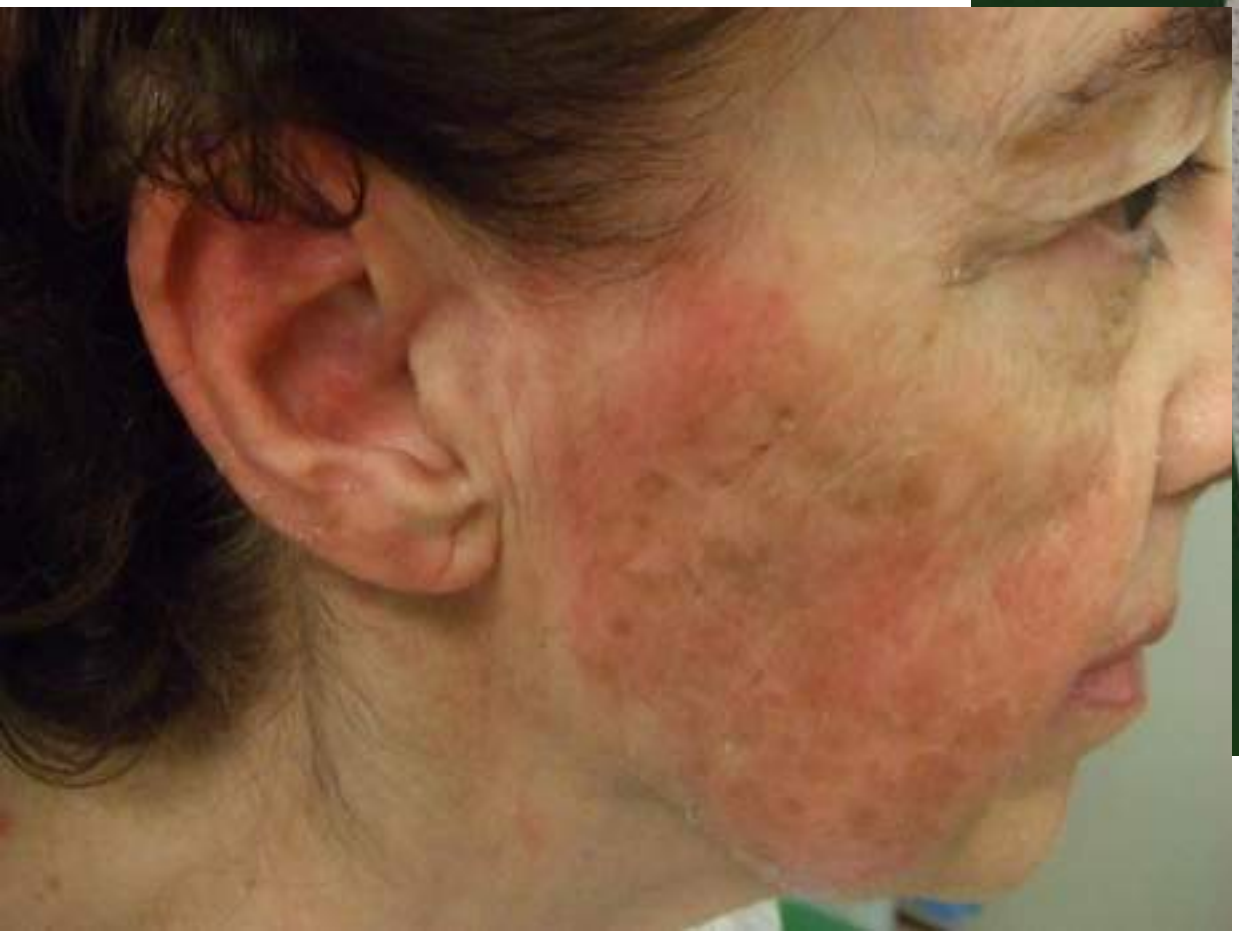


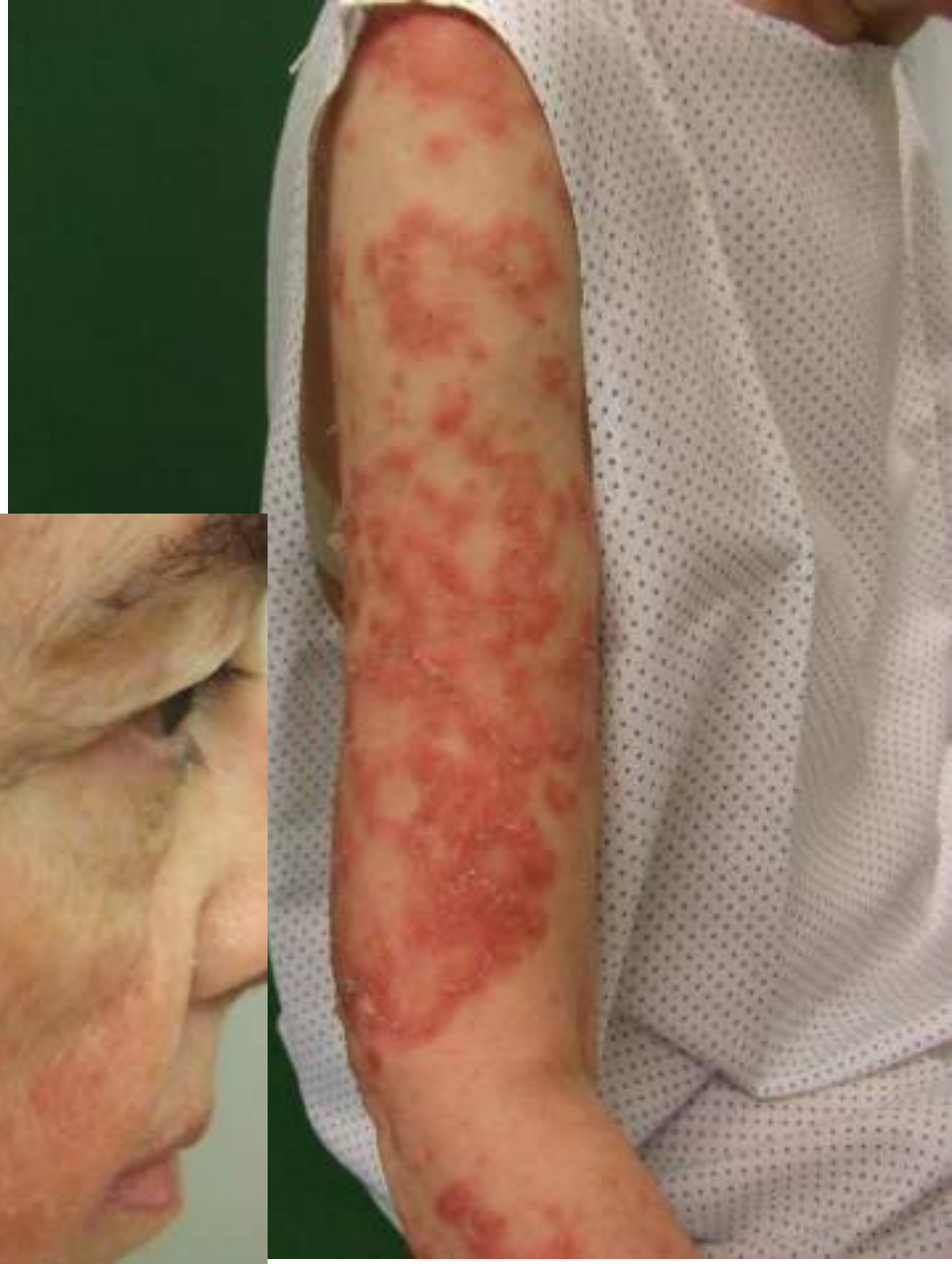


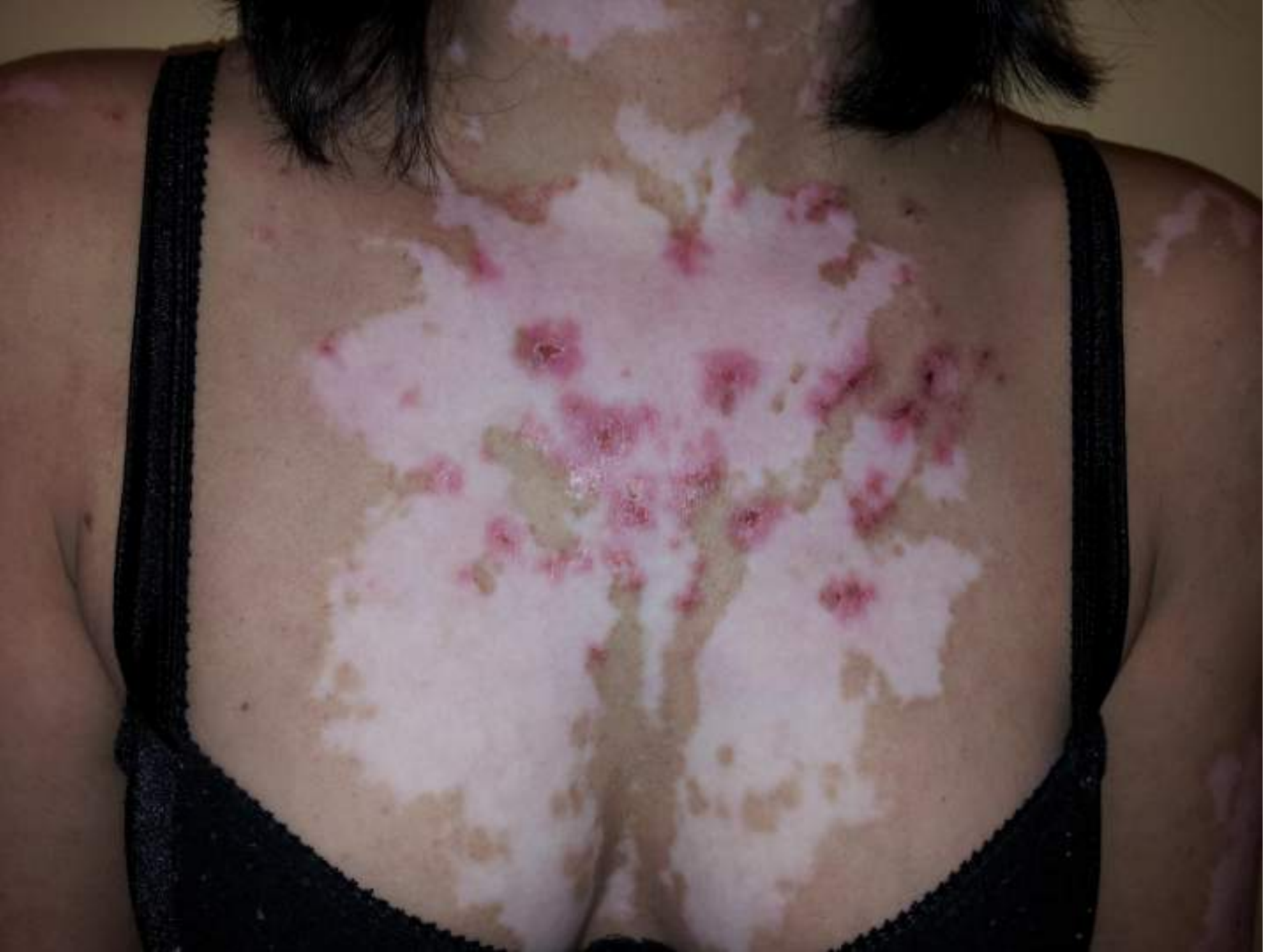


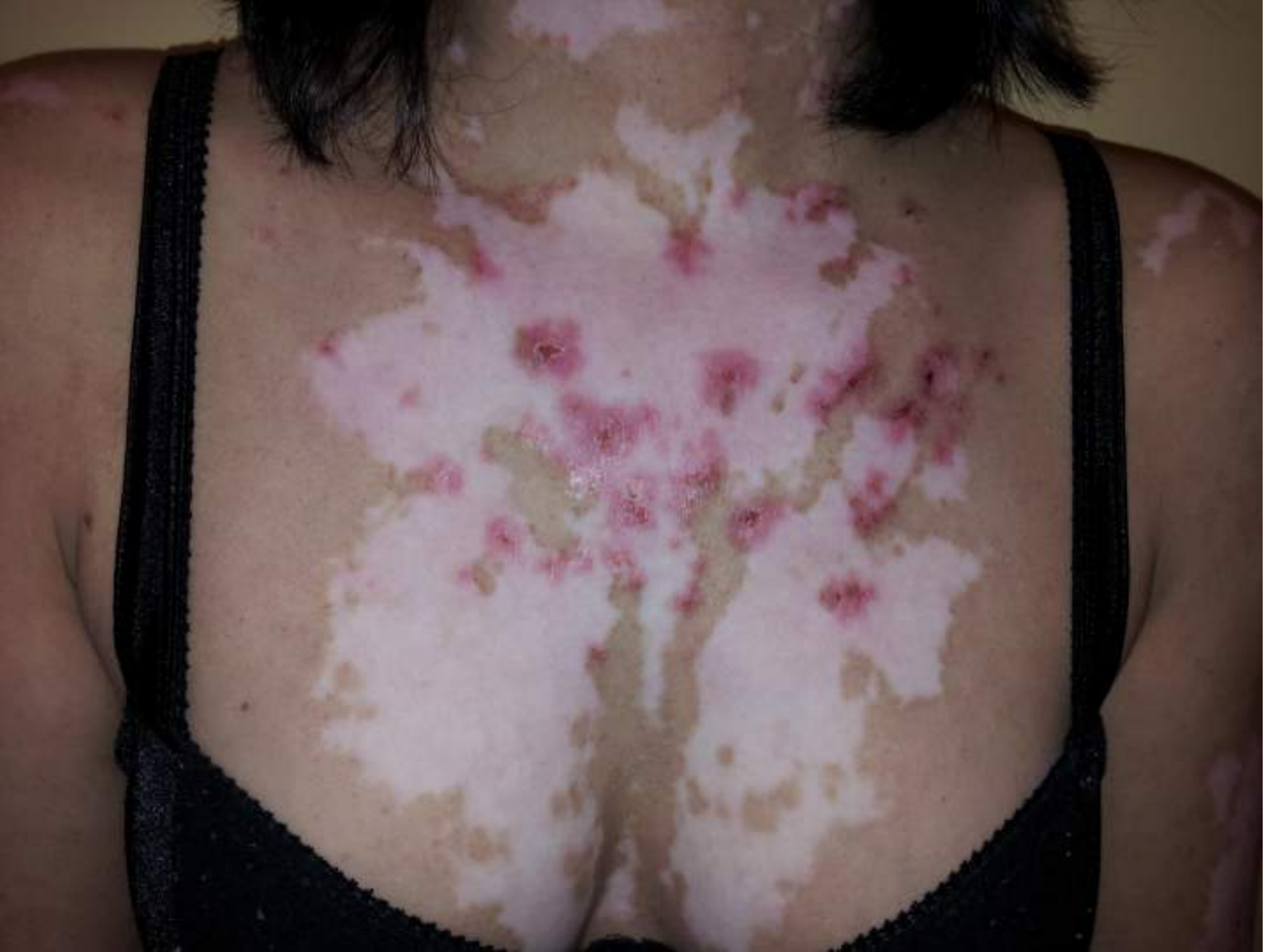


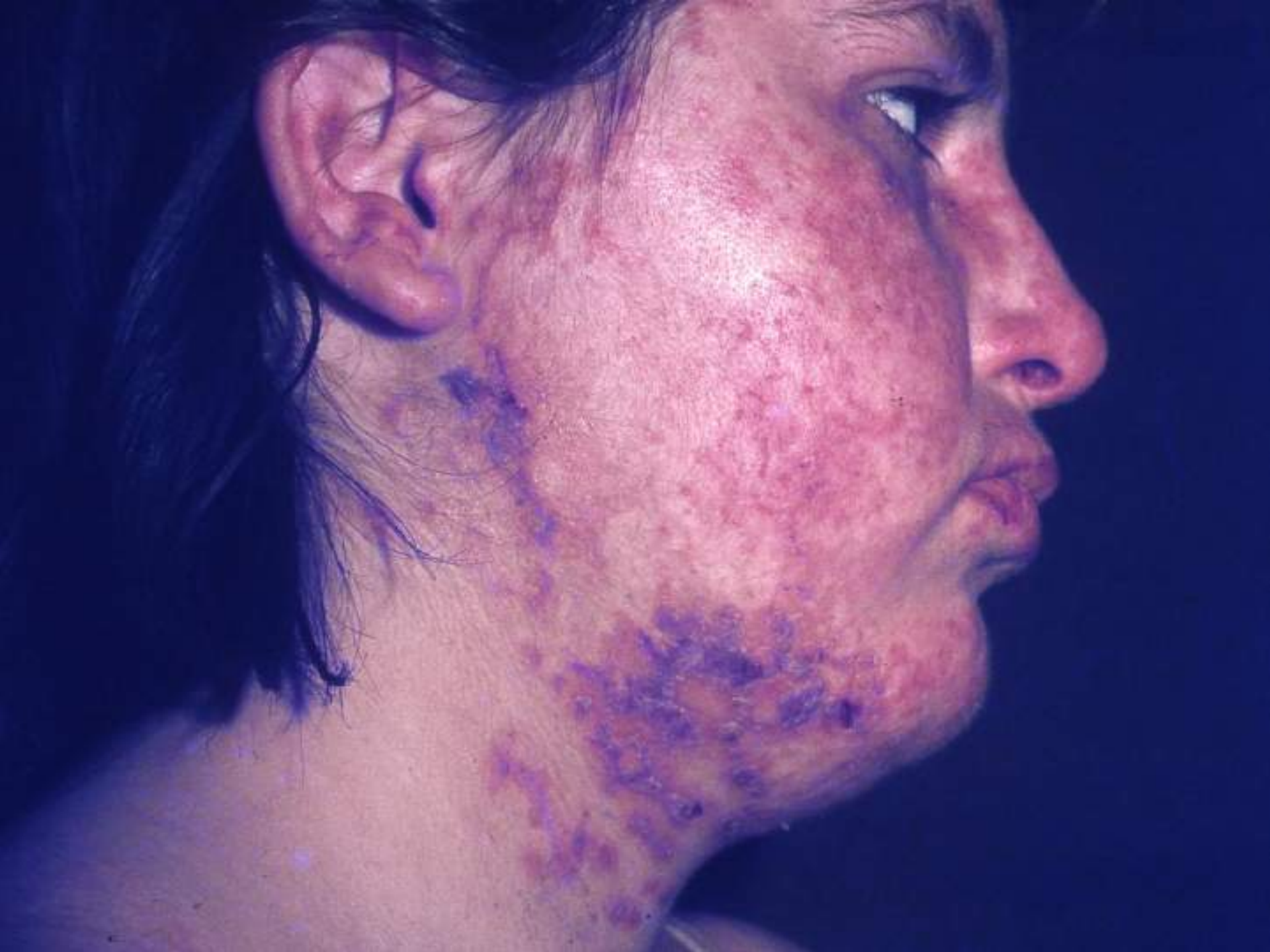


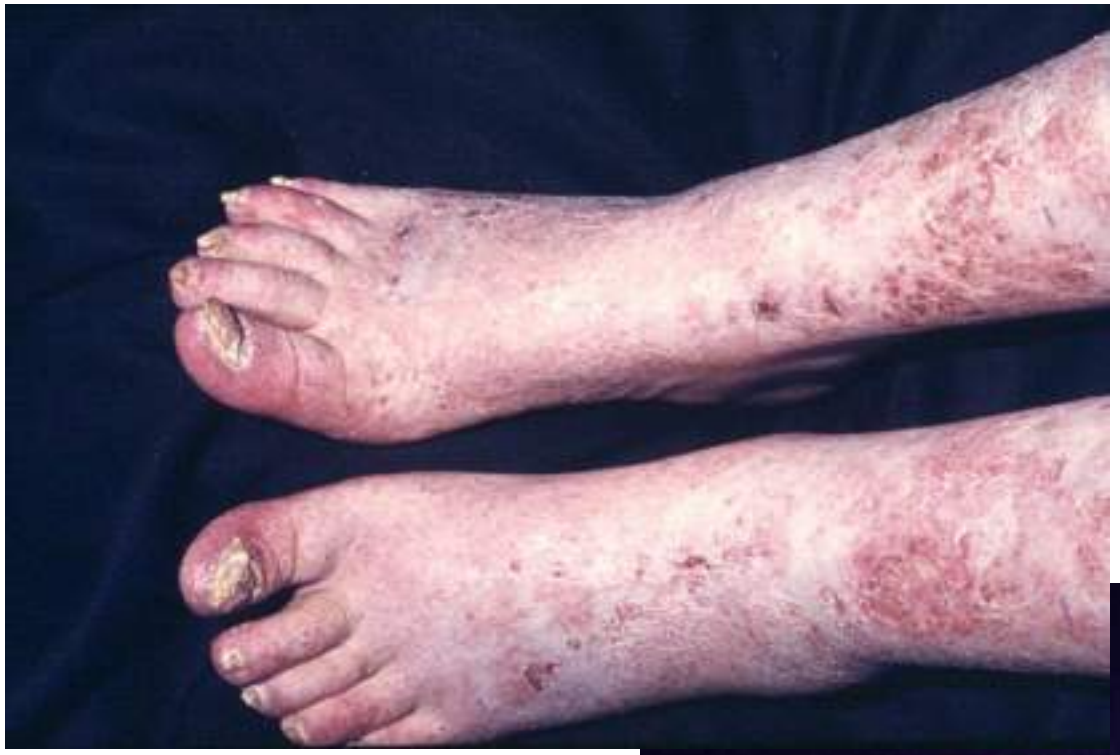


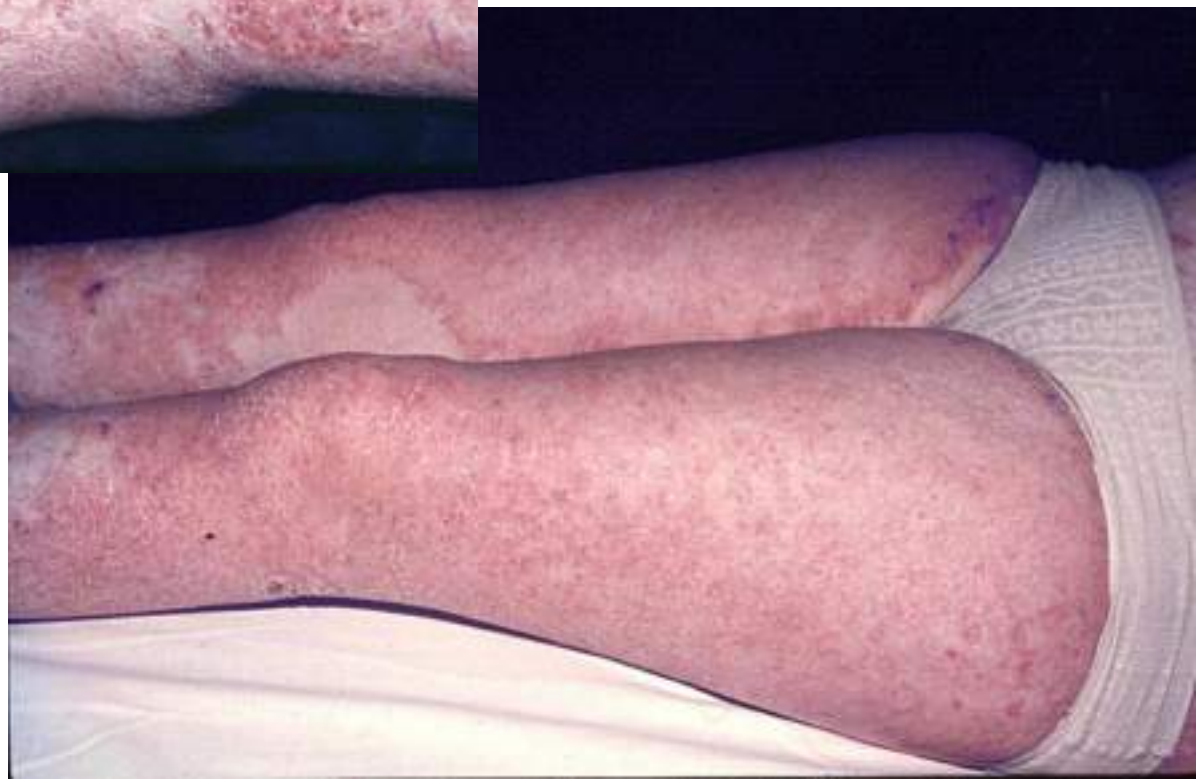


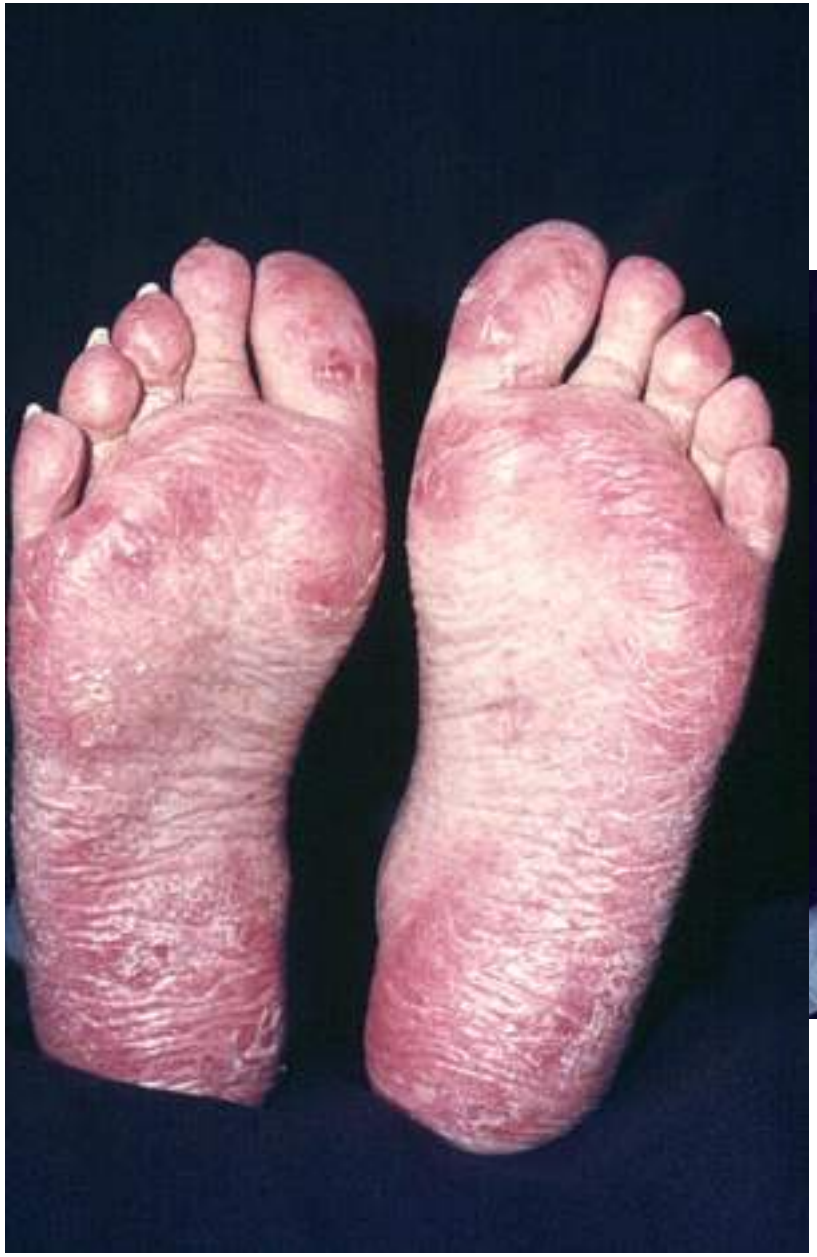


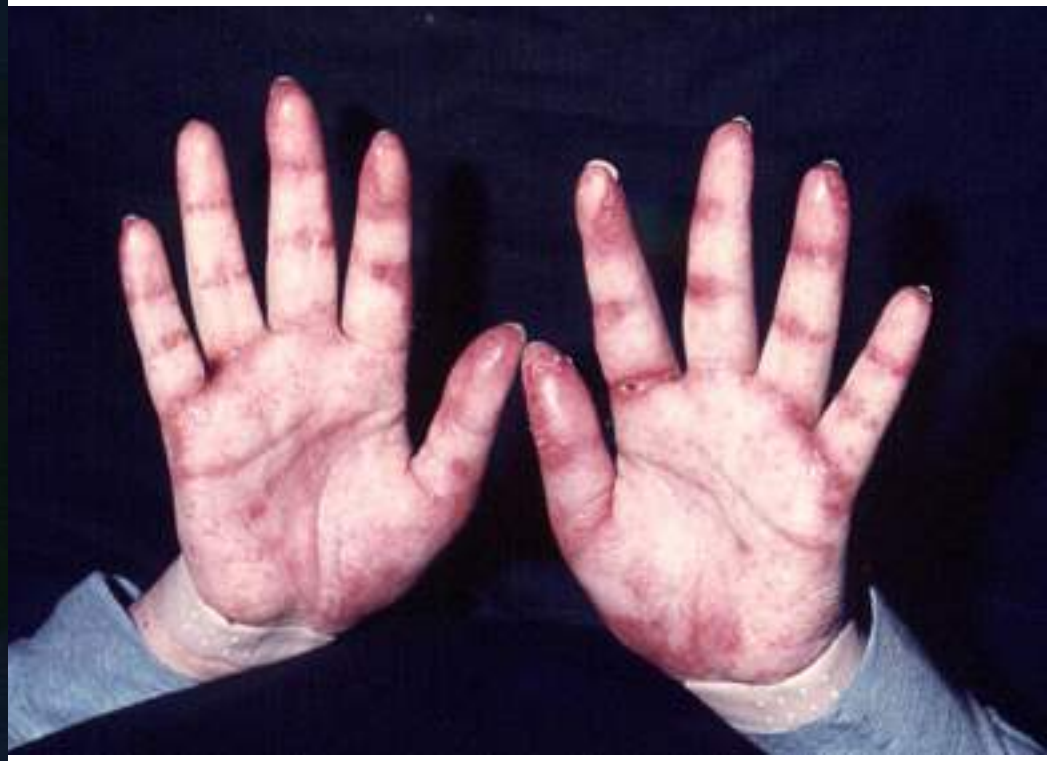


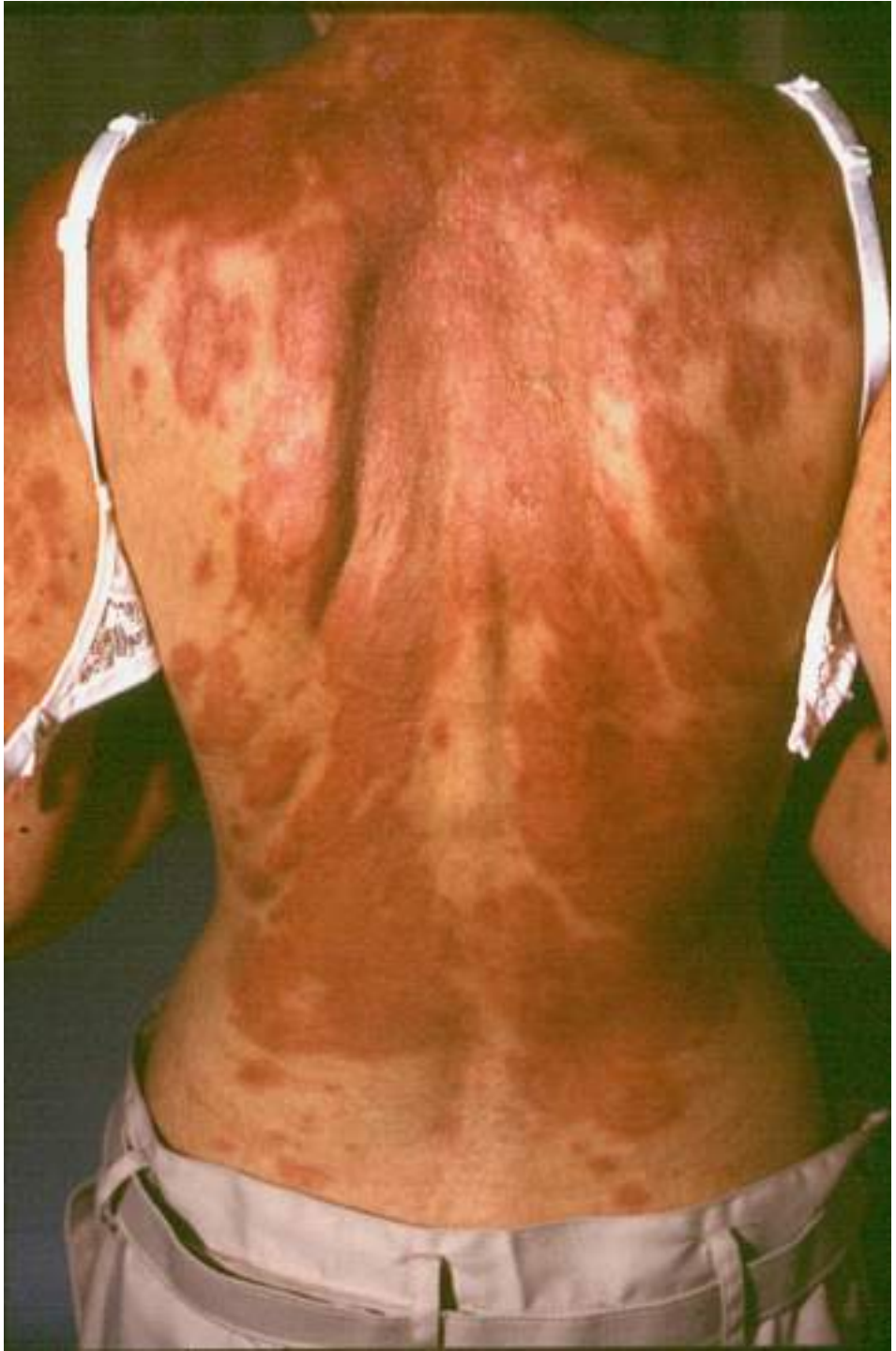


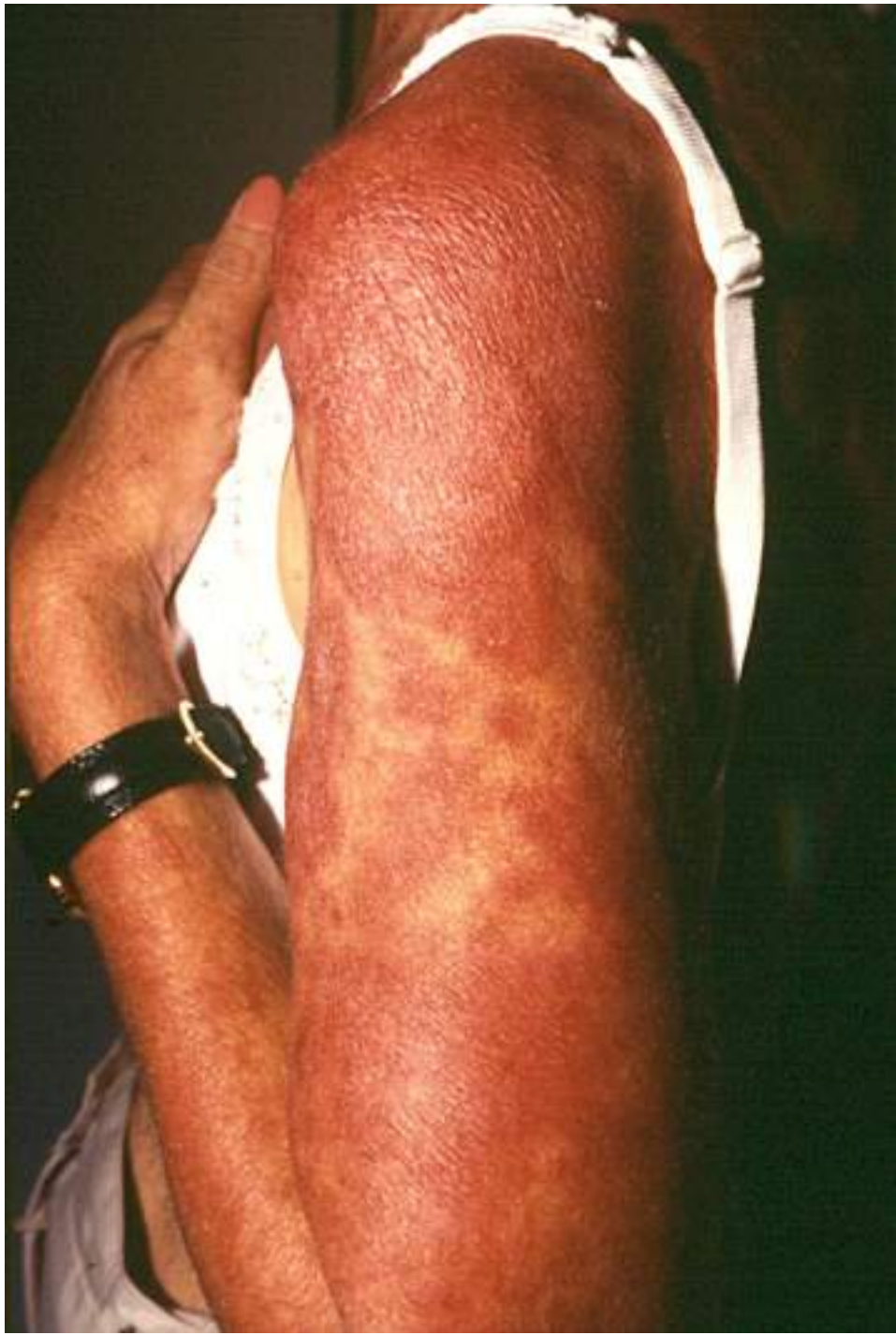


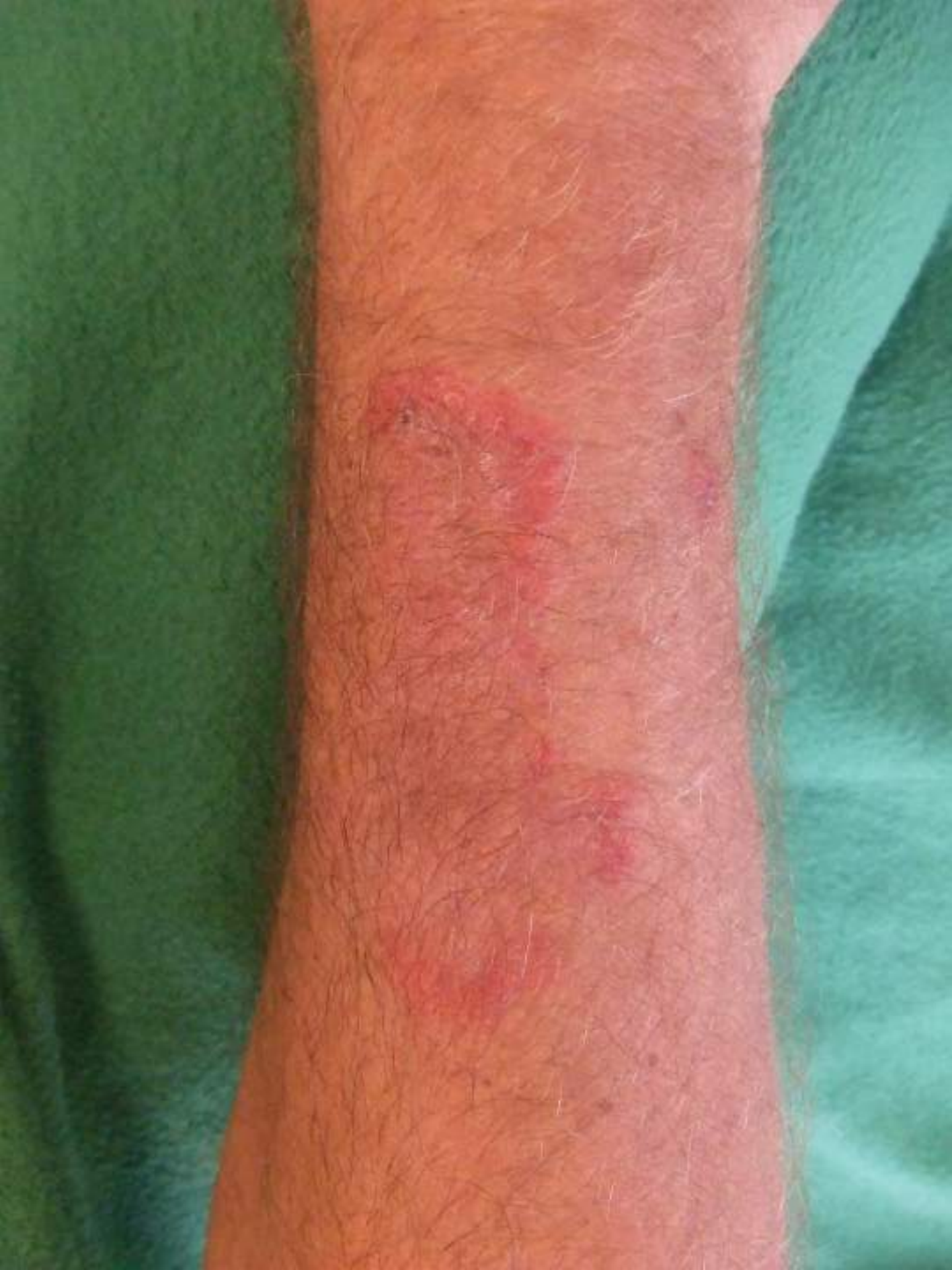




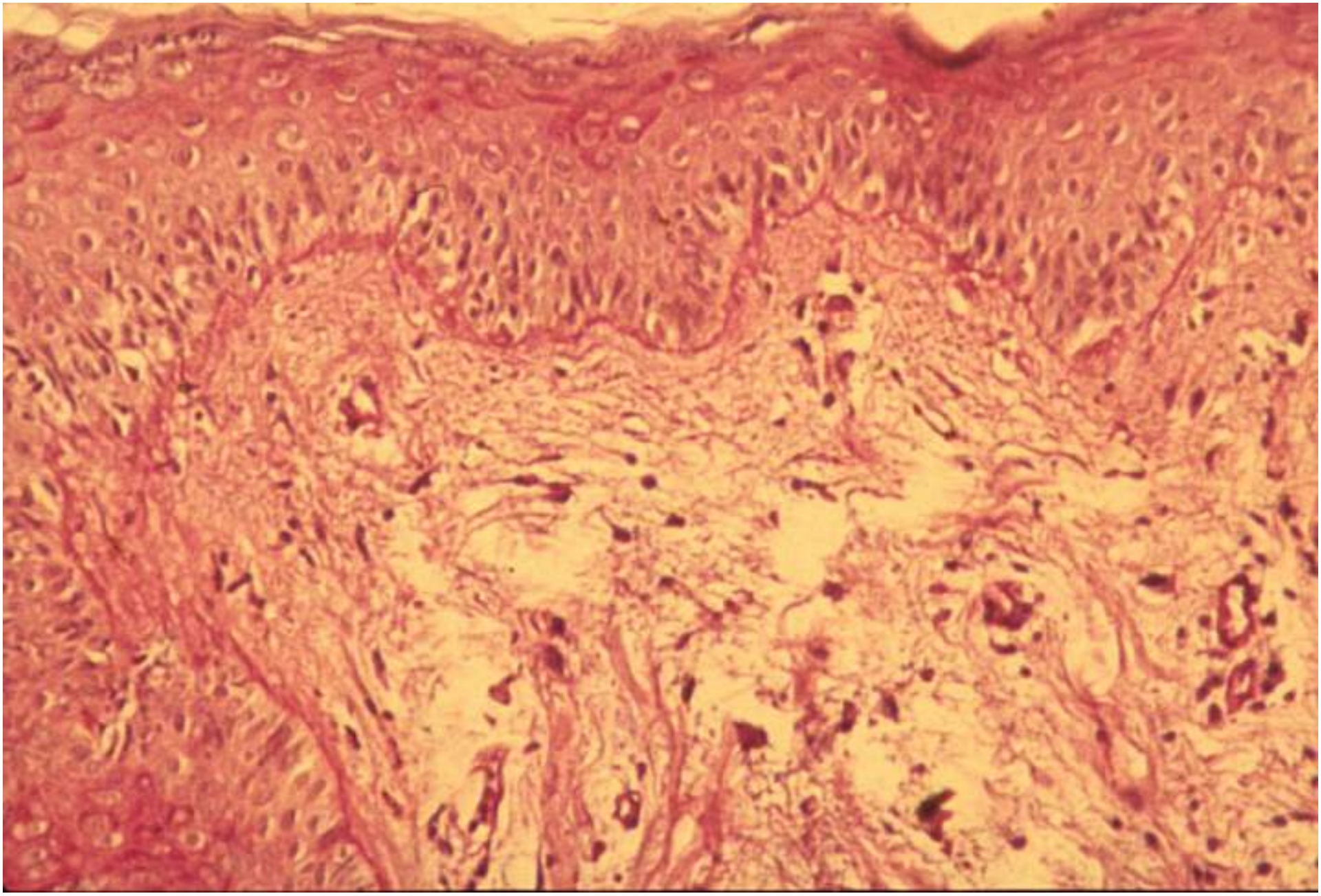


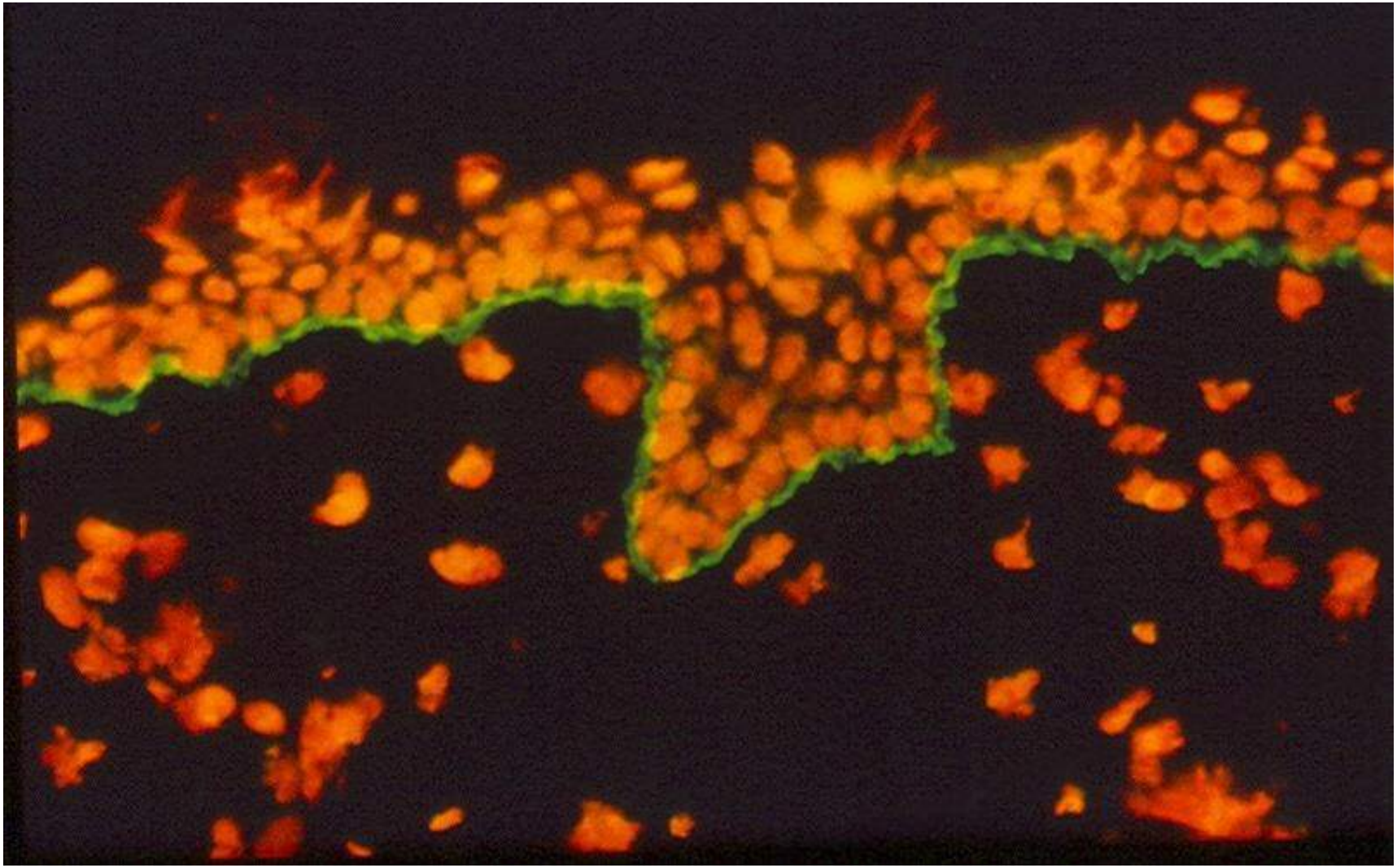






- ✓ Caracterizado inmunológicamente por ac antiRo (60 -100%)
- ✓ Presencia del ac anti La aproximadamente en la mitad de los casos anti Ro positivos.
- ✓ FAN + con Hep 2, moteado





- Asociaciones:

- ✓ Sdme de Sjögren
- ✓ Artritis reumatoidea
- ✓ LEN (1-2% con madres anti Ro positivas)
- ✓ Tiroiditis autoinmune.
- ✓ Angioedema hereditario
- ✓ ¿Paraneoplasia? *Clin Exp Dermatol* 2005; 30:655-658. Chaudry, Murphy White

- LECSA: tratamiento

- ✓ Fotoprotección
- ✓ Corticosteroides tópicos o intralesionales.
- ✓ Hidroxicloroquina 200 -400 mg día.
- ✓ Cloroquina 100- 200 mg día.
- ✓ Corticoides sistémicos (antiinflamatorio) 20 mg
- ✓ Talidomida, DAPS, Retinoides, IFN, inmunosupresores.

MEDICATIONS ASSOCIATED WITH DRUG-INDUCED SUBACUTE CUTANEOUS LUPUS ERYTHEMATOSUS

More common/higher risk*
- Terbinafine
- Thiazide diuretics (e.g. hydrochlorothiazide)
- TNF-α inhibitors
- Proton pump inhibitors (e.g. lansoprazole, pantoprazole, omeprazole)
- Calcium channel blockers (e.g. diltiazem, nifedipine, verapamil)
- Anti-epileptics (e.g. carbamazepine)
- Taxanes (e.g. docetaxel, paclitaxel)
- Thrombocyte inhibitors (e.g. ticlopidine)

Less common*
- ACE inhibitors (e.g. enalapril, lisinopril)
- β-blockers
- Doxorubicin
- Interferon-α and -β
- Leflunomide
- Ranitidine
- HMG-CoA reductase inhibitors ("statins")

*Medications are classified as being more common or having a higher risk if there were >10 cases reported in the literature as of 2016 or the relative risk in reference 49 was ≥2.0. Medications are classified as being less common if there have been 3–10 cases reported and the relative risk was <2.0.

Table 41.2 Medications associated with drug-induced subacute cutaneous lupus erythematosus (SCLE). ACE, angiotensin converting enzyme.

REVIEW ARTICLE

BJD
British Journal of Dermatology

A systematic review of drug-induced subacute cutaneous lupus erythematosus

G. Lowe, C.L. Henderson,* R.H. Grau,† C.B. Hansen and R.D. Sontheimer

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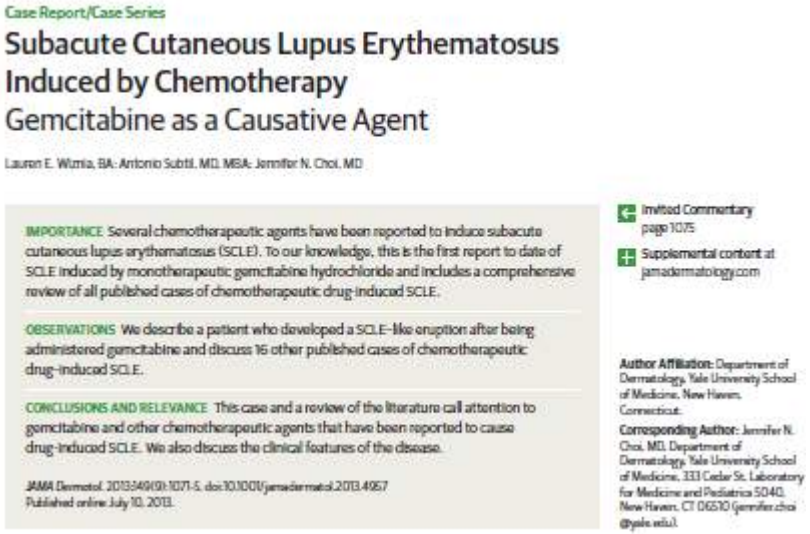
Invited Commentary

PRACTICE GAPS

Drug-Induced Subacute Cutaneous Lupus Erythematosus—Filling the Gap in Knowledge

Jeffrey P. Callen, MD



Case Report/Case Series

Subacute Cutaneous Lupus Erythematosus Induced by Chemotherapy
Gemcitabine as a Causative Agent

Lauren E. Wozniak, BA; Antonio Subtil, MD, MBA; Jennifer N. Choi, MD

IMPORTANCE Several chemotherapeutic agents have been reported to induce subacute cutaneous lupus erythematosus (SCLE). To our knowledge, this is the first report to date of SCLE induced by monotherapeutic gemcitabine hydrochloride and includes a comprehensive review of all published cases of chemotherapeutic drug-induced SCLE.

OBSERVATIONS We describe a patient who developed a SCLE-like eruption after being administered gemcitabine and discuss 16 other published cases of chemotherapeutic drug-induced SCLE.

CONCLUSIONS AND RELEVANCE This case and a review of the literature call attention to gemcitabine and other chemotherapeutic agents that have been reported to cause drug-induced SCLE. We also discuss the clinical features of the disease.

JAMA Dermatol. 2013;149(9):1071-5. doi:10.1001/jamadermatol.2013.4957
Published online July 10, 2013.

Invited Commentary
page 1075

Supplemental content at
jamadermatology.com

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Table 1 Drugs identified as causative of drug-induced subacute cutaneous lupus erythematosus (SCLE) in this report

Antihypertensives	40 of 117 reported cases: 34.2%
Calcium channel blockers	
Diltiazem[7,16]	6 cases
Verapamil[7,8]	5 cases
Nifedipine[7,16,18]	3 cases
Nitrendipine[3,5]	1 case
Diuretics	
Hydrochlorothiazide[7,16,23]	10 cases
Hydrochlorothiazide + triamterene[8]	3 cases
Chlorthiazide[5]	2 cases
Beta blockers	
Oxprenolol[22]	4 cases
Acebutolol[23]	1 case
Angiotensin-converting enzyme inhibitors	
Enalapril[26]	2 cases
Lisinopril[16]	1 case
Captopril[24]	1 case
Cilazapril[24]	1 case
Antifungals	30 of 117 reported cases: 25.6%
Terbinafine[11,14–16,20–42]	29 cases
Griseofulvin[13]	1 case
Chemotherapeutics	10 of 117 reported cases: 8.5%
Taxotere[16]	3 cases
Paclitaxel[16,38]	3 cases
Tamoxifen[39]	2 cases
Capecitabine[4,6,41]	2 cases
Antihistamines	9 of 117 reported cases: 7.7%
Terfenadine[42]	7 cases
Brompheniramine[43]	1 case
Cinnarizine + diethylpiperazine[44]	1 case
Immunomodulators	8 of 117 reported cases: 6.8%
Infliximab[7,17,31,44]	5 cases
Interferon α and β[3,6,45]	3 cases
Antiepileptics	3 of 117 reported cases: 2.6%
Carbamazepine[4,6,46]	2 cases
Phenytoin[46]	1 case
Statins	3 of 117 reported cases: 2.6%
Simvastatin[16,46]	2 cases
Pravastatin[46]	1 case
Biologics	2 of 117 reported cases: 1.7%
Rituximab[16]	1 case
Efalizumab[47]	1 case
Proton pump inhibitors	2 of 117 reported cases: 1.7%
Lansoprazole[42]	2 cases
Nonsteroidal anti-inflammatory drugs	2 of 117 reported cases: 1.7%
Naproxen[3,5]	1 case
Piroxicam[3,6]	1 case
Hormone-altering drugs	2 of 117 reported cases: 1.7%
Leuprorelin[48]	1 case
Anastrozole[48]	1 case
Ultraviolet therapy	2 of 117 reported cases: 1.7%
PUVA[34]	1 case
PUVA and UVB[49]	1 case
Others	4 of 117 reported cases: 3.4%
Bupropion[50]	1 case
Thiopronin[51]	1 case
Ticlopidine[52]	1 case
Hay with fertilizer[53]	1 case

The numbers in the table represent citations in references, and the drugs reported to be

1997 UPDATE OF THE 1982 AMERICAN COLLEGE OF RHEUMATOLOGY REVISED CRITERIA FOR CLASSIFICATION OF SYSTEMIC LUPUS ERYTHEMATOSUS*	
Criterion	**Definition**
1. Malar rash	Fixed erythema, flat or raised, over the malar eminences, tending to spare the nasolabial folds
2. Discoid rash	Erythematous raised patches with adherent keratotic scaling and follicular plugging; atrophic scarring may occur in older lesions
3. Photosensitivity	Skin rash as a result of unusual reaction to sunlight, by patient history or physician observation
4. Oral ulcers	Oral or nasopharyngeal ulceration, usually painless, observed by physician
5. Arthritis	Non-erosive arthritis involving two or more peripheral joints, characterized by tenderness, swelling or effusion
6. Serositis	a) **Pleuritis** – convincing history of pleuritic pain, rubbing heard by a physician, or evidence of pleural effusion *OR* b) **Pericarditis** – documented by ECG, rub or evidence of pericardial effusion
7. Renal disorder	a) Persistent **proteinuria** greater than 0.5 g/day or greater than 3+ if quantitation not performed *OR* b) **Cellular casts** – may be red cell, hemoglobin, granular, tubular or mixed
8. Neurologic disorder	a) **Seizures** – in the absence of offending drugs or known metabolic derangements, e.g. uremia, ketoacidosis or electrolyte imbalance *OR* b) **Psychosis** – in the absence of offending drugs or known metabolic derangements, e.g. uremia, ketoacidosis or electrolyte imbalance
9. Hematologic disorder	a) **Hemolytic anemia** with reticulocytosis *OR* b) **Leukopenia** – less than 4000/mm^3 total WBC on two or more occasions *OR* c) **Lymphopenia** – less than 1500/mm^3 on two or more occasions *OR* d) **Thrombocytopenia** – less than 100 000/mm^3 in the absence of offending drugs
10. Immunologic disorder	a) **Anti-DNA antibody** to **native DNA** in abnormal titer *OR* b) **Anti-Sm**: presence of antibody to Sm nuclear antigen *OR* c) Positive finding of **antiphospholipid antibodies** based on: (1) an abnormal serum level of IgG or IgM anti-cardiolipin antibodies; (2) a positive test result for lupus anticoagulant using standard methods; or (3) a false-positive serologic test for syphilis known to be positive for at least 6 months and confirmed by *Treponema pallidum* immobilization or fluorescent treponemal antibody absorption test (FTA-ABS)
11. Antinuclear antibody	An abnormal titer of antinuclear antibody by immunofluorescence (or an equivalent assay) at any point in time and in the absence of drugs known to be associated with "drug-induced lupus" syndrome

*The proposed classification is based on 11 criteria. For the purpose of identifying patients in clinical studies, a person shall be said to have systemic lupus erythematosus if any four or more of the 11 criteria are present, serially or simultaneously, during any interval of observation.

Table 41.4 1997 Update of the 1982 American College of Rheumatology revised criteria for classification of systemic lupus erythematosus[71,72]. ECG, electrocardiogram; Sm, Smith; WBC, white blood cell.

THE SYSTEMIC LUPUS INTERNATIONAL COLLABORATING CLINICS (SLICC) CLASSIFICATION SYSTEM – CLINICAL AND IMMUNOLOGIC CRITERIA

Clinical criteria

1. Acute cutaneous lupus, including:
   - Lupus malar rash (do not count if malar discoid)
   - Toxic epidermal necrolysis variant of SLE
   - Photosensitive lupus rash in the absence of dermatomyositis
   - Bullous lupus
   - Maculopapular lupus rash

OR

Subacute cutaneous lupus (non-indurated psoriasiform and/or annular polycyclic lesions that resolve without scarring, although occasionally with postinflammatory dyspigmentation or telangiectasias)

2. Chronic cutaneous lupus, including:
   - Classic discoid rash
     Localized (above the neck)
     Generalized (above and below the neck)
   - Hypertrophic (verrucous) lupus
   - Mucosal lupus
   - Lupus panniculitis (profundus)
   - Lupus erythematosus tumidus
   - Chilblain lupus
   - Discoid lupus erythematosus/lichen planus overlap

3. Oral ulcers*: palate, buccal, tongue *OR* nasal ulcers*

4. Nonscarring alopecia**

5. Synovitis involving 2 or more joints, characterized by swelling or effusion
OR tenderness in 2 or more joints and at least 30 minutes of morning stiffness

6. Serositis
   - Typical pleurisy for more than 1 day *OR* pleural effusions *OR* pleural rub
   - Typical pericardial pain (pain with recumbency improved by sitting forward) for more than 1 day *OR* pericardial effusion *OR* pericardial rub *OR* pericarditis by electrocardiography#

7. Renal
Urine protein-to-creatinine ratio (or 24-hour urine protein) representing 500 mg protein/24 hours *OR* red blood cell casts

8. Neurologic
   - Seizures
   - Psychosis
   - Mononeuritis multiplex##
   - Myelitis
   - Peripheral or cranial ne
   - Acute confusional stat

9. Hemolytic anemia

10. Leukopenia (<4000/mm^3 at least once)¶ *OR* lymphopenia (<1000/mm^3 at least once)¶¶

11. Thrombocytopenia (<100 000/mm^3 at least once)¶¶¶

Immunologic criteria

1. ANA level above laboratory reference range

Updating the American College of Rheumatology revised criteria for the classification of systemic lupus erythematosus. American College of Rheumatology website. <http://www.rheumatology.org/Portals/0/Files/1997%20Update%20of%201982%20Revised.pdf>.
Petri M, Orbai AM, Alarcón GS, et al. Derivation and validation of the Systemic Lupus International Collaborating Clinics classification criteria for systemic lupus erythematosus. Arthritis Rheum 2012;64:2677–86.

11. Thrombocytopenia (<100 000/mm^3 at least once)¶¶¶
Immunologic criteria
1. ANA level above laboratory reference range
2. Anti-dsDNA antibody level above laboratory reference range (or >2-fold the reference range if tested by ELISA)
3. Anti-Sm: presence of antibody to Sm nuclear antigen
4. Antiphospholipid antibody positivity as determined by any of the following: • Positive test result for lupus anticoagulant • False-positive test result for rapid plasma reagin • Medium- or high-titer anti-cardiolipin antibody level (IgA, IgG, or IgM) • Positive test result for anti-β2-glycoprotein I (IgA, IgG, or IgM)
5. Low complement: low C3, low C4, low CH50
6. Direct Coombs test in the absence of hemolytic anemia
*In the absence of other causes, such as vasculitis, Behçet disease, infection (herpesvirus), inflammatory bowel disease, reactive arthritis, and acidic foods. **Diffuse thinning or hair fragility with visible broken hairs in the absence of other causes such as alopecia areata, drugs, iron deficiency, and androgenic alopecia. #In the absence of other causes, such as infection, uremia, and Dressler pericarditis. ##In the absence of other known causes such as primary vasculitis. §In the absence of other known causes such as primary vasculitis, infection, and diabetes mellitus. §§In the absence of other causes, including toxic/metabolic, uremia, drugs. ¶In the absence of other known causes, such as Felty syndrome, drugs, and portal hypertension. ¶¶In the absence of other known causes, such as corticosteroids, drugs, and infection. ¶¶¶In the absence of other known causes, such as drugs, portal hypertension, and thrombotic thrombocytopenic purpura.

Table 41.5. The Systemic Lupus International Collaborating Clinics (SLICC) classification system – clinical and immunologic criteria[73]. Criteria are cumulative and need not be present concurrently. anti-dsDNA, anti-double-stranded DNA; ANA, antinuclear antibody; ELISA, enzyme-linked immunosorbent assay; SLE, systemic lupus erythematosus.

Updating the American College of Rheumatology revised criteria for the classification of systemic lupus erythematosus. American College of Rheumatology website. <http://www.rheumatology.org/Portals/0/Files/1997%20Update%20of%201982%20Revised.pdf>.

Petri M, Orbai AM, Alarcón GS, et al. Derivation and validation of the Systemic Lupus International Collaborating Clinics classification criteria for systemic lupus erythematosus. Arthritis Rheum 2012;64:2677–86.

Review

Novel paradigms in systemic lupus erythematosus

Thomas Dörner, Richard Furie

Lancet 2019; 393: 2344–58

Department of Medicine and Department of Rheumatology and Clinical Immunology, Charité Universitätsmedizin Berlin, Berlin, Germany (Prof T Dörner MD); German Rheumatism Research Center (DRFZ), Berlin, Germany (Prof T Dörner); and Division of Rheumatology Northwell Health and Zucker School of Medicine at Hofstra/Northwell, Great Neck, NY, USA

The heterogeneity of systemic lupus erythematosus (SLE), long recognised by clinicians, is now challenging the entire lupus community, from geneticists to clinical investigators. Although the outlook for patients with SLE has greatly improved, many unmet needs remain, chief of which is the development of safer and more efficacious therapies. To develop innovative therapies, a far better understanding of SLE pathogenesis as it relates to the array of clinical phenotypes is needed. Additionally, to efficiently achieve these goals, the lupus community needs to refine existing clinical research tools and better adapt them to overcome the obstacles created by the heterogeneity of manifestations. Here, we review progress towards the ultimate goal of safely reducing disease activity and preventing damage accrual and death. We discuss the new classification criteria from the European League Against Rheumatism and American College of Rheumatology, novel definitions of remission and low lupus disease activity, and new proposals for the histological classification of lupus nephritis. Recommendations for the treatment of SLE and novel approaches to drug development hold much promise to further enhance SLE outcomes.

Entry criterion			
Anti-nuclear antibodies at a titre of ≥1:80* on HEp-2 cells or an equivalent positive test			
Additive criteria Do not count a criterion if an explanation other than systemic lupus erythematosus is more likely Occurrence of a criterion on at least one occasion is sufficient At least one clinical criterion is required Criteria need not occur simultaneously Within each domain, only the highest weighted criterion is counted toward the total score			
Clinical domains and criteria	**Weight**	**Immunological domains and criteria**	**Weight**
Constitutional Fever	2	**Anti-phospholipid antibodies** Anti-cardiolipin antibodies or anti-β2GP1 antibodies or lupus anticoagulant	2
Cutaneous Non-scarring alopecia Oral ulcers Subacute cutaneous or discoid lupus Acute cutaneous lupus	 2 2 4 6	**Complement proteins** Low C3 or low C4 Low C3 and low C4	 3 4
Arthritis Either synovitis characterised by swelling or effusion in ≥two joints or tenderness in ≥two joints plus ≥30 min of morning stiffness	6	**Highly specific antibodies** Anti-dsDNA antibody† Anti-Smith antibody	 6 6
Neurological Delirium Psychosis Seizure	 2 3 5		
Serositis Pleural or pericardial effusion Acute pericarditis	 5 6		
Haematological Leucopenia Thrombocytopenia Autoimmune haemolysis	 3 4 4		
Renal Proteinuria >0·5 g/24 h Renal biopsy class II or V lupus nephritis Renal biopsy class III or IV lupus nephritis	 4 8 10		
Classify as systemic lupus erythematosus with a score of 10 or more if entry criterion fulfilled			

Figure 1: 2019 European League Against Rheumatism and American College of Rheumatology classification criteria for systemic lupus erythematosus

dsDNA=double-stranded DNA. HEp-2=human epithelial type 2. *Anti-nuclear antibody positivity should take the individual cutoff into account; the titre 1:80 has been derived from a broad literature review.[9] †In an assay with

- En los criterios clasificatorios, las lesiones cutáneas alcanzan una alta valuación. Solo estando por debajo de la nefritis lupica y el lab.
- Los criterios de clasificación, excluye a los simuladores lúpicos, reconoce casos tempranos.
- Los criterios de clasificación define cohortes, con gran especificidad para estudios clínicos.
- Distinto a criterios diagnósticos, más subjetivos y menos específicos.
- Solo comité de expertos

- Estos criterios clasificatorios alcanzan una sensibilidad del 96.4% y una especificidad del 93.4%
- Los del SLICC (Systemic Lupus International Collaborating Clinics) tiene 96.7% de sensibilidad y 83.7% de especificidad.
- ACR (American College of Rheumatology) 82,8% de sensibilidad y 93.4 de especificidad.
- La llave de ingreso a este sistema es el FAN (+ del 99,5% de la cohorte

- El tratamiento debe evitar el daño de la enfermedad y la iatrogenia o efectos colaterales de los remedios en cuestión por eso se introducen los conceptos de ESTADO DE BAJA INTENSIDAD DE LA ENFERMEDAD LÚPICA Y DEFINICIÓN DE REMISIÓN
- El belimumab y los antipalúdicos serían los únicos que presentan una actividad preventiva
- La dosis de HCQ aconsejada por los oftalmólogos es 5mg/kg (ver concentración en sangre)

Adjunctive or supportive therapy

UV protection, management of comorbidities: cardiovascular (blood pressure, hyperlipidaemia, smoking cessation), infectious (immunisations), and osteoporosis (vitamin D supplementation) risk factors

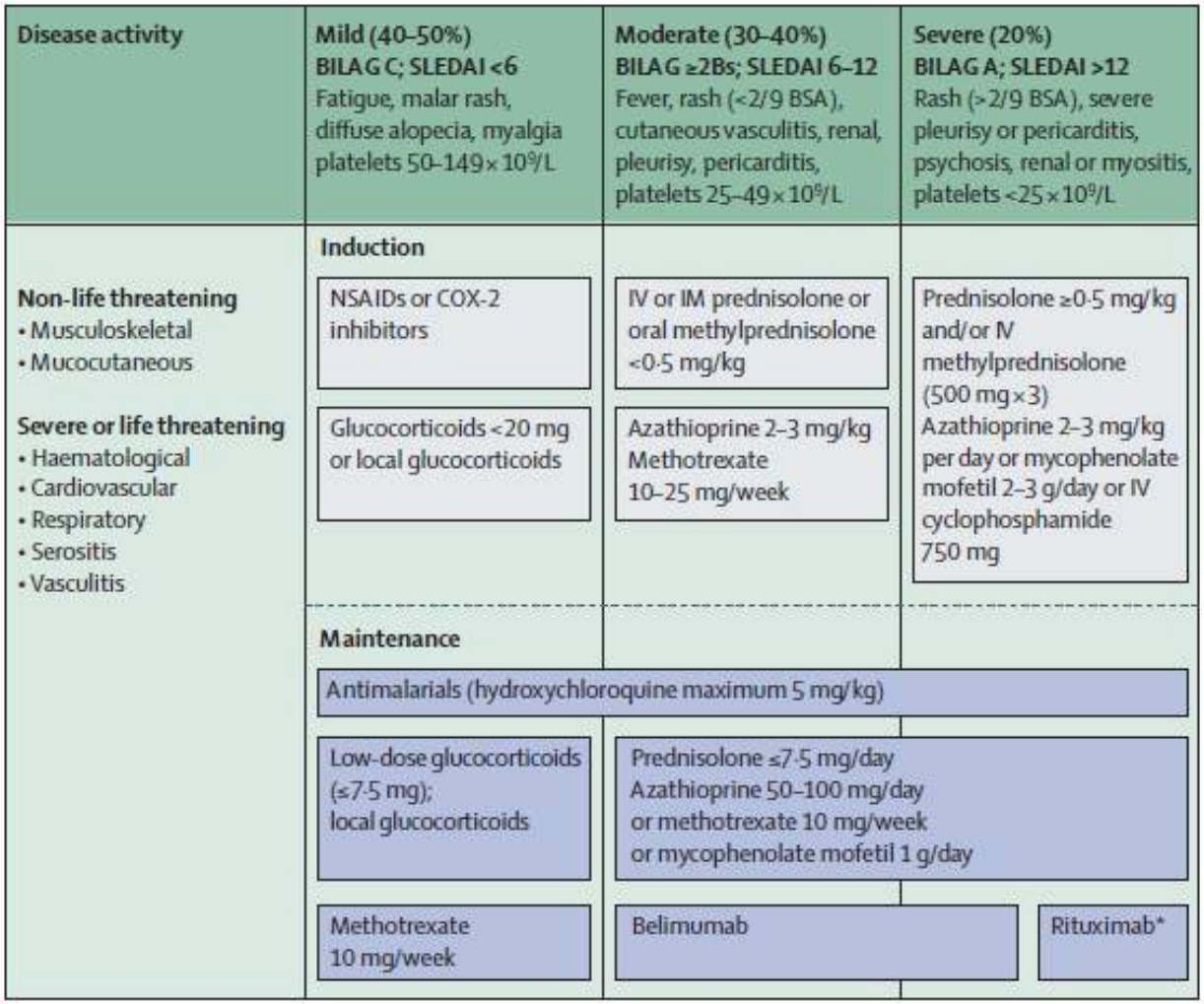
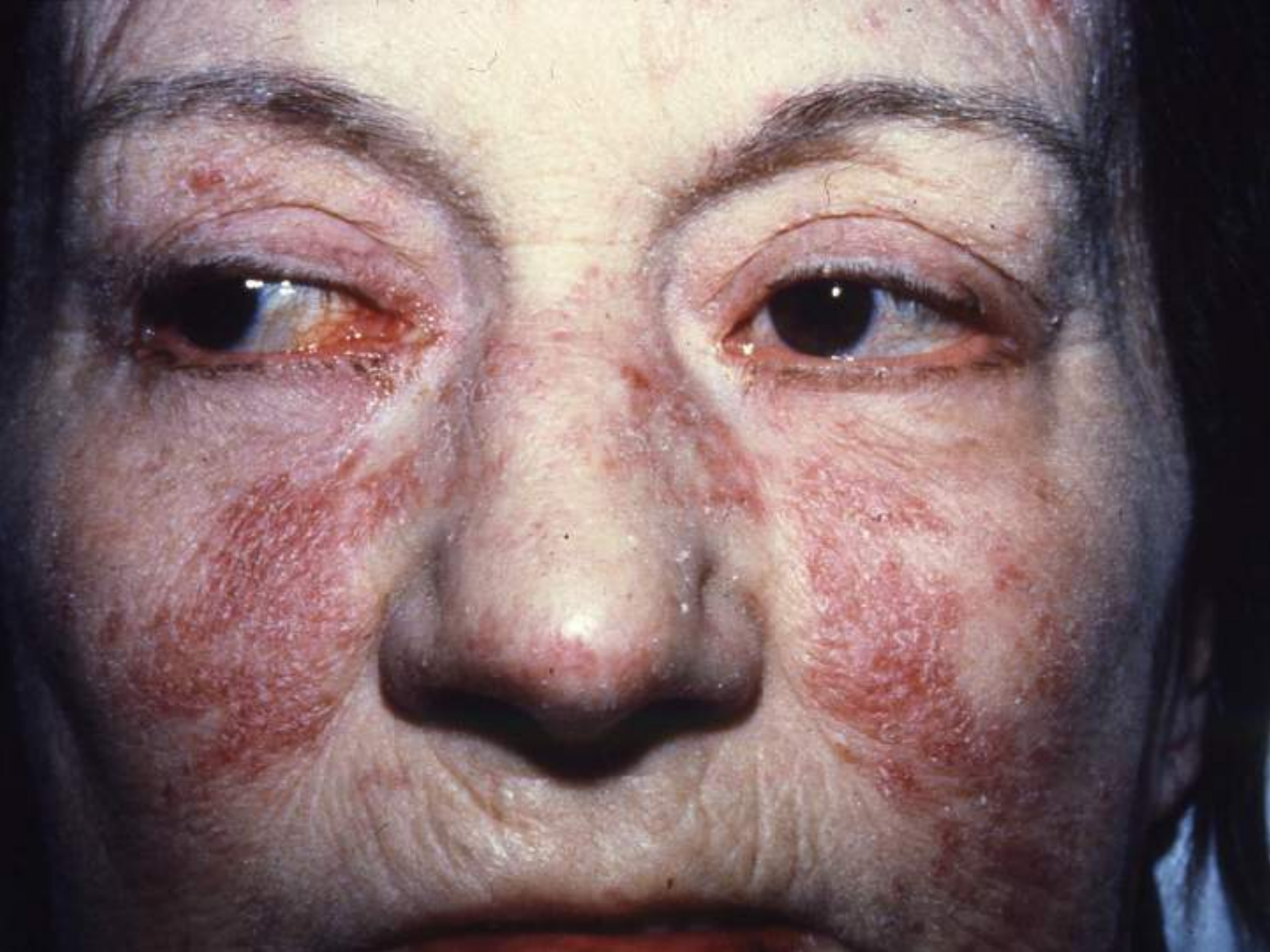
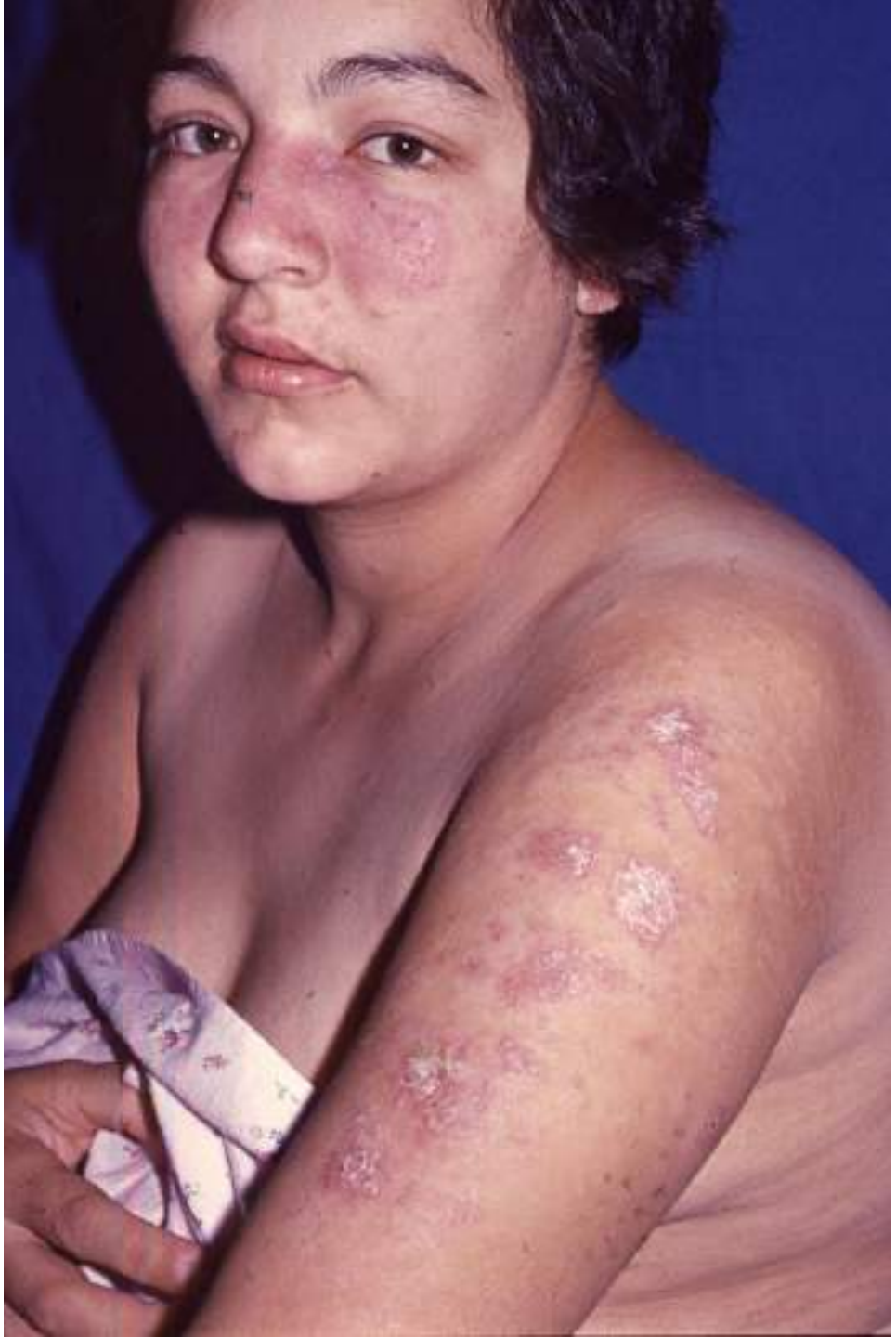


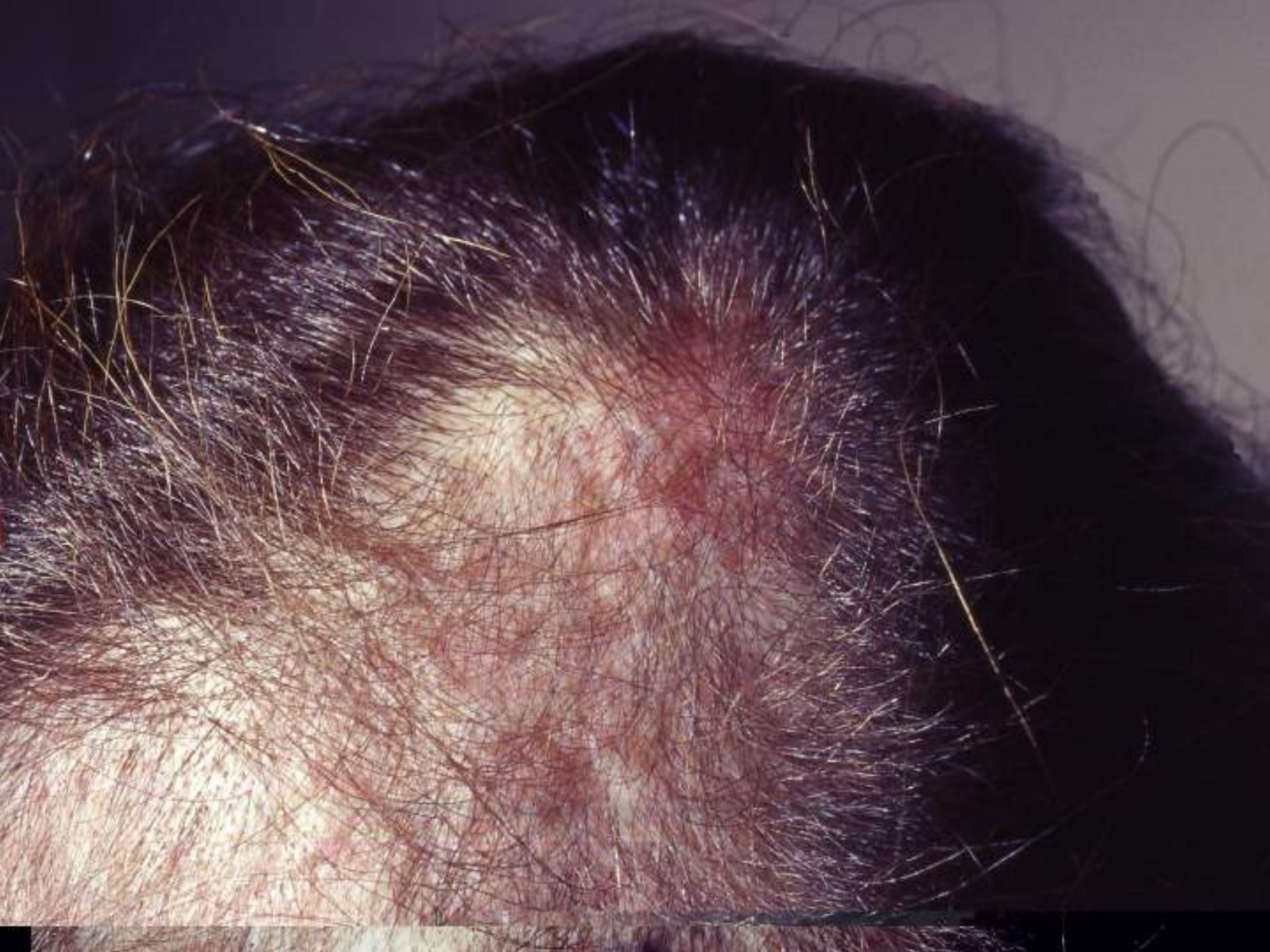
***Figure 2*: Possible treatment algorithms for induction and maintenance in extra-renal systemic lupus erythematosus**

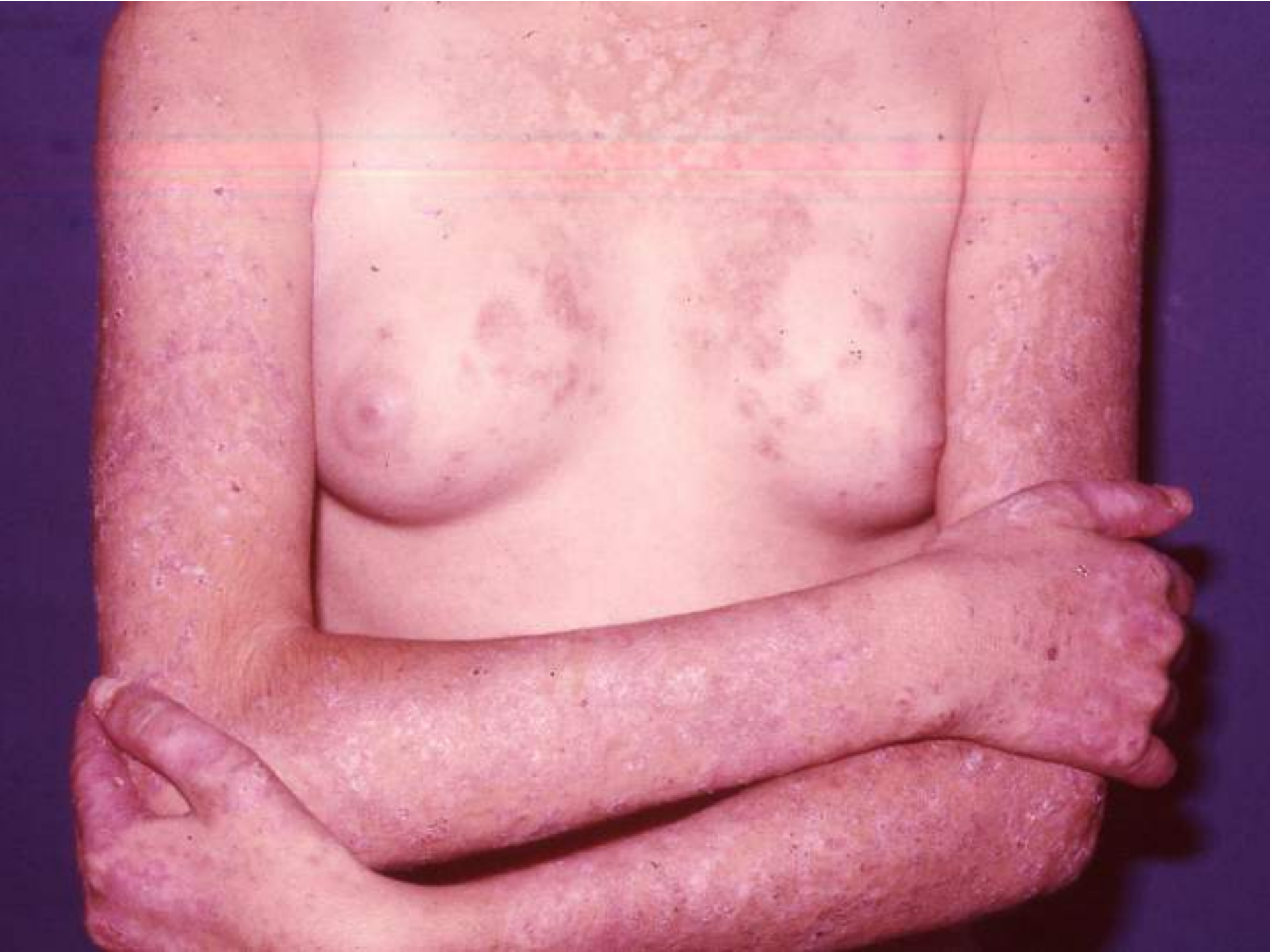
Developed according to the British Society of Rheumatology guidelines for the management of systemic lupus erythematosus in adults.[3] BILAG=British Isles Lupus Assessment Group. BSA=body surface area. IM=intramuscular. IV=intravenous. NSAID=non-steroidal anti-inflammatory drug. SLEDAI=Systemic Lupus Erythematosus Disease Activity Index. UV=ultraviolet. *Still an experimental treatment.

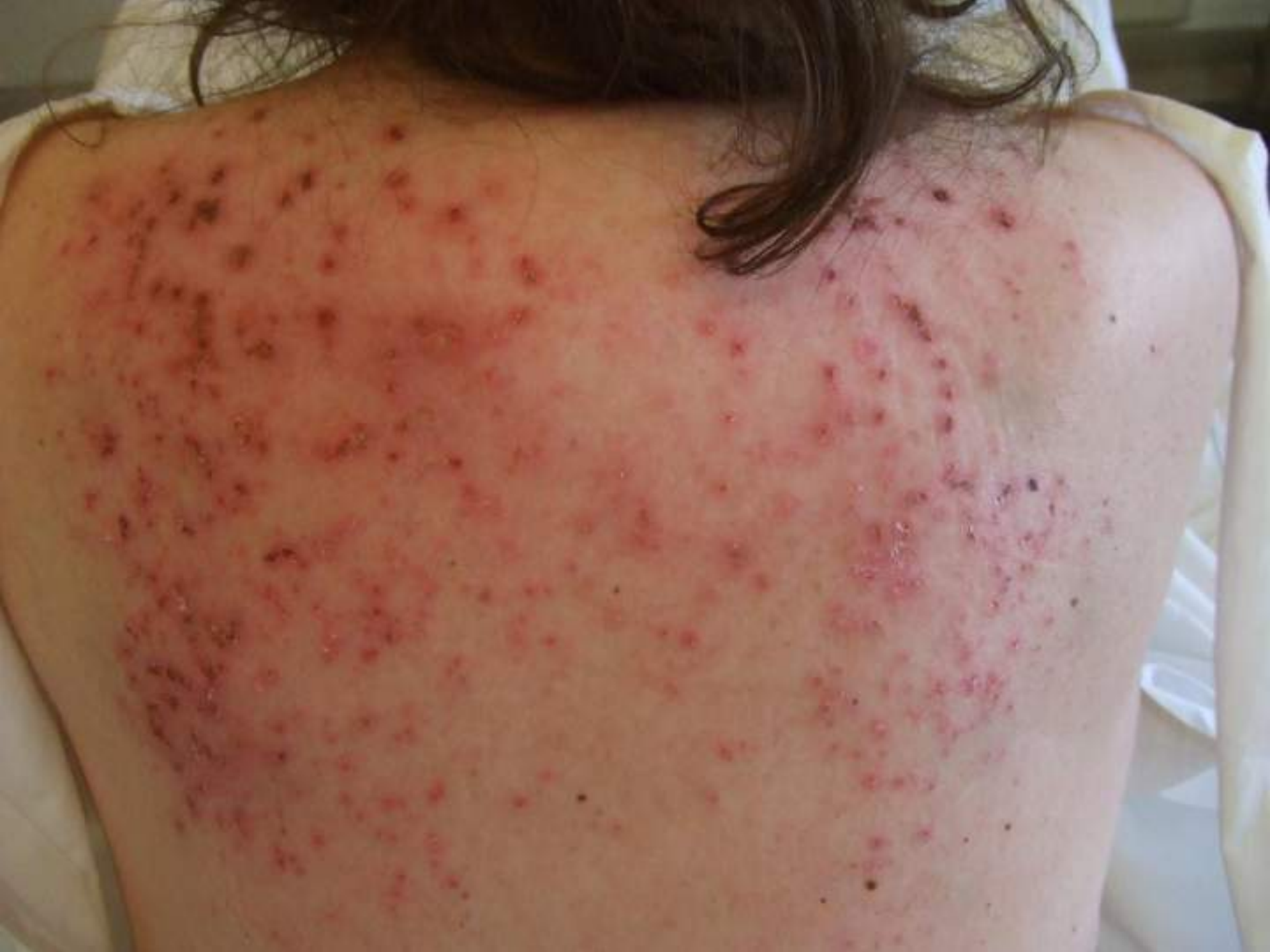
- Jerarquizan al micofenolato vs otros inmunosupresores para ahorrar corticoides en el LES extrarenal.
- Belimumab 10mgkg cada 4 semanas. Para LES extrarenales. Disminuye y retrasa el daño del LES.
- Se está evaluando la combinación o efectuar tratamientos sucesivos con rituximab

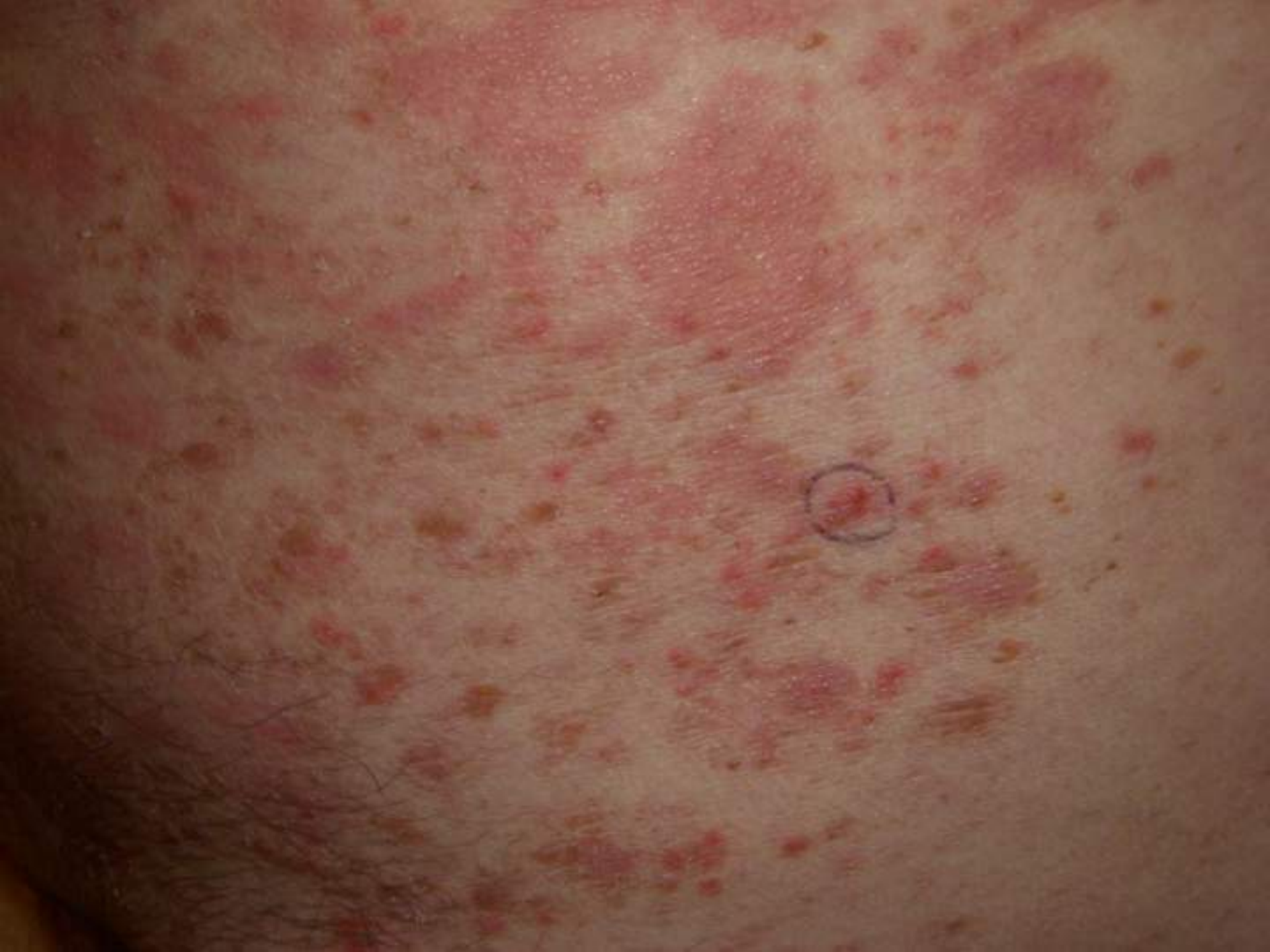












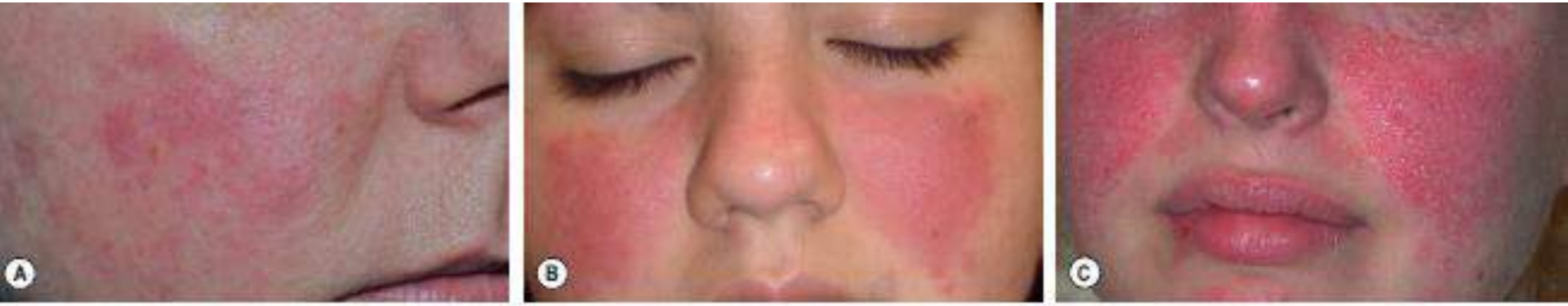


Fig. 41.9 Acute cutaneous lupus erythematosus (ACLE). The facial erythema, often referred to as a "butterfly rash" may be variable (**A**), edematous (**B**) or have associated scale (**C**). The presence of small erosions can aid in the clinical differential diagnosis. *A, Courtesy, Kalman Watsky, MD.*

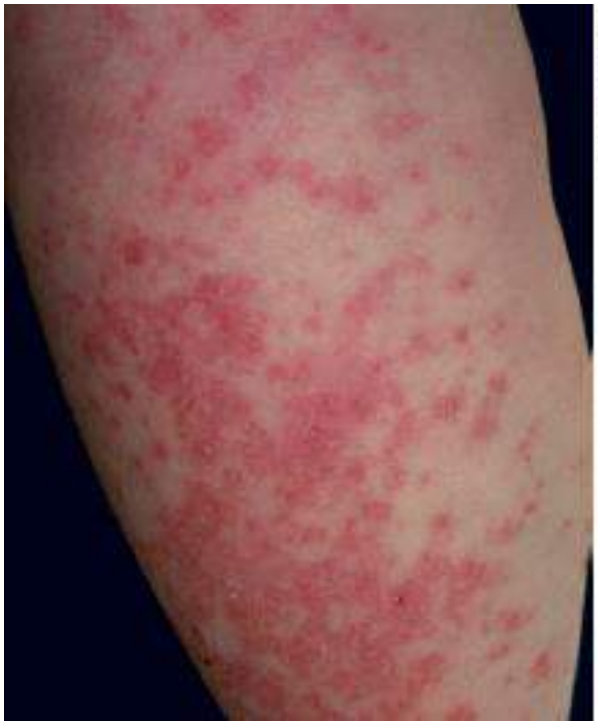
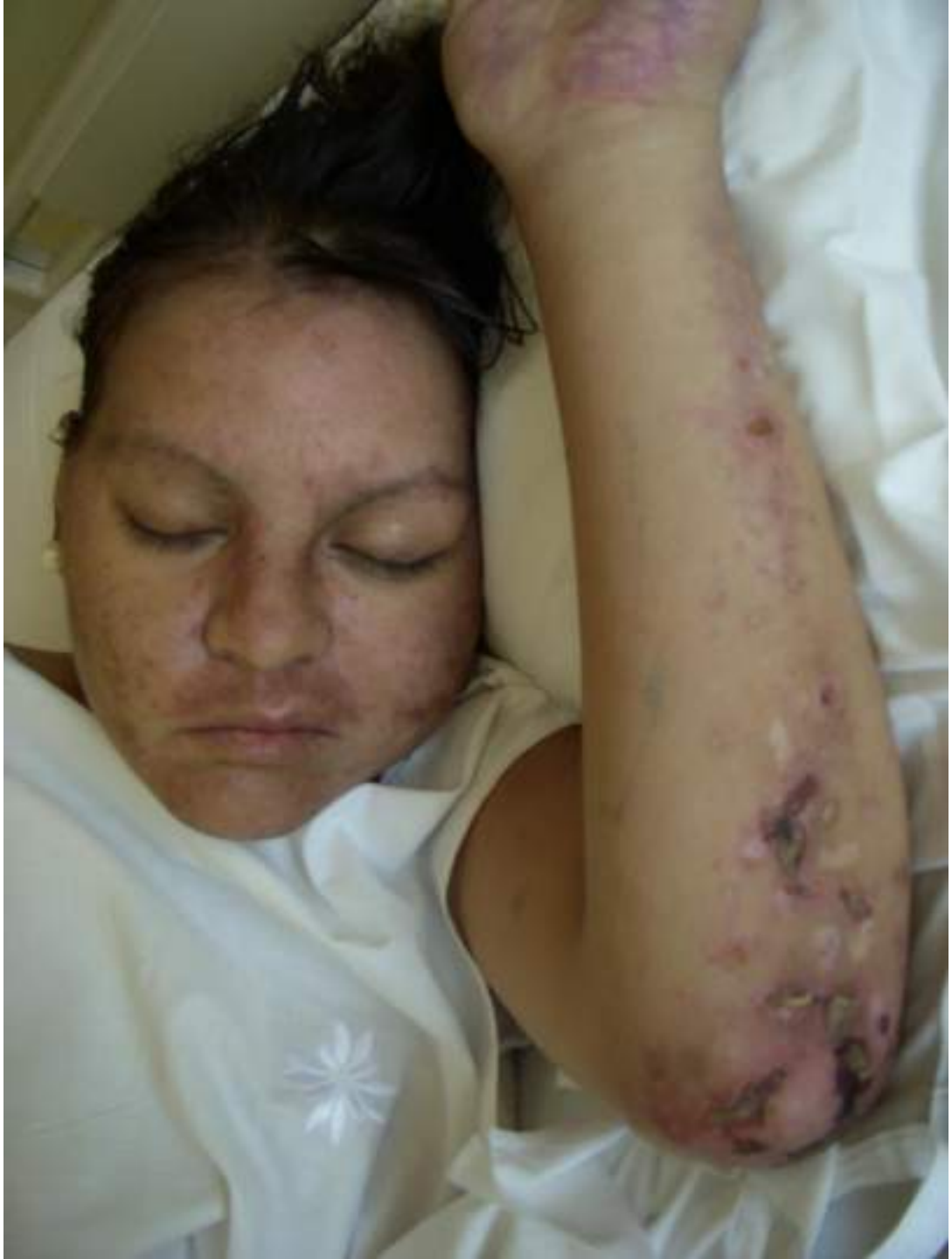
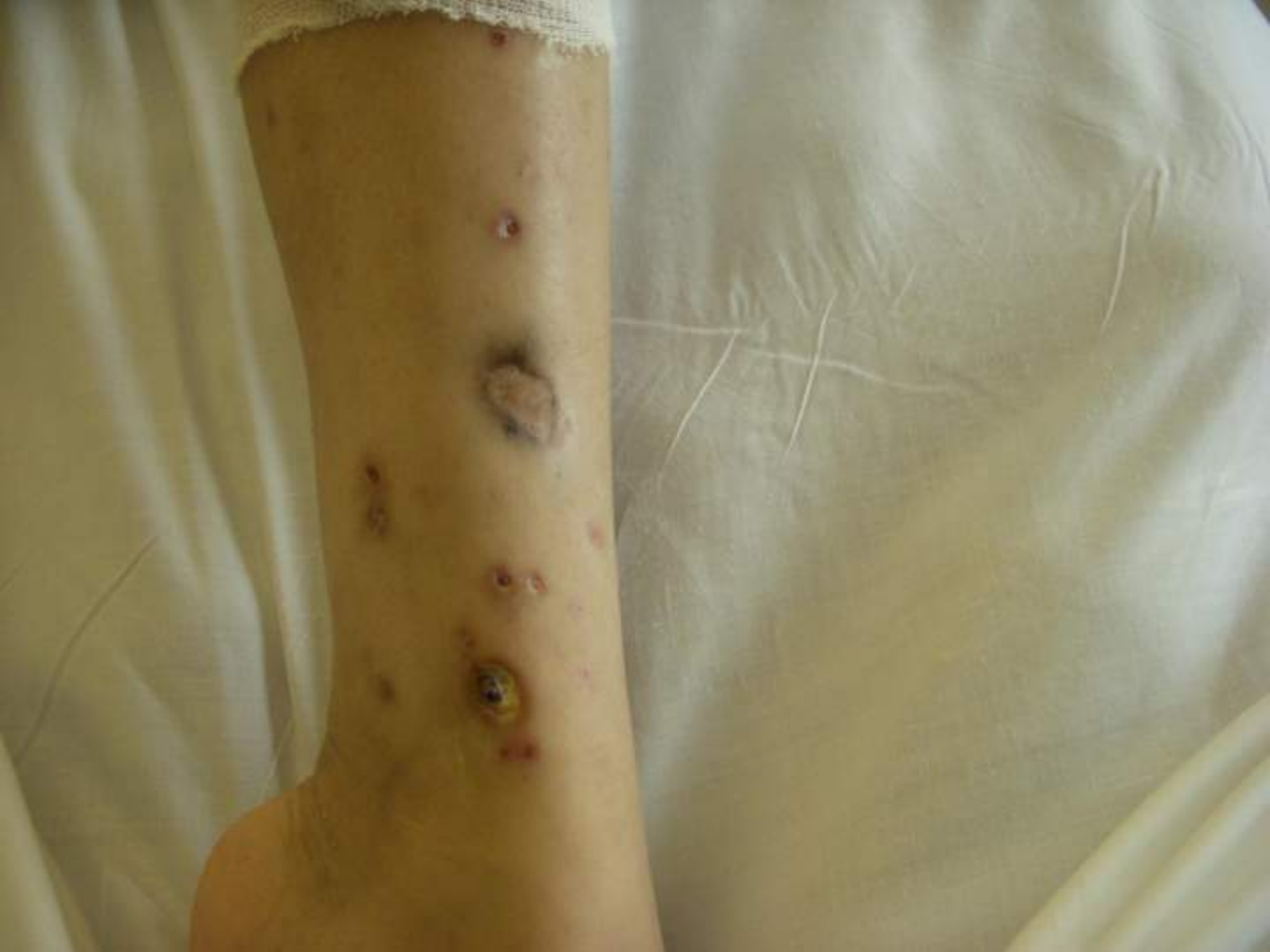


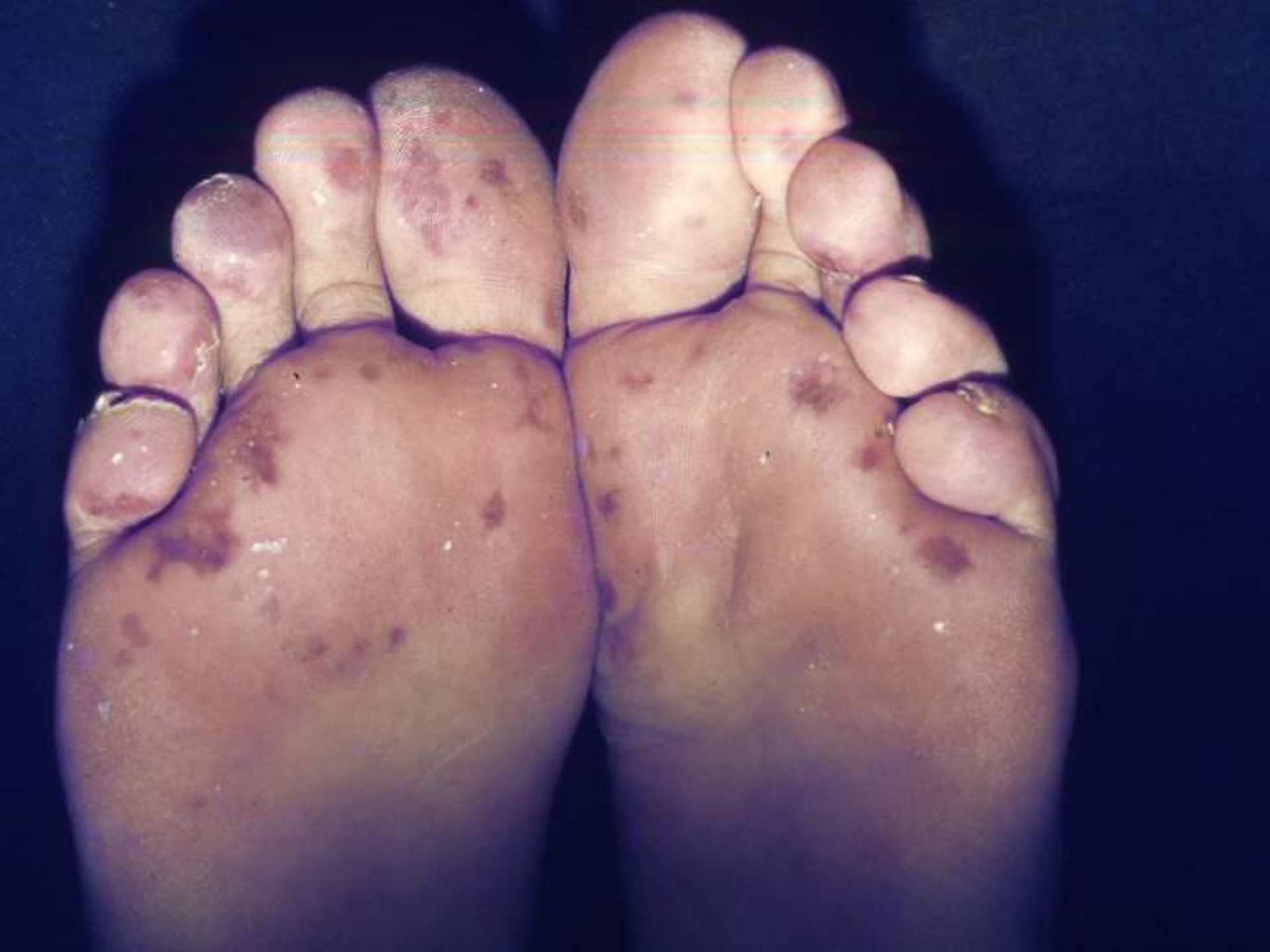
Fig. 41.10 Acute cutaneous lupus erythematosus (ACLE). This patient had ACLE lesions on the arms as well as the face.

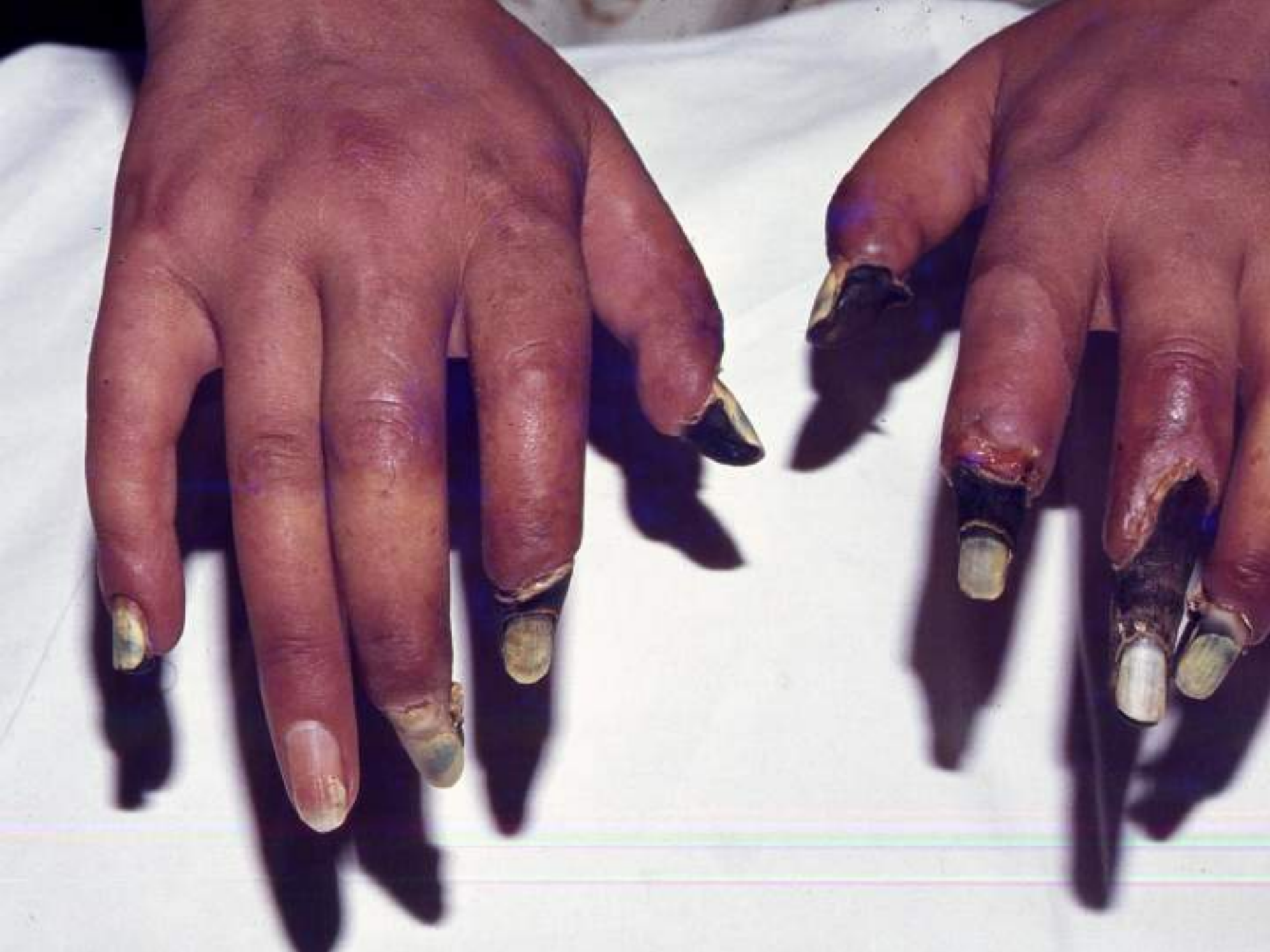
CUTANEOUS FINDINGS (NONSPECIFIC) THAT SUGGEST THE DIAGNOSIS OF SYSTEMIC LUPUS ERYTHEMATOSUS
Diffuse non-scarring alopecia
Raynaud phenomenon
Nail fold (periungual) telangiectasias and erythema
Vasculitis
• Urticarial vasculitis
• Small vessel vasculitis (e.g. palpable purpura)
• Polyarteritis nodosa-like lesions
• Ulcerations
Cutaneous signs of antiphospholipid syndrome
• Livedo reticularis
• Ulcerations
• Acrocyanosis
• Atrophie blanche-like lesions
• Degos-like lesions
• Livedoid vasculopathy
Palmar erythema
Papular and nodular mucinosis
Sweet syndrome-like neutrophilic dermatosis

Table 41.6 Cutaneous findings (nonspecific) that suggest the diagnosis of systemic lupus erythematosus. These are in addition to skin signs of other autoimmune connective tissue diseases, which raise the possibility of an overlap syndrome.









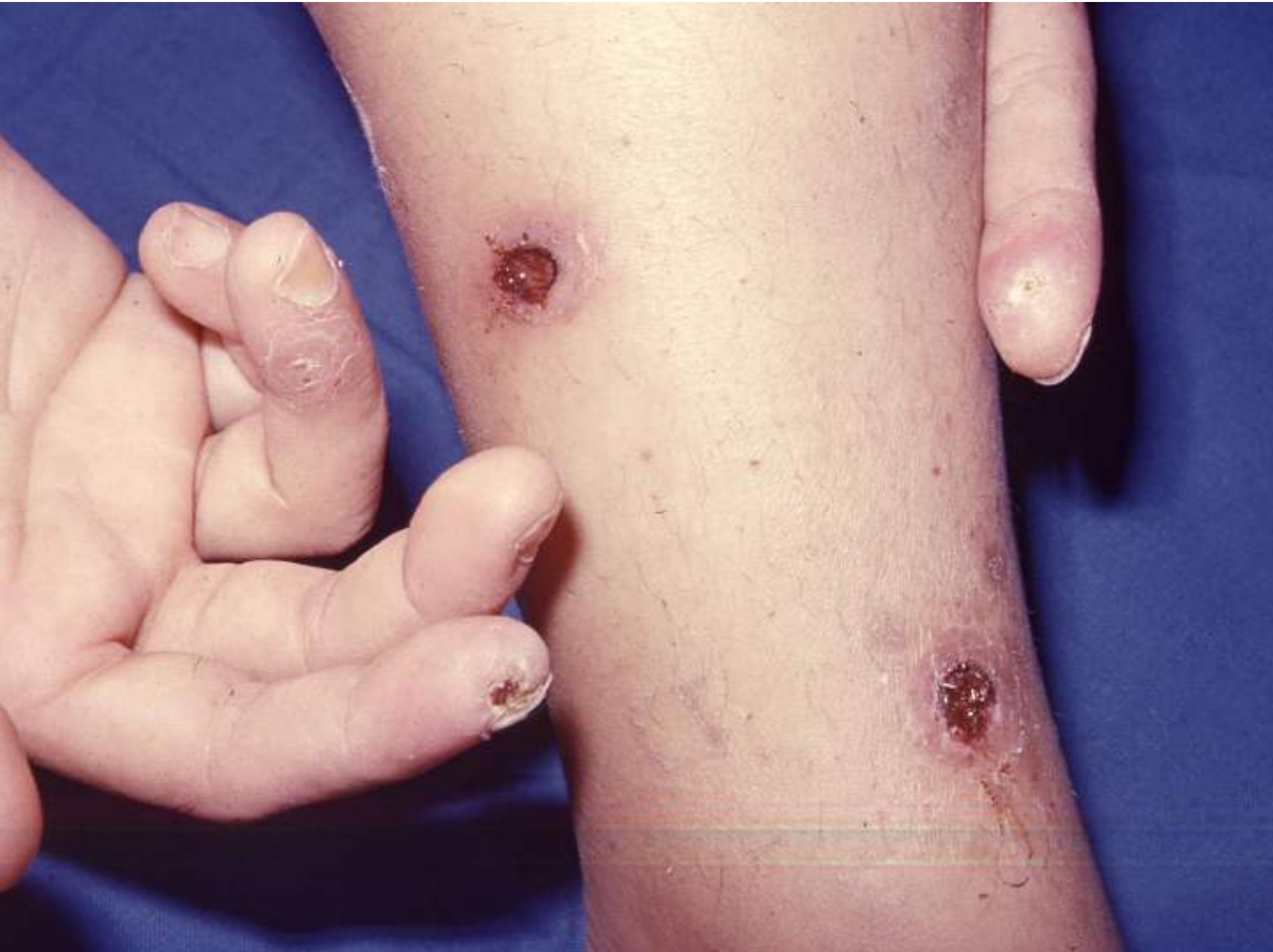


Table 2. Treatment Approaches for SLE.*

Aspirin†
Glucocorticoids†
Immunosuppressive agents
Cyclophosphamide
Methotrexate
Azathioprine
Mycophenolate mofetil
Modulation of B-cell function or numbers
Reestablishment of tolerance
B-cell depletion
B-cell–directed cytokines
Blockade of B-lymphocyte stimulator (belimumab)†
TACI–immune globulin (atacicept)
Blockade of the interleukin-6 receptor (tocilizumab)
Interruption of T-cell–B-cell interaction
Blockade of CD40 ligand
CTLA4–immune globulin
Blockade of inducible costimulator
Reestablishment of tolerance in T cells
Autoantigen-derived peptides
Blockade of type I interferon
Inhibition of toll-like receptor
Hydroxychloroquine†
Hormone manipulation (dehydroepiandrosterone)
Modulation of cell signaling
Spleen tyrosine kinase (fostamatinib)
Janus kinase
Rho kinase
Calcium/calmodulin-dependent protein kinase IV
Calcineurin (dipyridamole)
Mammalian target of rapamycin (sirolimus)

- Lupus Eritematoso Sistémico: Terapéutica

✓ Hidroxicloroquina: inhibel la función de toll – like receptors que contribuyen a la autoinmunidad.

✓ Pulsos de ciclofosfamida IV en forma mensual o bimensual son útiles para la nefritis.

✓ Los glucocorticoides y la aspirina son las otras drogas aprobadas por la FDA.

- Lupus Eritematoso Sistémico: Terapéutica

- ✓ BELIMUMAB es un ac contra la citoquina estimuladora de los linfocitos b (BLyS). Favorece la apoptosis e inhibe el paso de LB a plasmocitos.
- ✓ Ha resultado en un pequeño pero significativo beneficio clínico para pacientes con LES suaves o moderados.
- ✓ Contraindicado en infecciones cr.

- Lupus Eritematoso Sistémico: Terapéutica

- ✓ BELIMUMAB se administra en forma IV, durante 1 hora, 10mg/kg. Días 0 -14 28 y luego mensualmente.
- ✓ Frecuentemente reacciones en las primeras administraciones (hospital de día)
- ✓ Se administra si fracasan los tratamientos convencionales.

- Lupus Eritematoso Sistémico: Terapéutica

✓ BELIMUMAB se observa resultado en un tercio de los pacientes, efectos adversos en otro tercio y nada en otro tercio.

✓ Cuando hay resultados los brotes son menos frecuentes, mejora la artritis y la piel, el laboratorio (anti ADN y C) y ahorra corticoides.

- Lupus Eritematoso Sistémico: Terapéutica

✓ Efectos adversos del BELIMUMAB: hipotensión y angioedema, dolor de cabeza, artralgias, fatiga y nausea de corta duración.

✓ OJO INFECCIONES.

✓ BELIMUMAB + RITUXIMAB ??

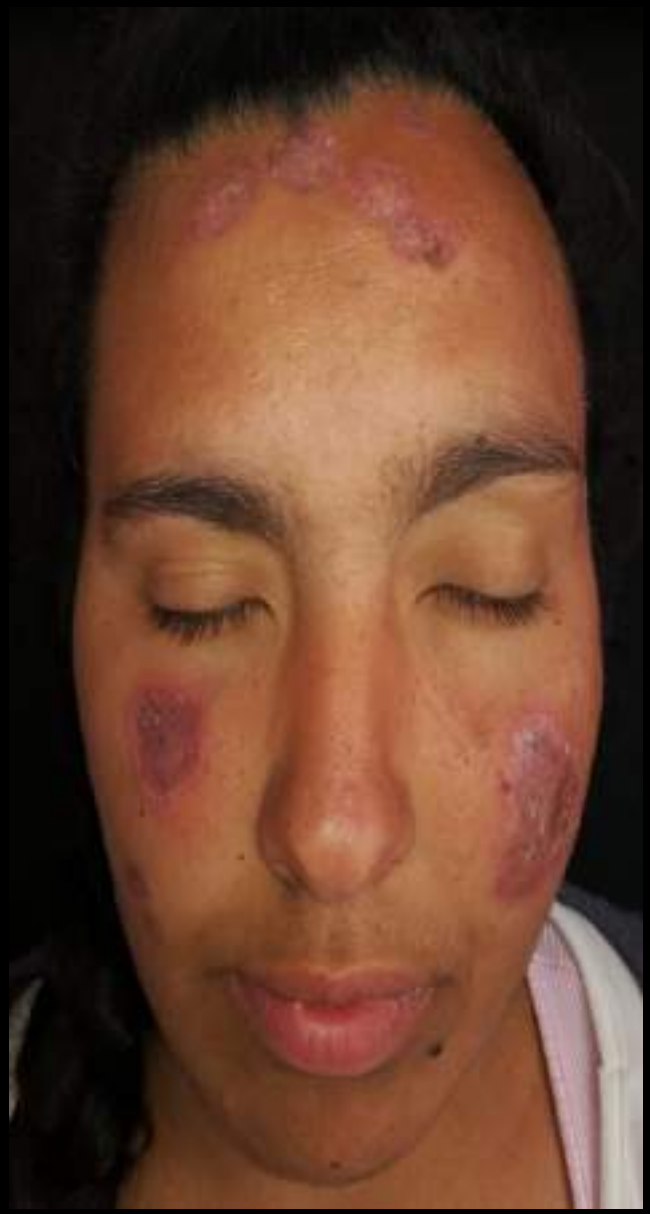
✓ EPRATUZUMAB?

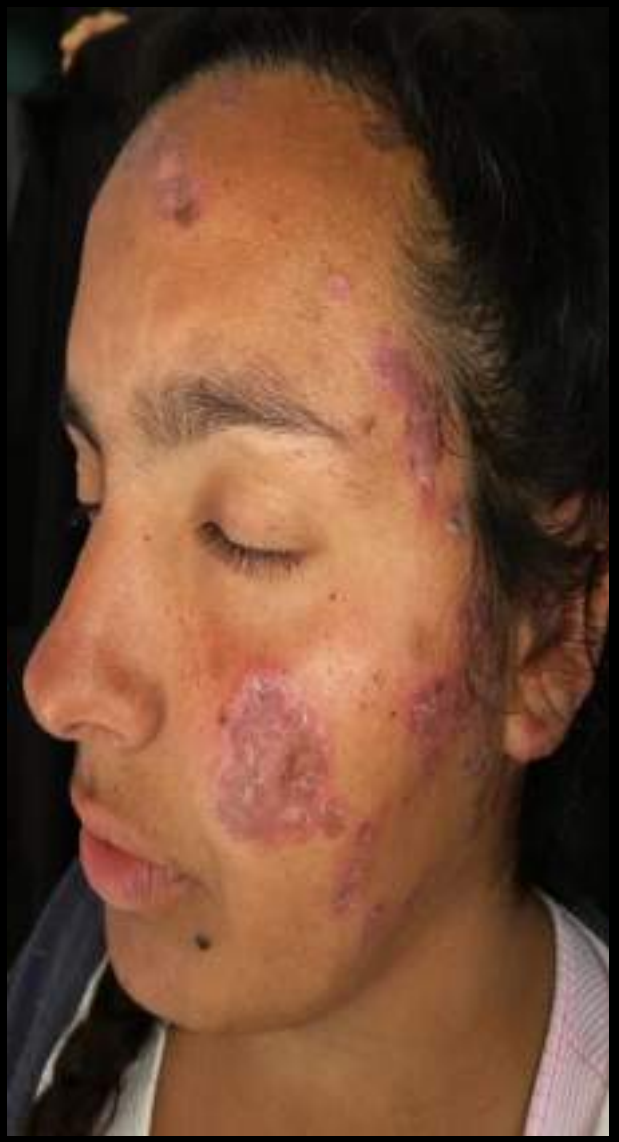
MUCHAS GRACIAS

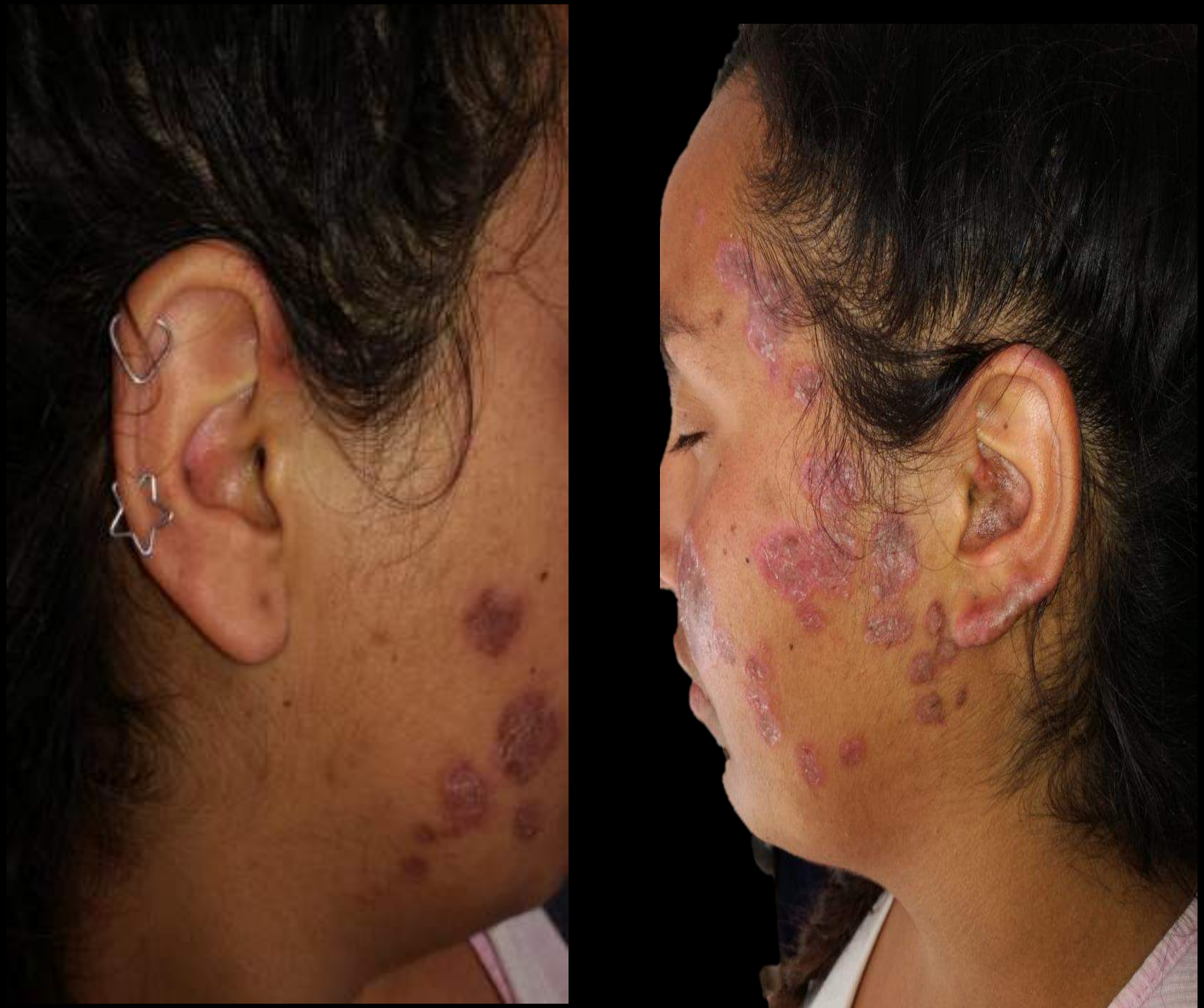
osvaldostringa@gmail.com

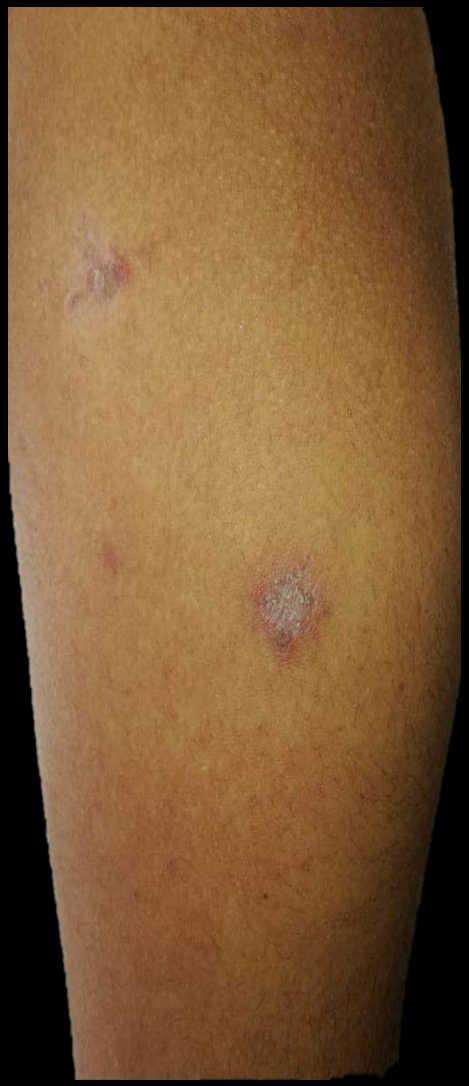
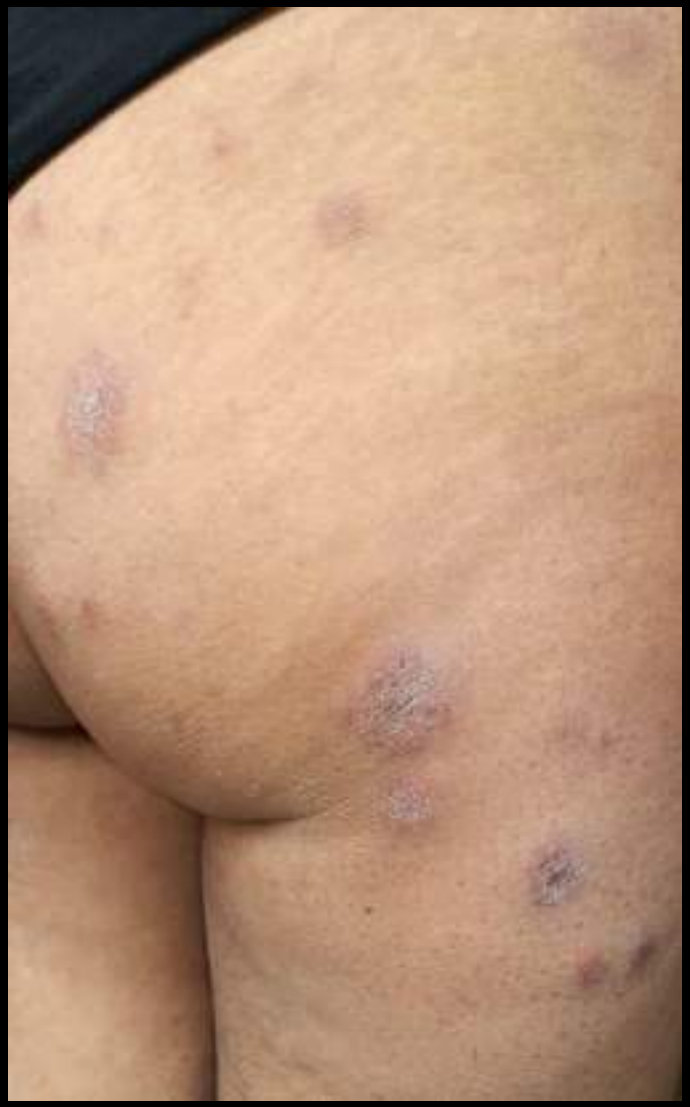
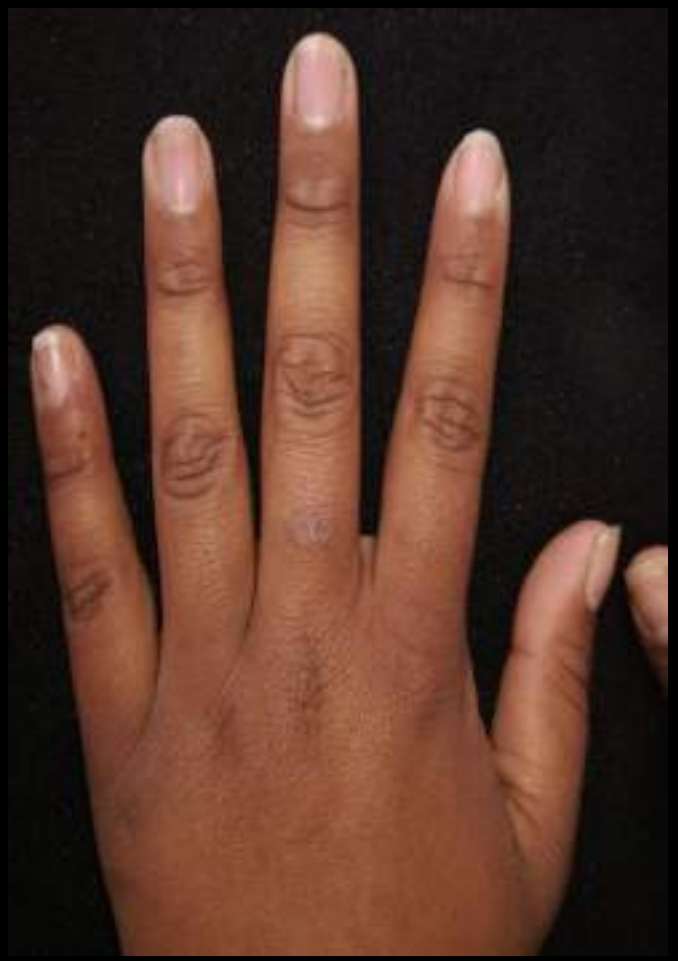
CASO CLÍNICO

Mathys, S; Perez, S; Alonso, M; Carranza, D; Dhabar, M; Stringa, O; Pascutto, C.







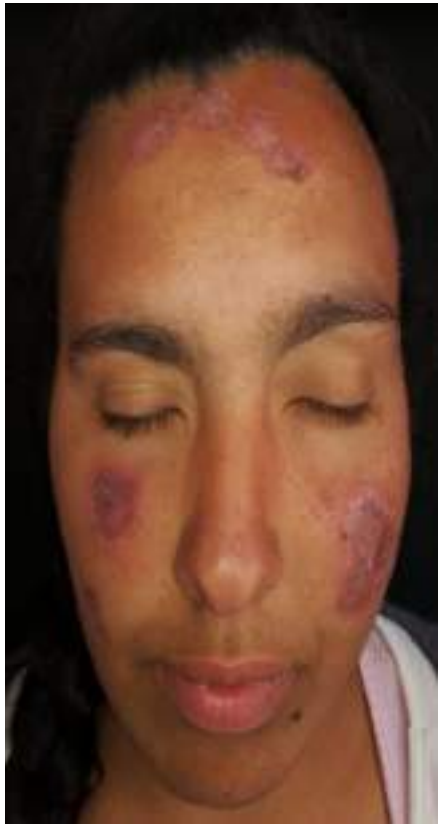




ANTECEDENTES PERSONALES

Paciente	• **Femenino. 22 años**
Antecedentes	• **Aorta bicúspide** • **Sordera oído izquierdo e hipoacusia derecha congénita con requerimiento de cirugía en la infancia** • **Abuela materna: AR**
Medicación habitual	• **No refiere.**

MOTIVO DE CONSULTA

- **Dermatosis pruriginosa en rostro, lóbulos de la oreja, glúteos y MMII de 9 meses de evolución.**
- **Fue tratada previamente en otra institución con crema triple, Ac. Fusídico y Acnoxin sin respuesta.**

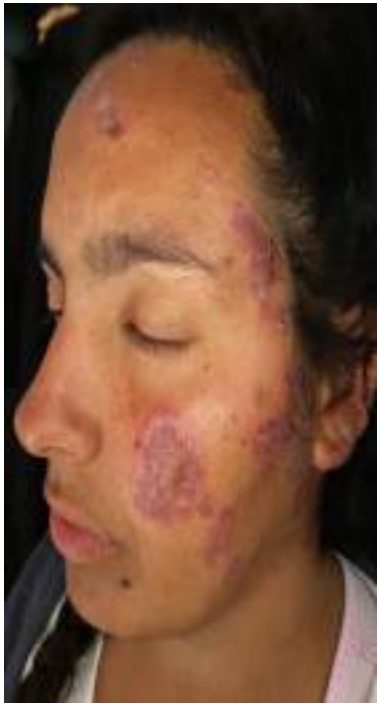


ESTUDIOS REALIZADOS EXTERNOS

JUNIO 2019

LABORATORIO

Hto 44
Hb 14,3
Plq 285.000
TP 85 KPTT 32
VDRL NR
TSH 1,22
FAN 1/80: patrón nuclear Moteado fino



JUNIO 2019

MICOLÓGICO cultivo y directo (rostro) EXTERNO

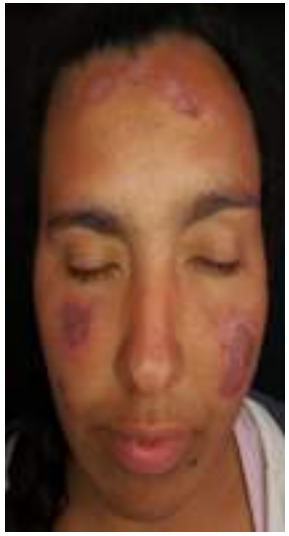
NEGATIVO

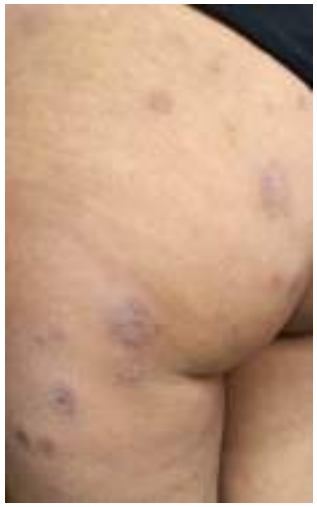
JULIO 2019

BIOPSIA (rostro**) EXTERNO**

"Hallazgo vinculable a papula fibrótica con foliculitis crónica asociada"

CONDUCTA





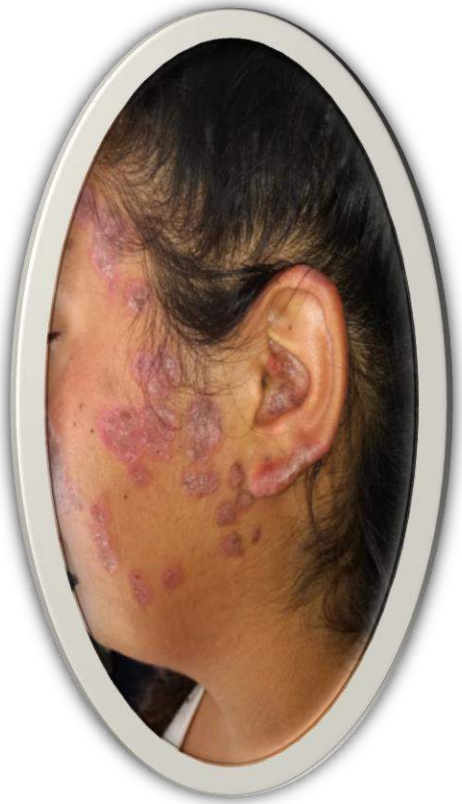
BX X3

1- AP lesión
2- IF lesión
3- IF perilesional

IDX:

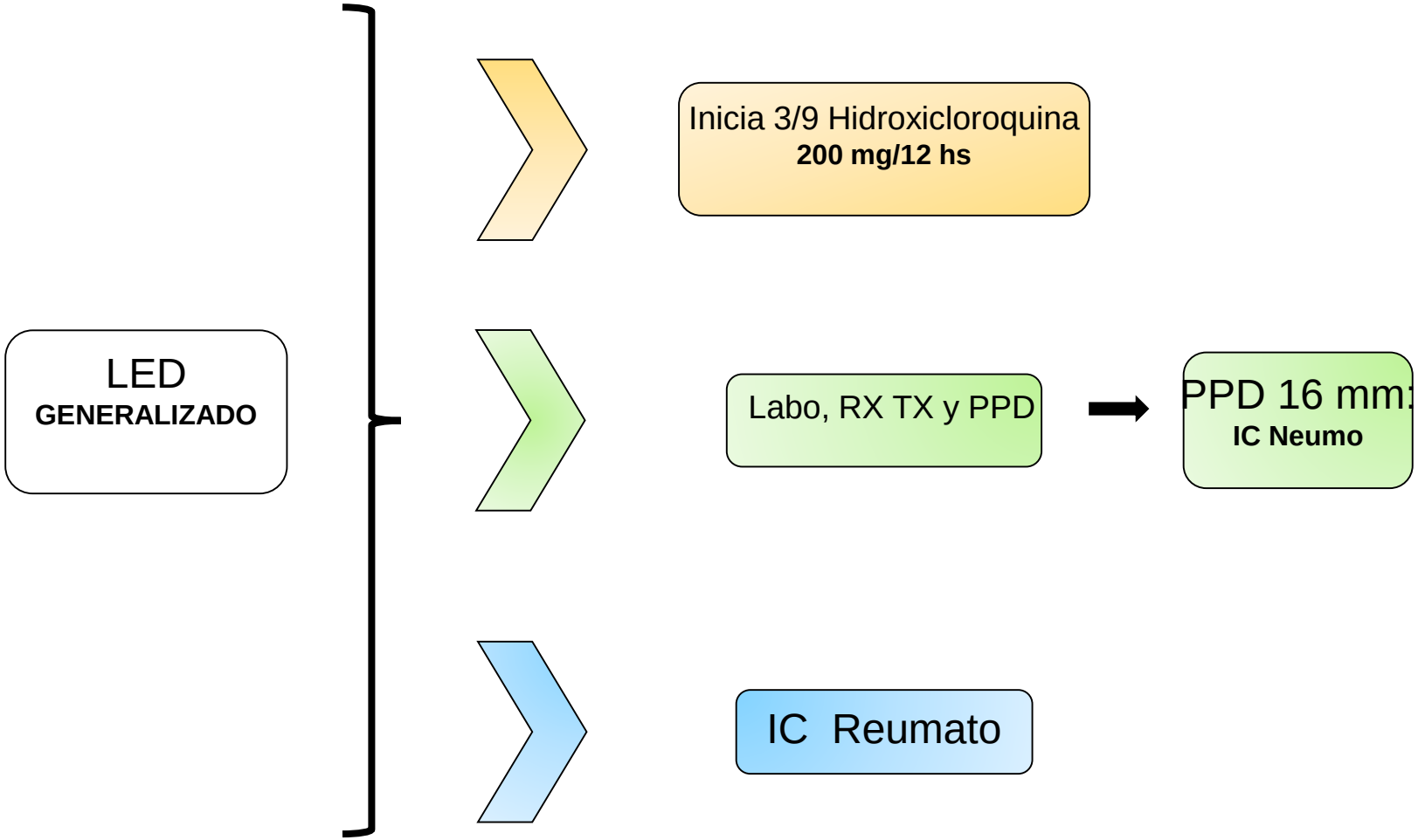
LED GENERALIZADO

DIAGNÓSTICO



LED
GENERALIZADO

CONDUCTA


LED
GENERALIZADO
Inicia 3/9 Hidroxicloroquina
200 mg/12 hs
Labo, RX TX y PPD
PPD 16 mm:
IC Neumo
IC Reumato

LUPUS ERITEMATOSO CUTÁNEO

Lupus **Eritematoso** cutáneo

- AGUDO
  - Localizada
  - Generalizada
  - Tipo NET
- SUBAGUDO
  - Anular
  - Papuloescamosa
  - Inducida por drogas
- CRÓNICO
  - **L.E. Discoide**
    - Localizada
    - **Generalizada**
  - **Paniculítis lúpica**
  - **L.E. Tumidus**
  - **L.E. Chiblain**
  - **Overlap sme**

JEADV 2017, 31, 389–404

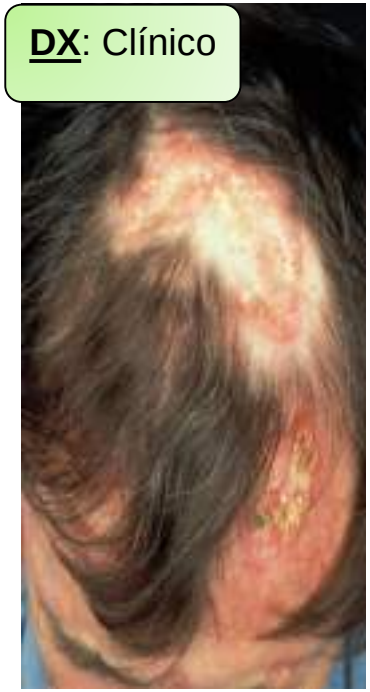
S2k guideline for treatment of cutaneous lupus erythematosus – guided by the European Dermatology Forum (EDF) in cooperation with the European Academy of Dermatology and Venereology (EADV)

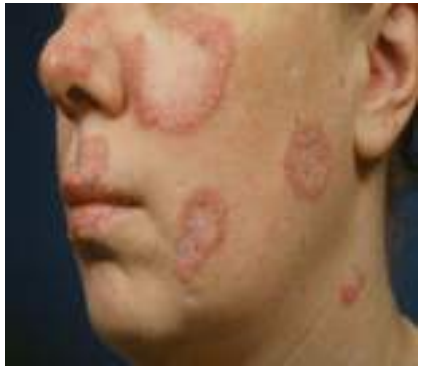
A. Kuhn, C. Aberer, Z. Bata-Csörgő, M. Caproni, A. Diehl, C. Forconi, R. Gläser, H.-W. Hödgen, A. Landmann, B. Majewski, F. Myong, R. Oberau, A. Ranki, J.C. Szepietowski, B. Yen-Pogar

LUPUS ERITEMATOSO DISCOIDE

- **Es una enfermedad crónica, de etiología autoinmunitaria, que afecta la piel, las mucosas y las faneras en áreas fotoexpuestas.**
- **Mayor frecuencia entre los 20 y 40 años, con un predominio mujer/hombre de 2 a 1.**
- **Tiene una variedad localizada y una generalizada de acuerdo a si se manifiesta por arriba o debajo del cuello.**

DX: Clínico





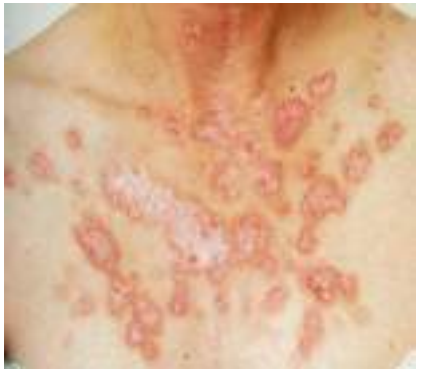
LED +LES (20%) tienen aumentado el riesgo de fotosensibilidad,anti Sm y leucopenia pero menor riesgo para serositis y artitis que LES sin LED

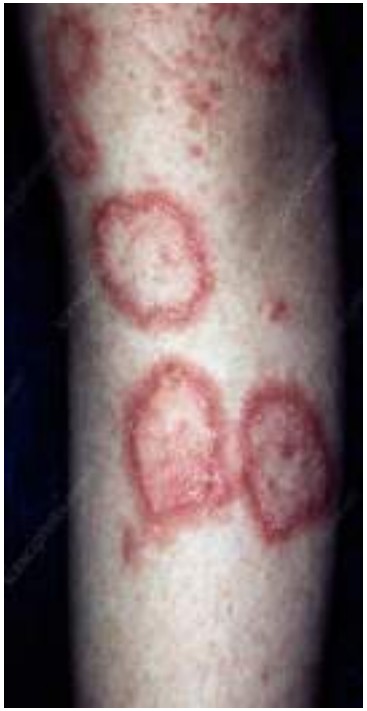
LABO

ANA (Títulos bajos)

FR +

VES (20%)

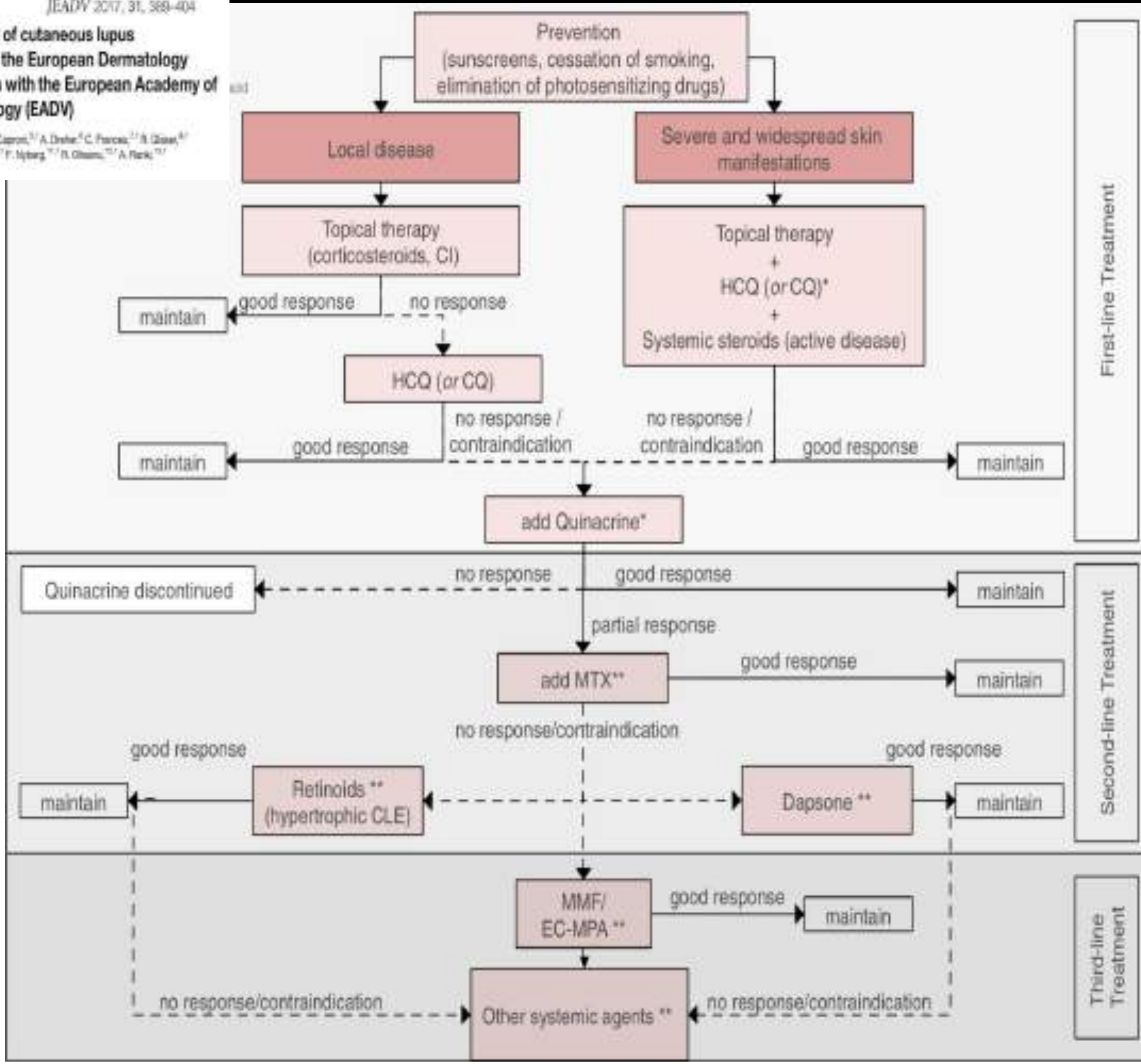




GUIDELINES JEADV 2017, 31, 389–404

S2k guideline for treatment of cutaneous lupus erythematosus – guided by the European Dermatology Forum (EDF) in cooperation with the European Academy of Dermatology and Venereology (EADV)

A. Kuhn, E. Aberer, Z. Bata-Csörgő, M. Caproni, A. Dreher, C. Frances, R. Gläser, H.-W. Klötgen, A. Landmann, B. Marinovic, F. Nyberg, R. Olteanu, A. Ranki, J.C. Szepietowski, B. Volc-Platzer



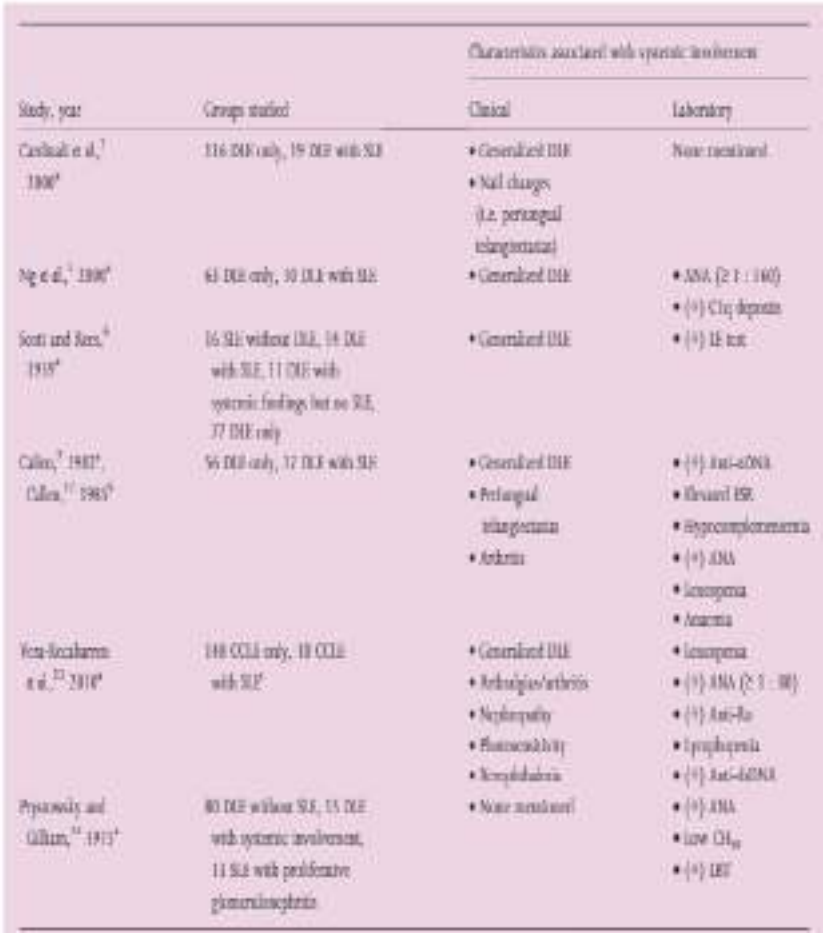
BJD British Journal of Dermatology

Determining risk factors for developing systemic lupus erythematosus in patients with discoid lupus erythematosus

B.F. Chong J. Song N.J. Olsen

REVIEW ARTICLE ptember 2011

Objetivo: comparar la correlación **c**línica y de laboratorio del LED con **c**ompromiso sistémico, es decir, dilucidar **qué pacientes con LED tienen mayor riesgo de desarrollar LES.**



Study, year	Groups studied	Characteristics associated with systemic involvement: Clinical	Laboratory
Cardinali et al.,[7] 1998*	116 DLE only, 19 DLE with SLE	• Generalized DLE • Nail changes (i.e. periungual telangiectasia)	None mentioned
Ng et al.,[8] 1998*	61 DLE only, 10 DLE with SLE	• Generalized DLE	• ANA (≥ 1 : 160) • (+) $C1q$ deposits
Scott and Rees,[9] 1959*	16 SLE without DLE, 14 DLE with SLE, 11 DLE with systemic findings but no SLE, 37 DLE only	• Generalized DLE	• (+) LE test
Callen,[3] 1983*, Callen,[11] 1985*	96 DLE only, 17 DLE with SLE	• Generalized DLE • Periungual telangiectasia • Arthritis	• (+) Anti-nDNA • Elevated ESR • Hypocomplementemia • (+) ANA • Leucopenia • Anaemia
Vera-Recabarren et al.,[12] 2004*	148 CCLE only, 18 CCLE with SLE	• Generalized DLE • Arthralgias/arthritis • Nephropathy • Photosensitivity • Neutropenia	• Leucopenia • (+) ANA (≥ 1 : 80) • (+) Anti-Ro • Lymphopenia • (+) Anti-dsDNA
Prystowsky and Gilliam,[13] 1973*	80 DLE without SLE, 15 DLE with systemic involvement, 11 SLE with proliferative glomerulonephritis	• None mentioned	• (+) ANA • Low CH_{50} • (+) LET

30% generalizado y 7.3% localizado

43% generalizado y 14% localizado

13% generalizado y 1% localizado

BJD British Journal of Dermatology

Determining risk factors for developing systemic lupus erythematosus in patients with discoid lupus erythematosus

B.F. Chong J. Song N.J. Olsen

REVIEW ARTICLE ptember 2011

Resultados:

1- La frecuencia de progresión del LED va del 0-28%
2- El intervalo desde el dx de LED hasta la progresión a LES fue entre 0 y 34 años siendo mas del 70% en los 1eros 5 años.

FACTORES CLÍNICOS DE LED ASOCIADOS CON LES

- LED generalizado
- cambios ungueales: telangiestasias periungueales
- artralgias y artritis en IFP y rodillas

FACTORES DE LABORATORIO ASOCIADOS CON LES EN LED

-VES aumentado
-ANA +
-Alteraciones hematológicas (anemia, leucopenia)

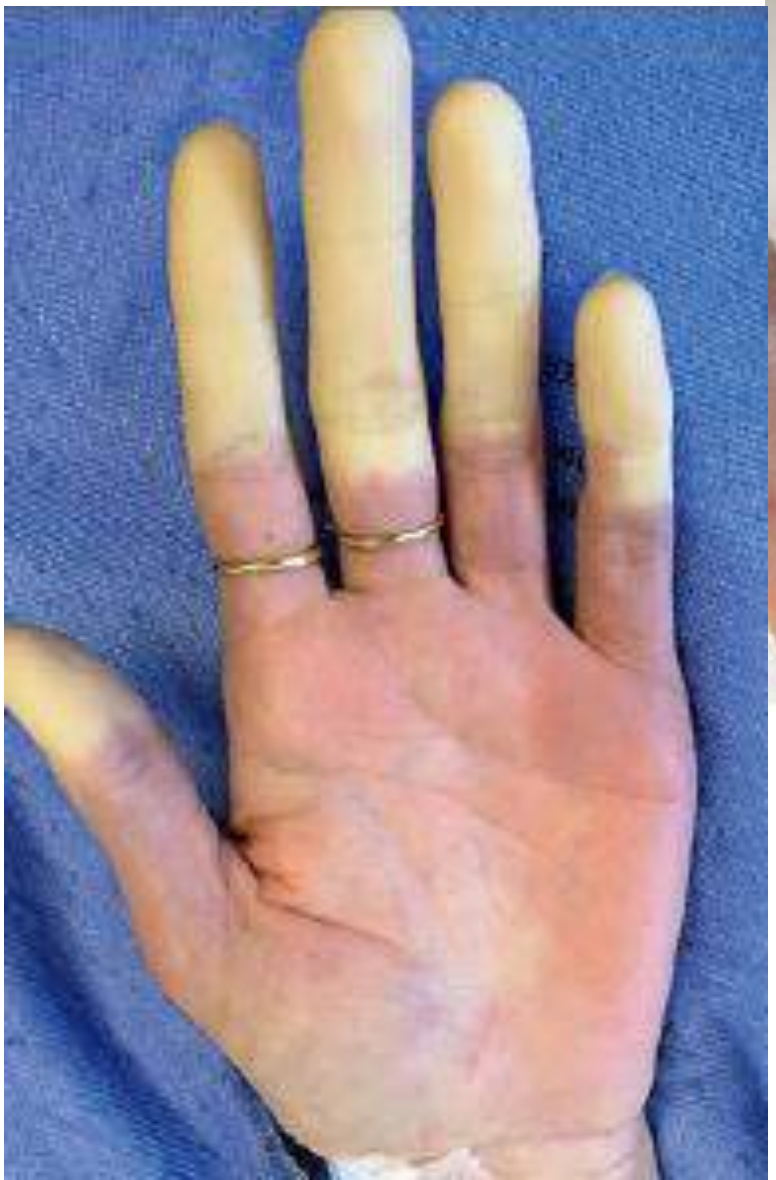
INTERÉS DEL CASO

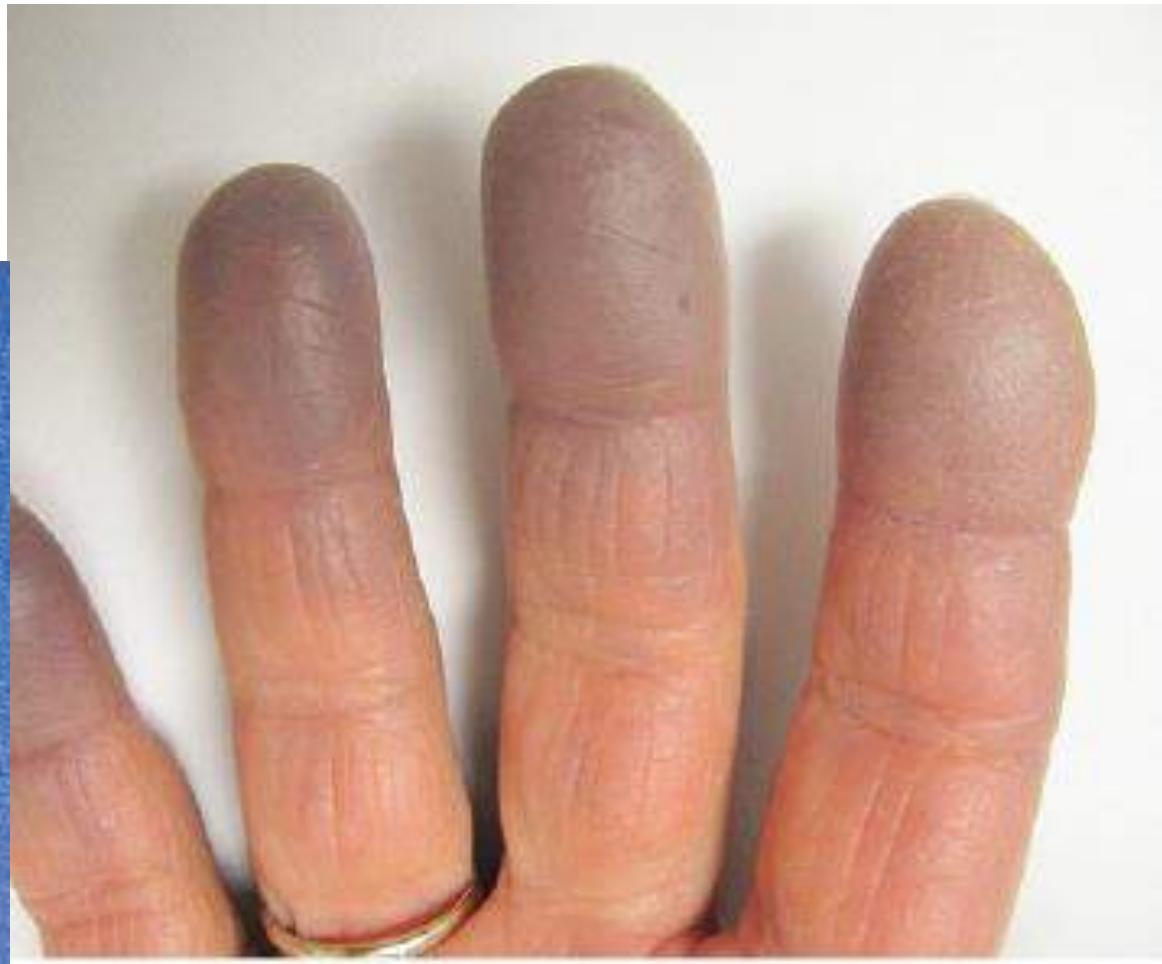
1- Presentar un caso de LED atípico por su forma generalizada

2-Enfatizar la importancia del seguimiento estricto de éstos pacientes ya que tienen mayor riesgo de progresión a LES

Muchas gracias!

osvaldostringa@gmail.com





Raynaud (blanco, azul y rojo)

	Primario(3-5% de la población)	**Secundario**
Sexo (F/M)	20/1	4/1
Edad de comienzo	Pubertad	Mayor de 25 años
Frecuencia de ataques	Menos de 5 x día	5 – 10 x día
Precipitantes	Frio y emociones	Frío
Injuria isquémica	NO	SI
Capilaroscopía anormal	Negativa	95%
Otros fenómenos vasomotores	SI	SI
FAN	Negativo o bajos títulos	90%
Anticentrómero	Negativo	50-60%
Anti Scl 70	Negativo	20-30%

The NEW ENGLAND JOURNAL of MEDICINE

REVIEW ARTICLE

Edward W. Campion, M.D., *Editor*

Raynaud's Phenomenon

Fredrick M. Wigley, M.D., and Nicholas A. Flavahan, Ph.D.

From the Division of Rheumatology (F.M.W.) and the Department of Anesthesiology and Critical Care Medicine (N.A.F.), Johns Hopkins University School of Medicine, Baltimore. Address reprint requests to Dr. Wigley at the Division of Rheumatology, Johns Hopkins University School of Medicine, 5200 Eastern Ave., Suite 4100, Mason F. Lord Bldg., Center Tower, Baltimore, MD 21224, or at fwig@jhmi.edu.

N Engl J Med 2016;375:556-65.
DOI: 10.1056/NEJMra1507638

In his 1862 thesis, Maurice Raynaud describes the condition afflicting a 26-year-old female patient: "Under the influence of a very moderate cold . . . she sees her fingers become ex-sanguine, completely insensible, and of a whitish yellow color. This phenomenon happens often without reason, lasts a variable time, and terminates by a period of very painful reaction, during which the circulation is re-established little by little and recurs to the normal state."[1] The term "Raynaud's disease" was used to describe these vascular events until Hutchinson, who argued that multiple etiologic factors could be responsible, introduced the concept of "Raynaud's phenomenon."[2] Although results vary according to sex, local environmental climate,[3] and work exposures,[4] most population-based surveys estimate the prevalence of the disorder in the general population at 3 to 5%.[5] We currently classify patients into two groups: those with primary Raynaud's phenomenon, which is diagnosed when no underlying disease is found; and those with secondary Raynaud's phenomenon, which is diagnosed when there is associated disease. This review provides an update on new insights into the mechanism and pathogenesis of Raynaud's phenomenon and on current approaches to the management of this disorder.[6]

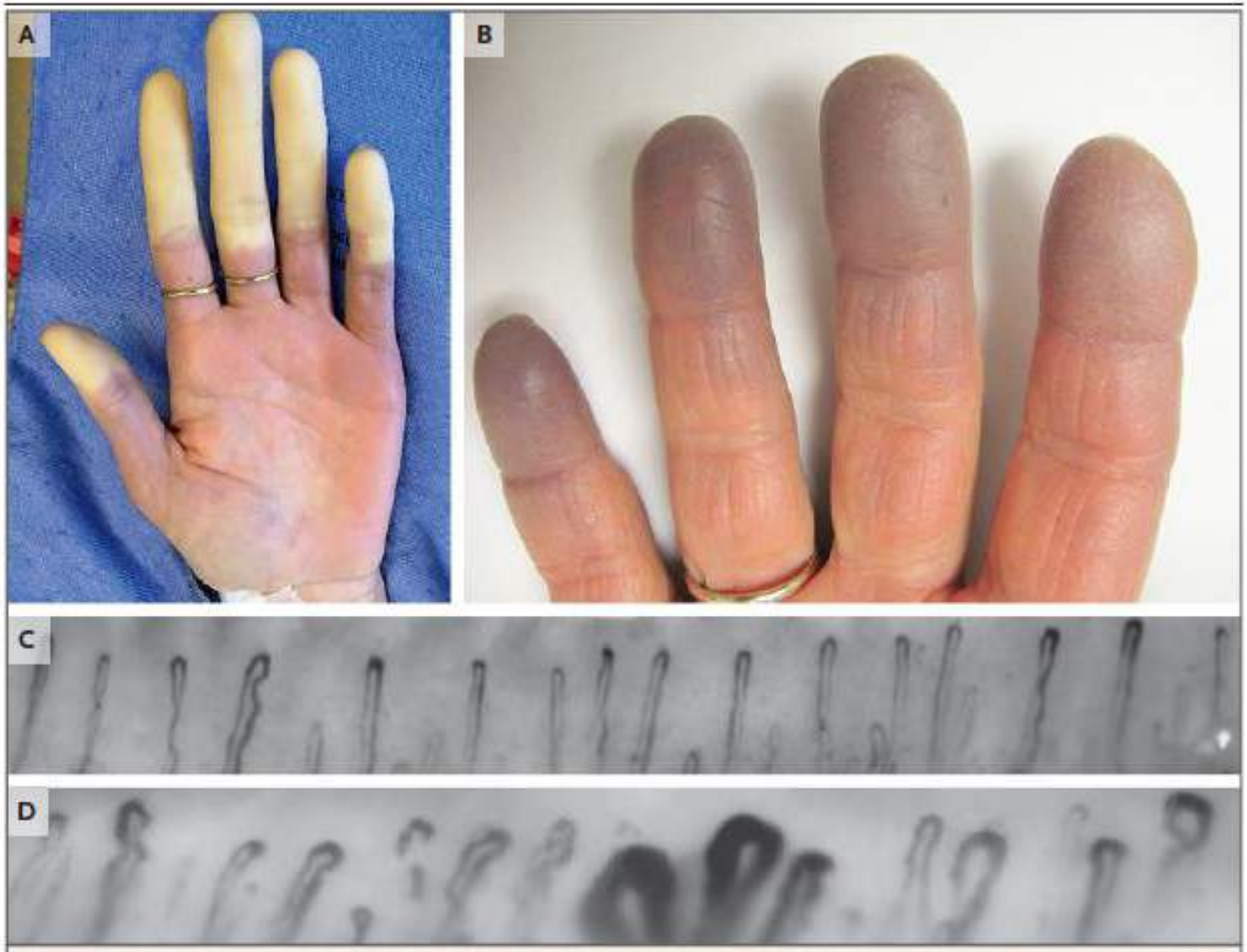


Figure 1. Findings in Patients with Raynaud's Phenomenon.

Panel A shows the pallor phase, and Panel B the cyanotic phase. Panel C shows normal nailfold capillaries, which would be indicative of healthy persons or those with primary Raynaud's phenomenon, and Panel D the enlarged capillary loops that are typical of scleroderma microvascular disease, as seen with the use of capillaroscopy.

Table 1. Drug Treatment of Raynaud's Phenomenon.*

Agent	Dose
Calcium-channel blocker	
Nifedipine	10–30 mg 3 times daily orally
Sustained-release nifedipine	30–120 mg daily orally
Amlodipine	5–20 mg daily orally
Felodipine	2.5–10.0 mg twice daily orally
Isradipine	2.5–5.0 mg twice daily orally
Diltiazem†	30–120 mg 3 times daily orally
Sustained-release diltiazem†	120–300 mg daily orally
Phosphodiesterase-5 inhibitor	
Sildenafil	20 mg 3 times daily or 50 mg twice daily
Tadalafil	20 mg every other day
Vardenafil	10 mg twice daily
Sympatholytic agent: prazosin	1–5 mg twice daily
Angiotensin II–receptor type 1 antagonist: losartan	25–100 mg daily orally
Selective serotonin reuptake inhibitor: fluoxetine	20–40 mg daily orally
Vasodilator: nitroglycerin	$^1/_4$–$^1/_2$ in. of 2% ointment applied topically daily
Other vasoactive drug	
Pentoxifylline	400 mg 3 times daily orally
Botulinum toxin	50–100 units per hand
Prostaglandin	
Epoprostenol‡	0.5–6.0 ng per kilogram per min intravenously for 6 to 24 hr for 2 to 5 days
Iloprost§	0.5–2.0 ng per kilogram per min intravenously for 6 to 24 hr for 2 to 5 days

* Adapted from Wigley.[27]
† Diltiazem is not as effective as the dihydropyridine class of calcium-channel blockers.[22]
‡ The Food and Drug Administration has approved the use of epoprostenol for

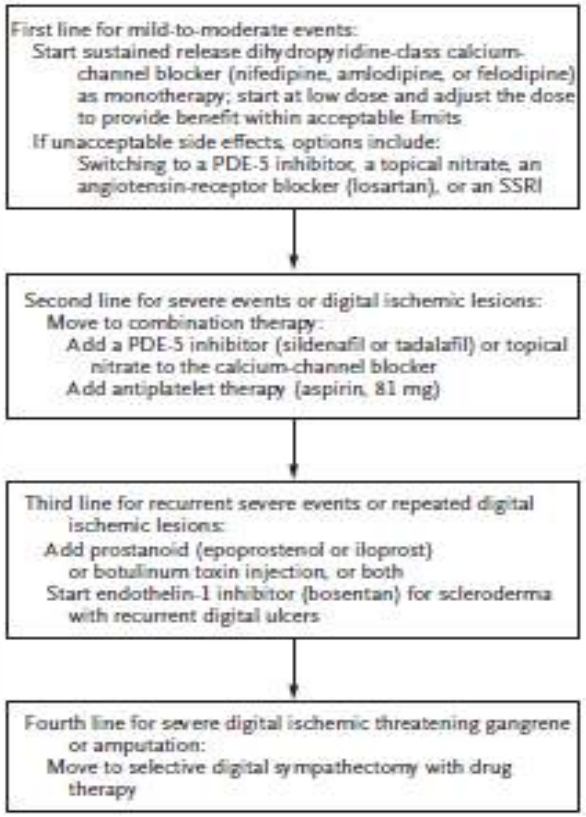
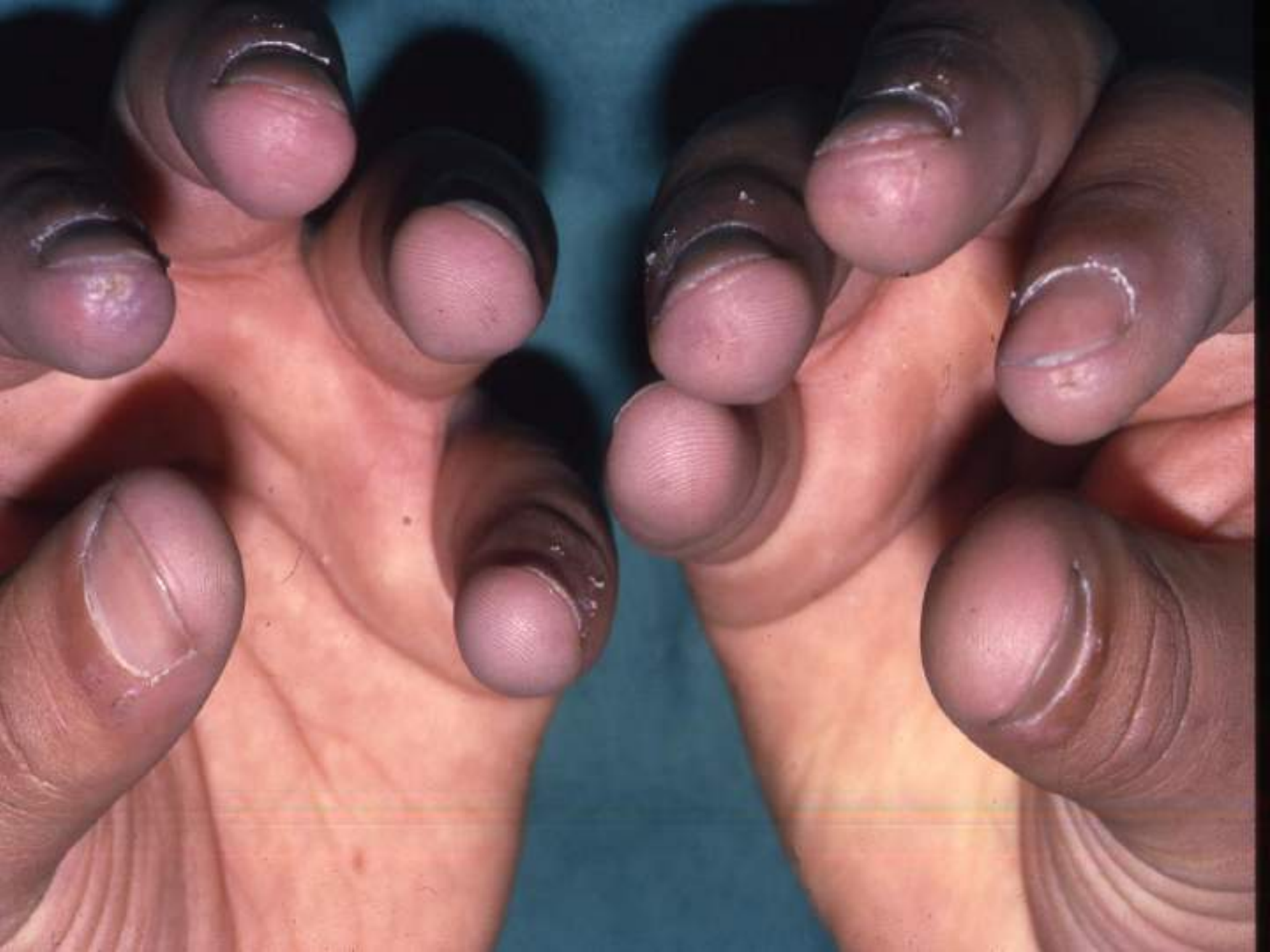
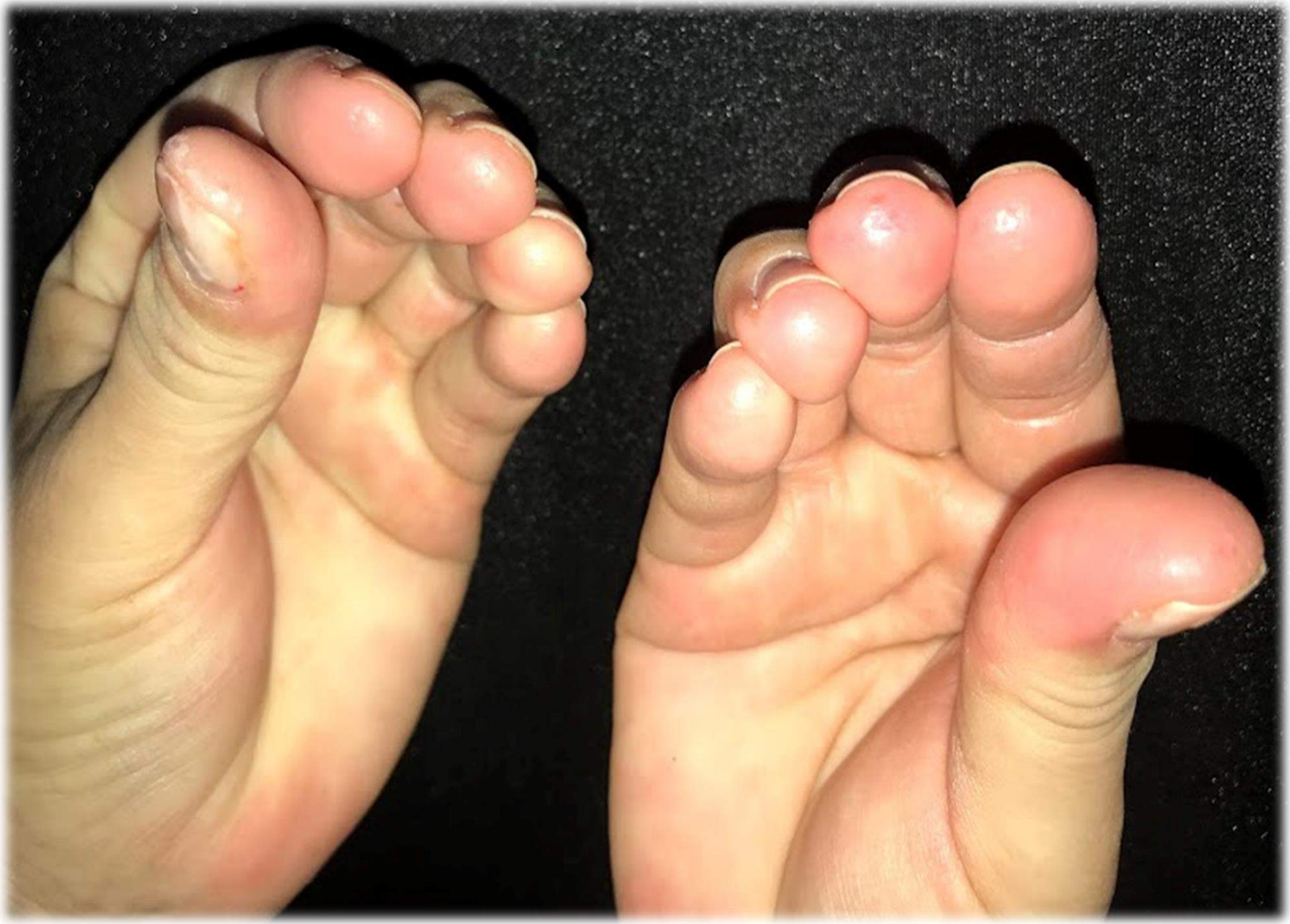


Figure 3. Current Practices in the Management of Raynaud's Phenomenon.

PDE-5 denotes phosphodiesterase type 5, and SSRI selective serotonin reuptake inhibitor.

review[29] provided moderate-quality evidence that oral calcium-channel blockers are minimally effective in the treatment of primary Raynaud's phenomenon as measured by the frequency of attacks; there were 1.72 fewer attacks per week (95% confidence interval [CI], 0.60 to 2.84) with





Esclerodermia sistémica

	DIFUSA (%)	LIMITADA(%)
Raynaud	90	99
Inflamación de dedos	95	90
Frotes de tendón	70	5
Artralgias	98	90
Calcinosis	20	40
Telangiectasias	60	90
Esofago	80	90
Intestino delgado	40	60
Enf intersticial pulmonar	70	35
Hipertensión pulmonar	15-20	20-25

Esclerodermia sistémica

	DIFUSA (%)	LIMITADA(%)
Cardiomiopatia	15	10
Crisis renal	20	1
Sd Sicca	15	35
FAN (moteado o nucleolar)	90	90
Anticentrómero	5-30	50-90
Anti Scl 70	20-60	10-15
Sobrevida a 5 a.	70	90
Sobrevida a 10 a.	50	70

Muchas gracias!

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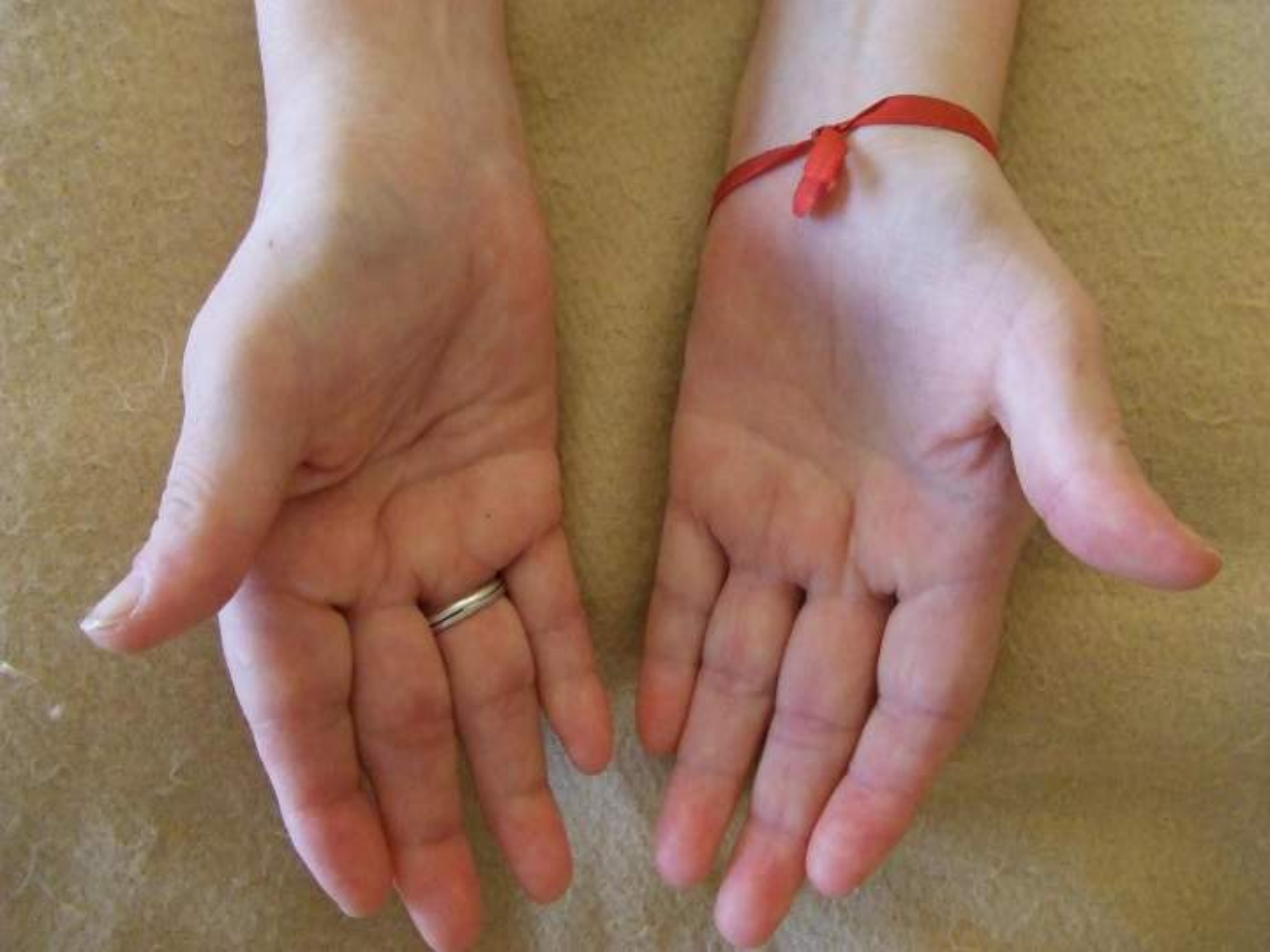

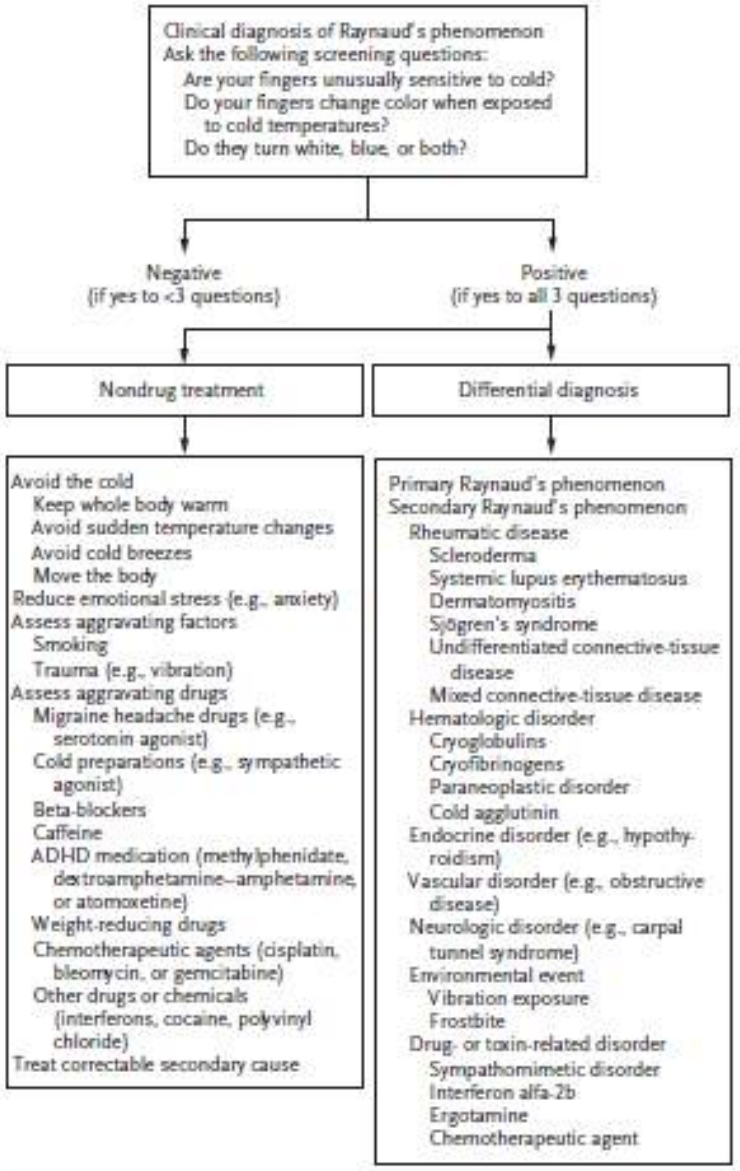

Figure 2. Nondrug Treatment and Clinical Diagnosis of Raynaud's Phenomenon.
ADHD denotes attention deficit–hyperactivity disorder.