Cutaneous T-cell lymphoma – combination modalities in treatment

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Cutaneous T-cell lymphoma (CTCL)

- **Larger spectrum of diseases with two characteristic features:**
- **1. Malignant expansion of T- cells clones stopped on the way from bone marrow precursor cells to helper cells**
- **2. Forming and location of lymphoma in the skin**

CTCL[1]: EORTC[2] Classification

- Indolent
  - Mycosis fungoides (MF)
  - Mycosis fungoides plus follicular mucinosis
  - Pagetoid reticulosis
  - Large-cell CTCL, CD30+
  - Lymphomatoid papulosis
- Aggressive
  - Sézary syndrome (SS)
  - Large-cell CTCL, CD30-
  - Immunoblastic T-cell lymphoma
  - Pleomorphic T-cell lymphoma
- Provisional
  - Granulomatous slack skin
  - CTCL, pleomorphic small/medium-sized T-cell lymphoma
  - Subcutaneous panniculitis-like T-cell lymphoma

[1] CTCL Cuteanous T-Cell Lymphoma, [2] EORTC European Organisation for Research and Treatment of Cancer

Cutaneous T-cell lymphoma

- **Three stages of CTCL with epidermotrophism:**
  - **I. Eczematoid stage (premycotic, patch stage)**
  - **II. Infiltrative stage (plaque stage)**
  - **III. Tumor stage**
- **The disease usually proceeds from stage to stage, various alterations of more stages can be present simultaneously as well.**

CTCL: Stage and Prognosis

	IA	IB	IIA	IIB	III	IVA	IVB
5-year DSS (%) *	100	96	68	80	40	0	
10-year DSS (%)	98	83	68	42	20	0	
Median survival (yr)	>32	12.1	10.0	2.9	3.6-4.6	1.1	1.1
ODP (%) †	9	20	34				
5-year RFS** (%)	50	36	9				
10-year RFS (%)	31	3					

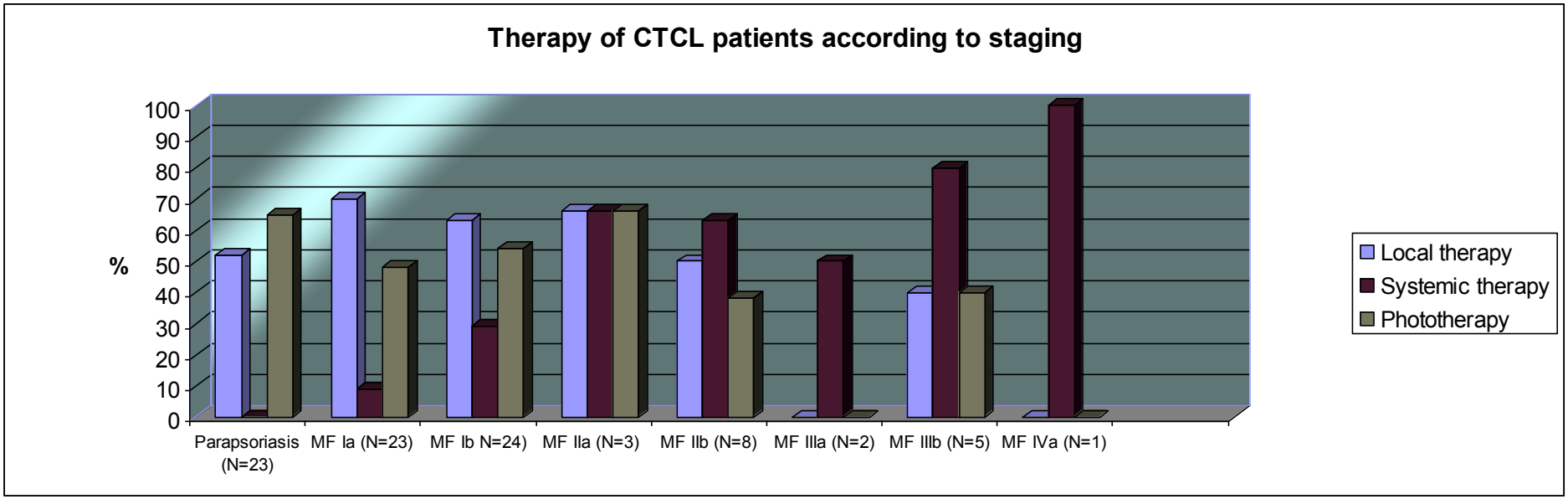
[1] DSS, disease-specific survival; [2] ODP, overall disease progression; [3] RFS, relapse-free survival

Methods used for CTCL treatment in the Ist Dept. of Derm. in Brno

- **Topically**: steroids
  tar
- **Phototherapy**: UVB 311 nm
  SUP
  CUP
  PUVA
- **Photodynamic therapy**
- **Systemic treatment**: acitretin
  Interferon α2a
  Interferon α2b
  (steroids)
  bexarotene
- **Radiotherapy** in co-operation with Dept. of Oncology

Our experience with combination of therapeutical modalities for advanced CTCL

- PUVA / UVB 311nm + retinoids
- PUVA + interferons
- PUVA + retinoids + interferons
- PUVA + retionoids + interferons + radiotherapy
- PUVA + bexarotene
- Other combinations

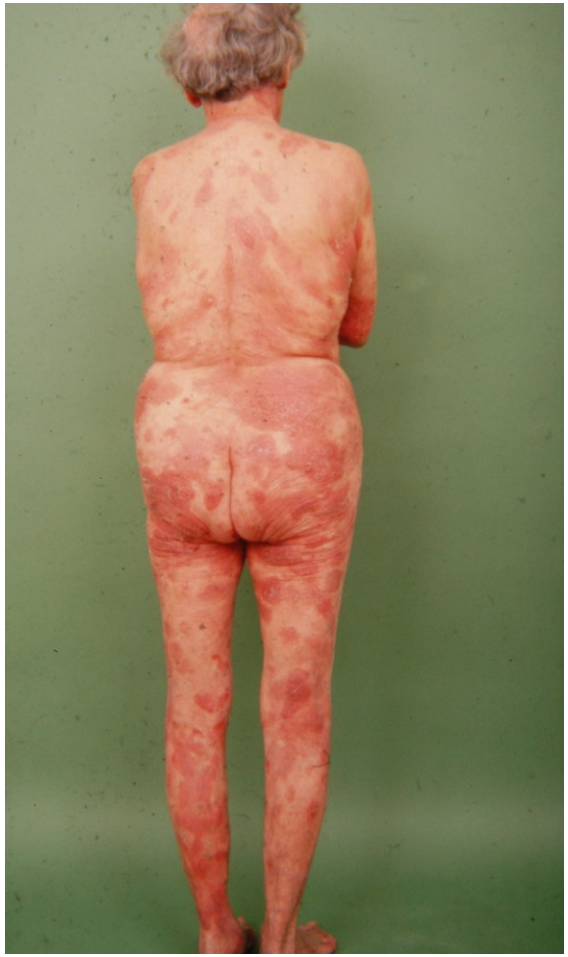

Therapy of CTCL patients according to staging
%
100
90
80
70
60
50
40
30
20
10
0
Parapsoriasis (N=23)
MF Ia (N=23)
MF Ib N=24)
MF IIa (N=3)
MF IIb (N=8)
MF IIIa (N=2)
MF IIIb (N=5)
MF IVa (N=1)
Local therapy
Systemic therapy
Phototherapy

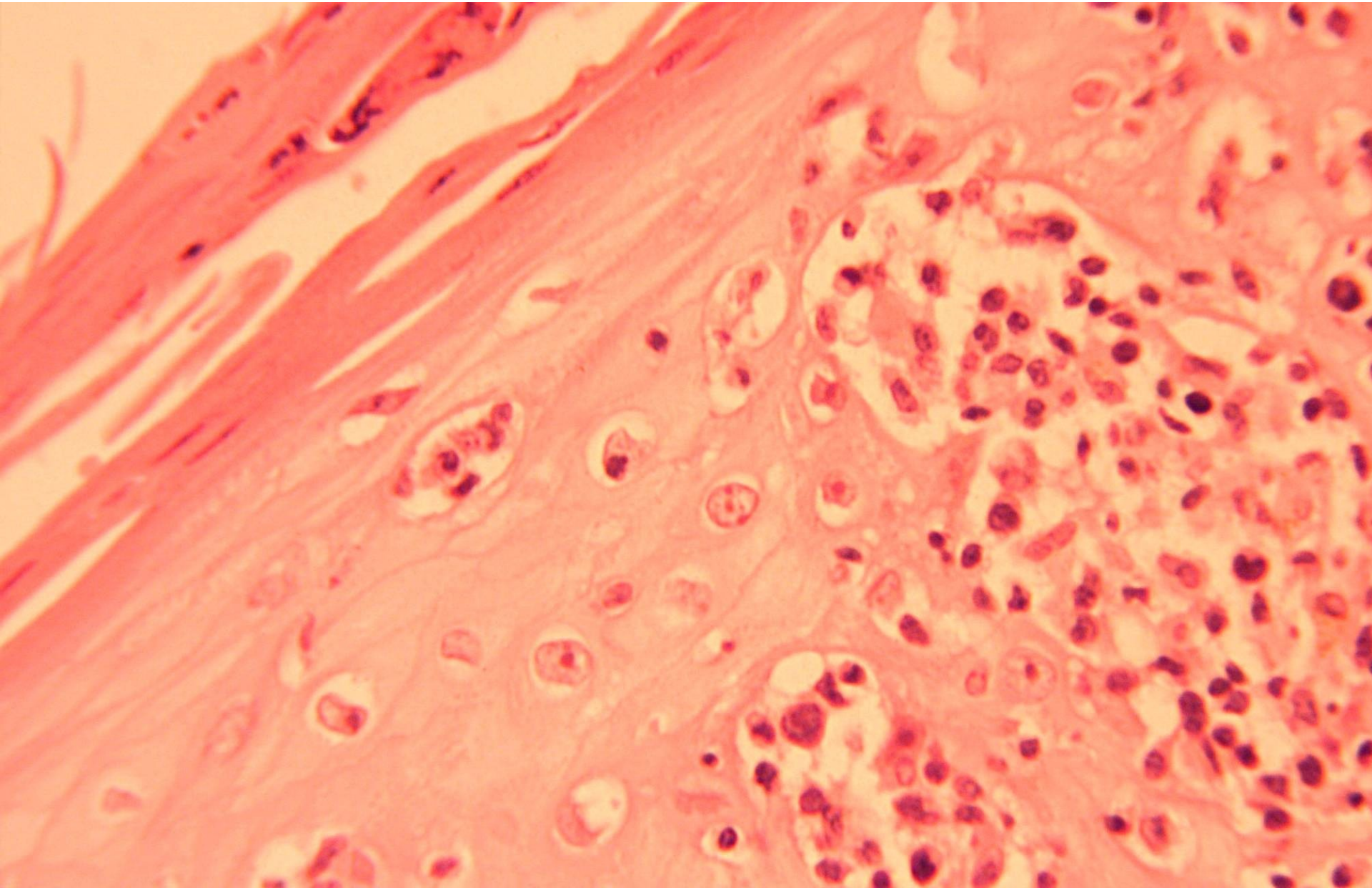
Bexarotene Properties

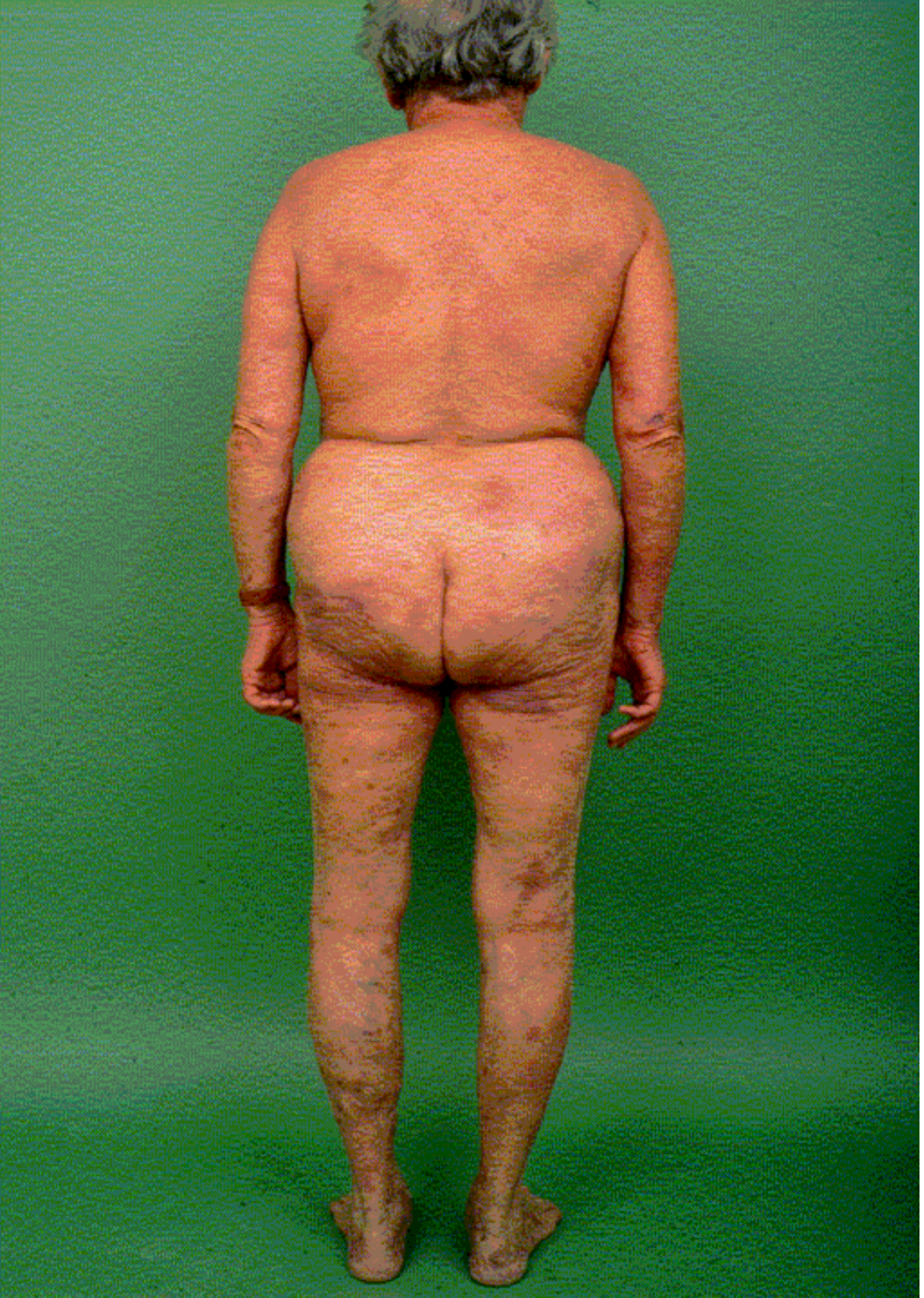
- Novel retinoid rexinoid
- Selective retinoid X receptor (RXR) antagonist
- Modulates expression of genes regulated by retinoid response elements
- Available as topical or systemic treatment
- Mono- or combination therapy

Bexarotene: Adverse Events

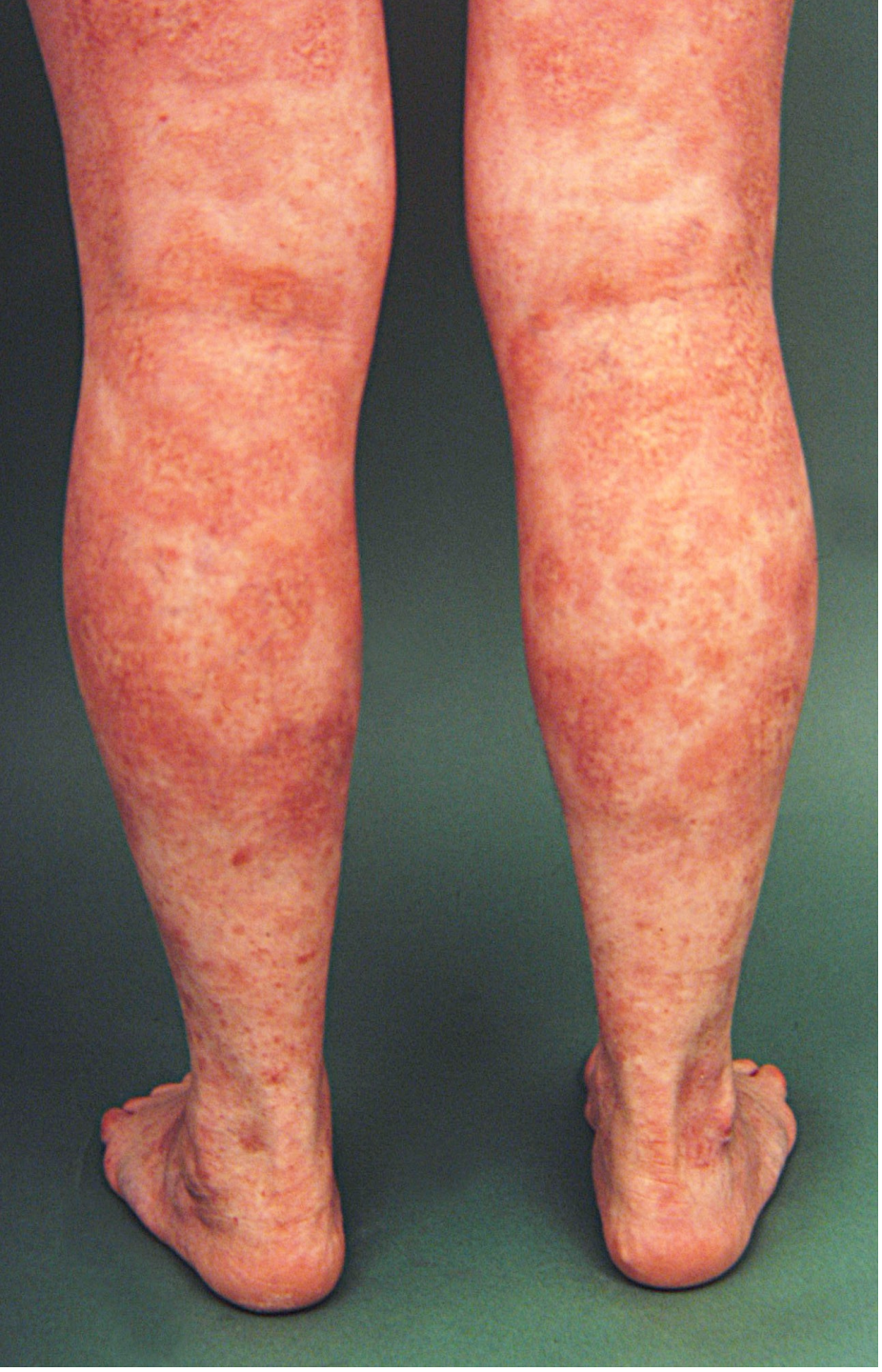
Adverse event	Incidence by initial dose ($mg/m^2/day$) 300 (n=84)	> 300 (n=53)
Hyperlididaemia	79%	79%
Hypercholestolaemia	32%	62%
Headache	30%	42%
Hypothyroidism	29%	53%
Pruritus	25%	15%
Asthaenia	20%	45%
Leukopenia	17%	47%
Rash	17%	23%
Infection	13%	23%
Exfoliative dermatitis	10%	28%
Diarrhoea	7%	42%
Anaemia	6%	25%
Anorexia	2%	23%



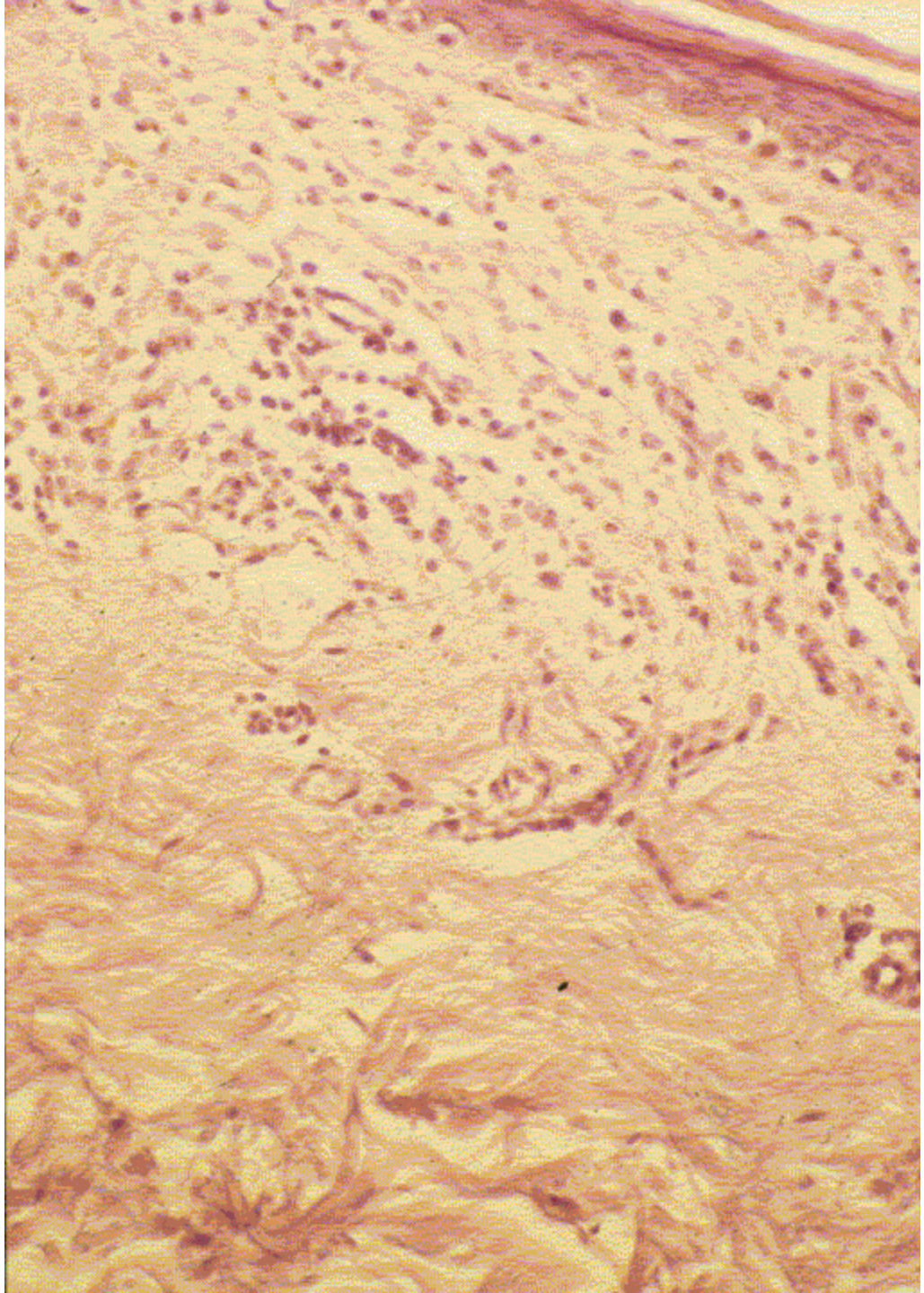


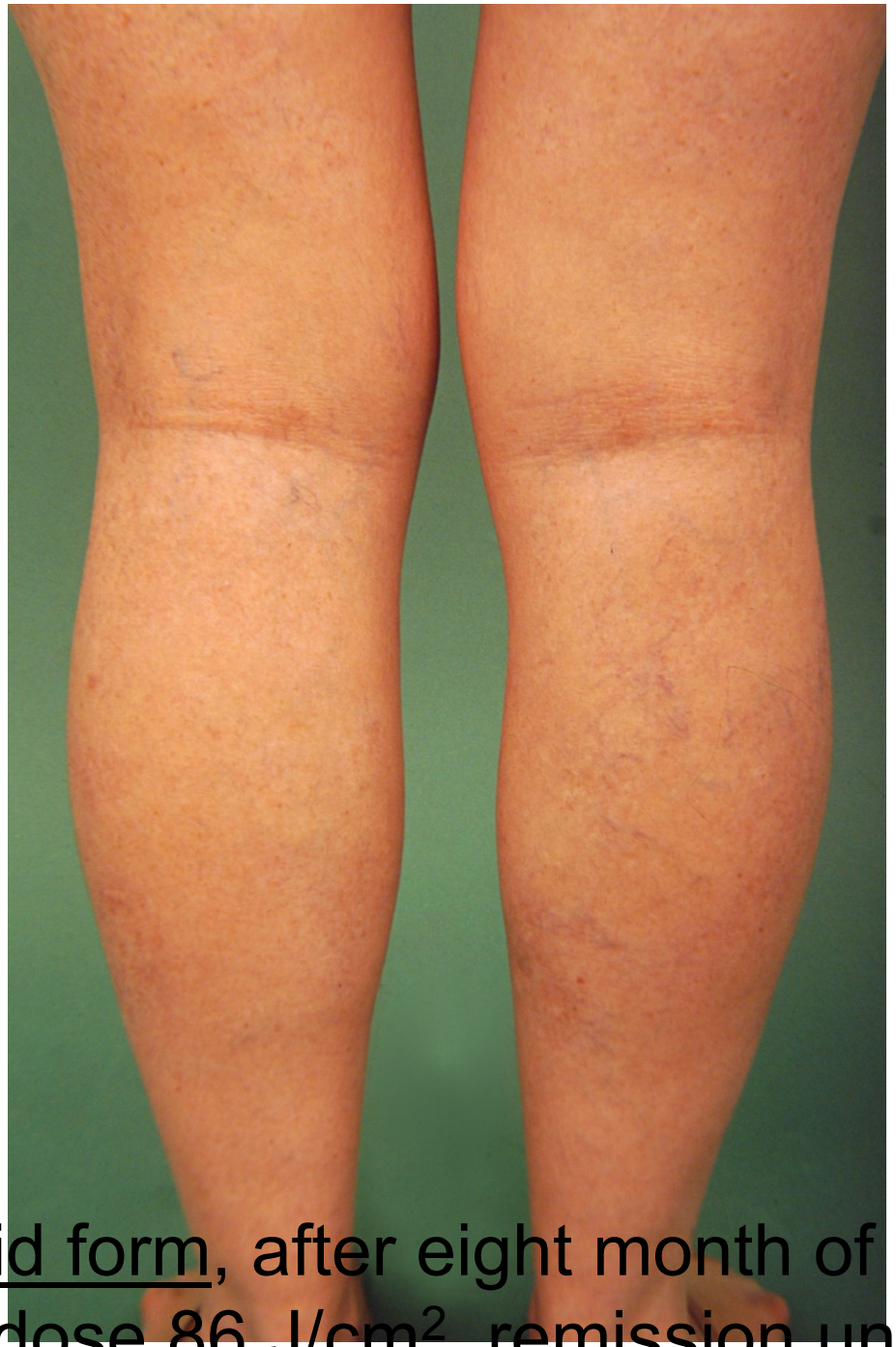


MF, after six month of PUVA

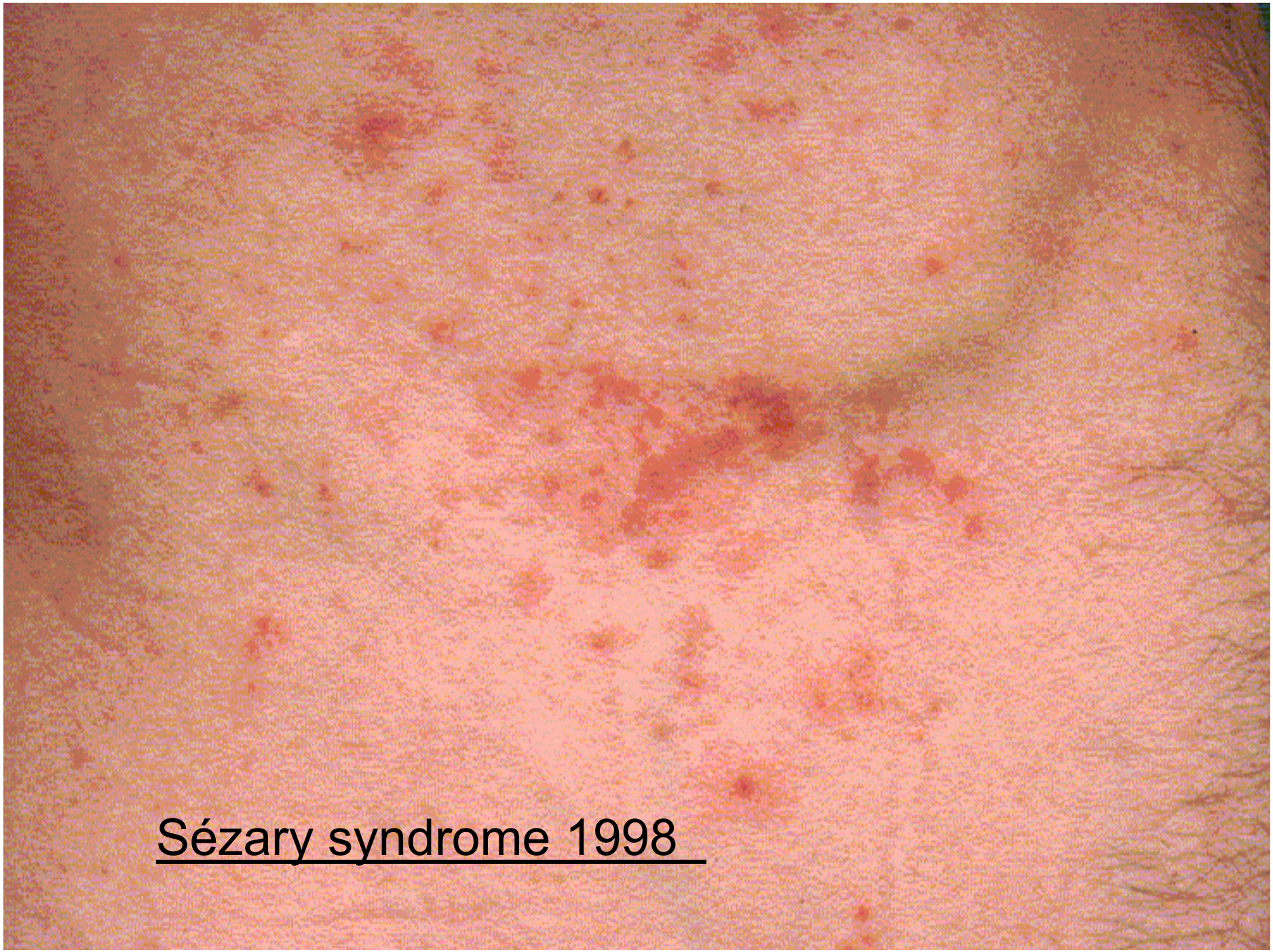


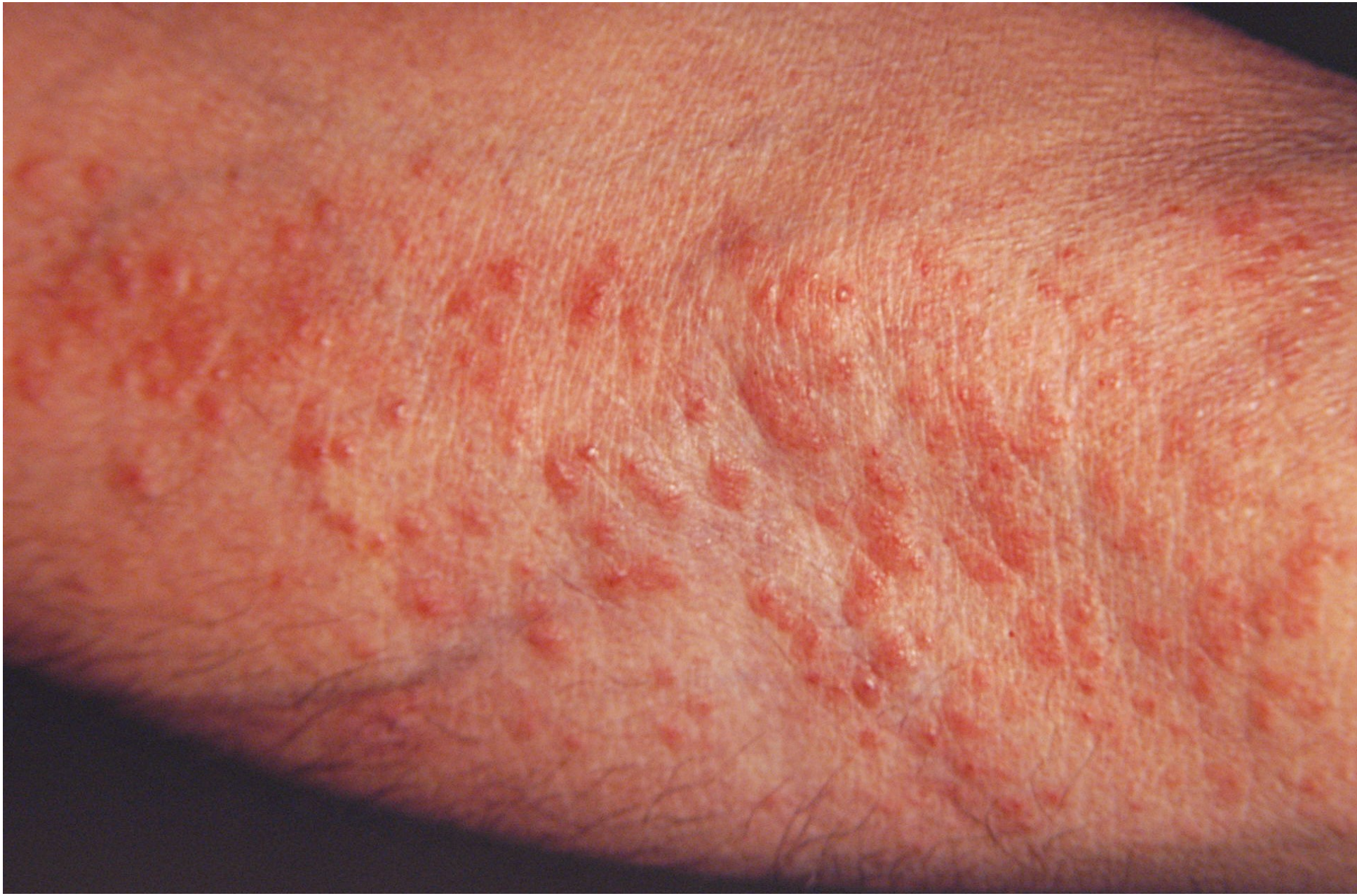
MF, lichenoid form, 1999

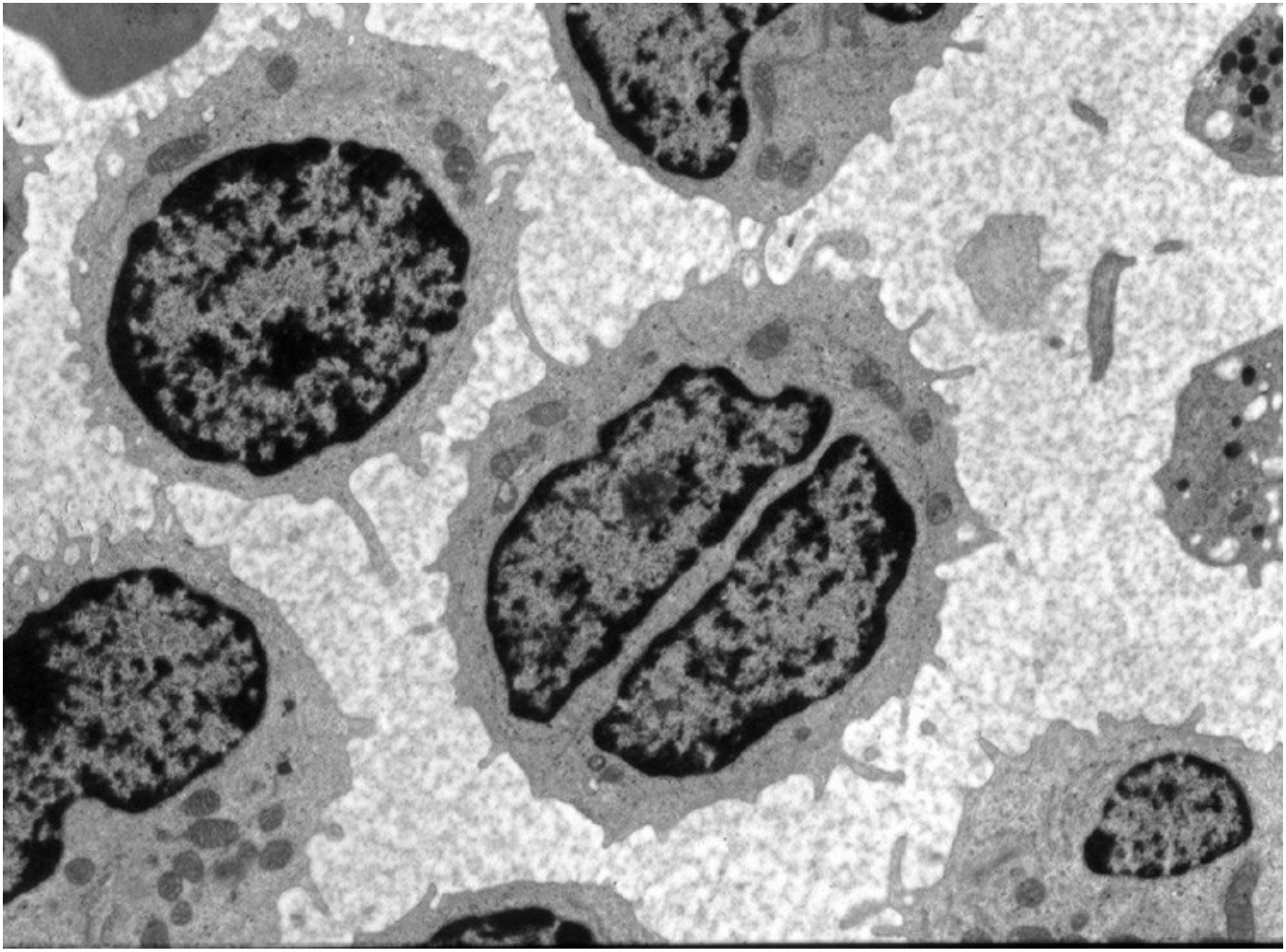


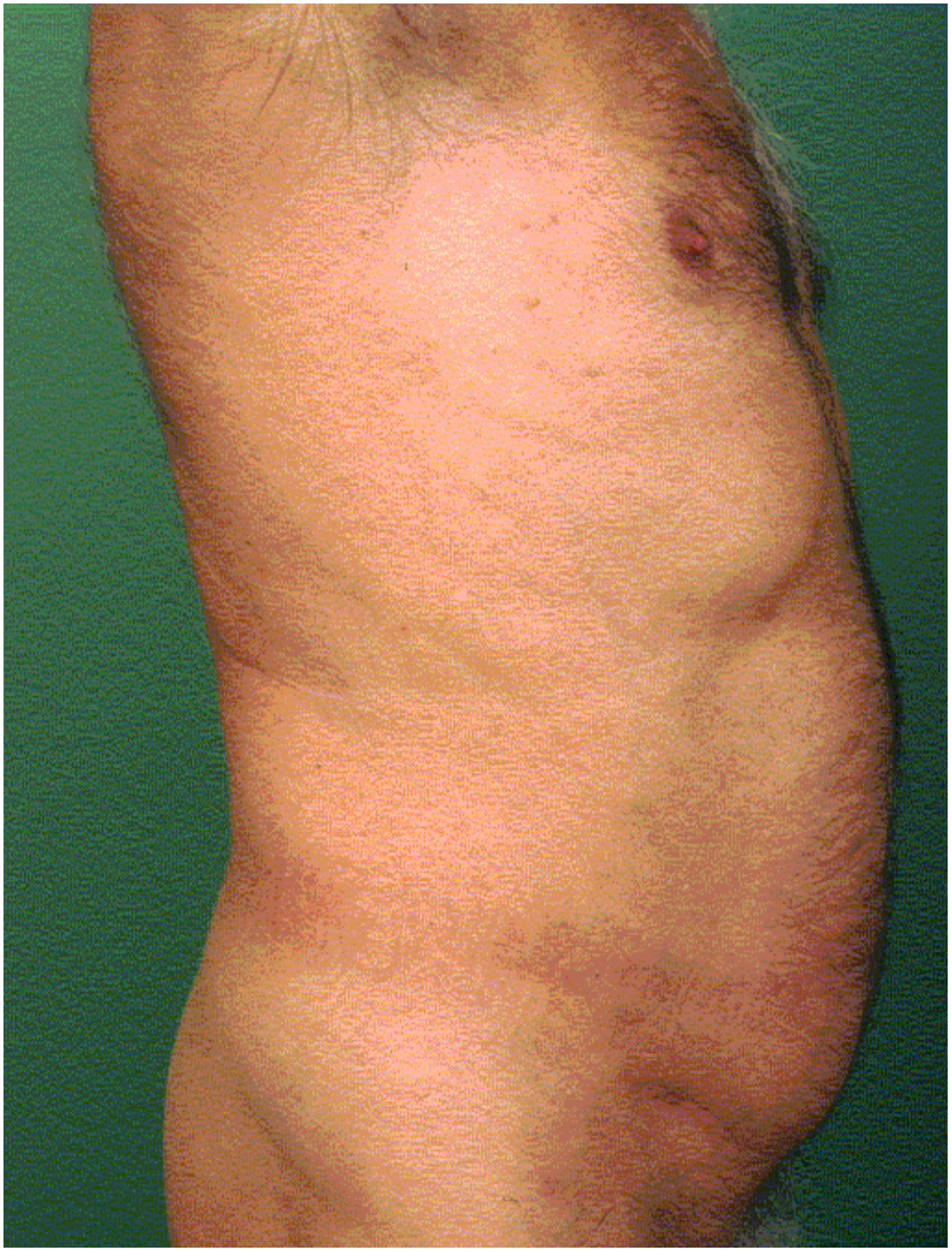


MF, lichenoid form, after eight month of PUVA, cumulative dose 86 J/cm^2, remission until now

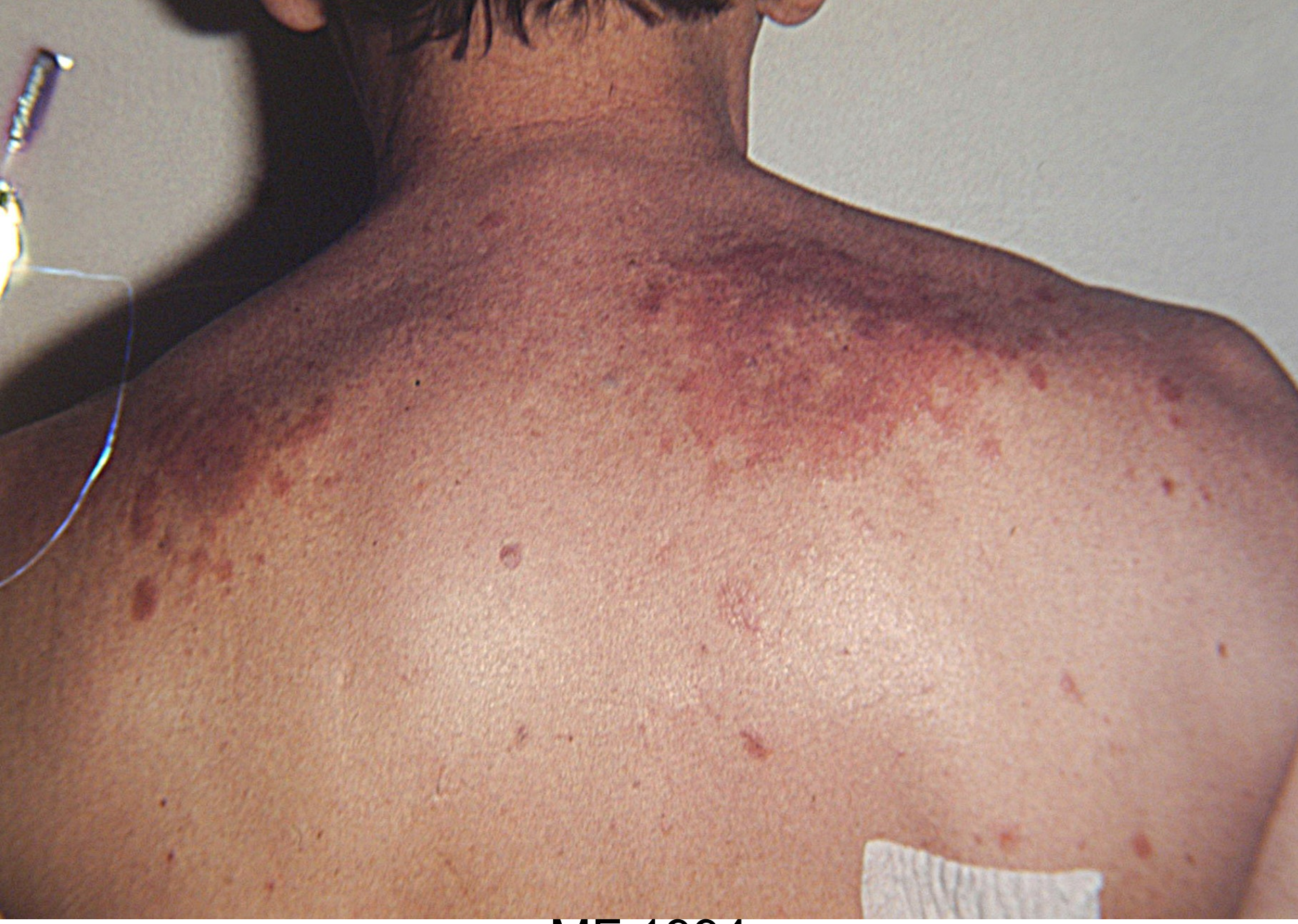

Sézary syndrome 1998



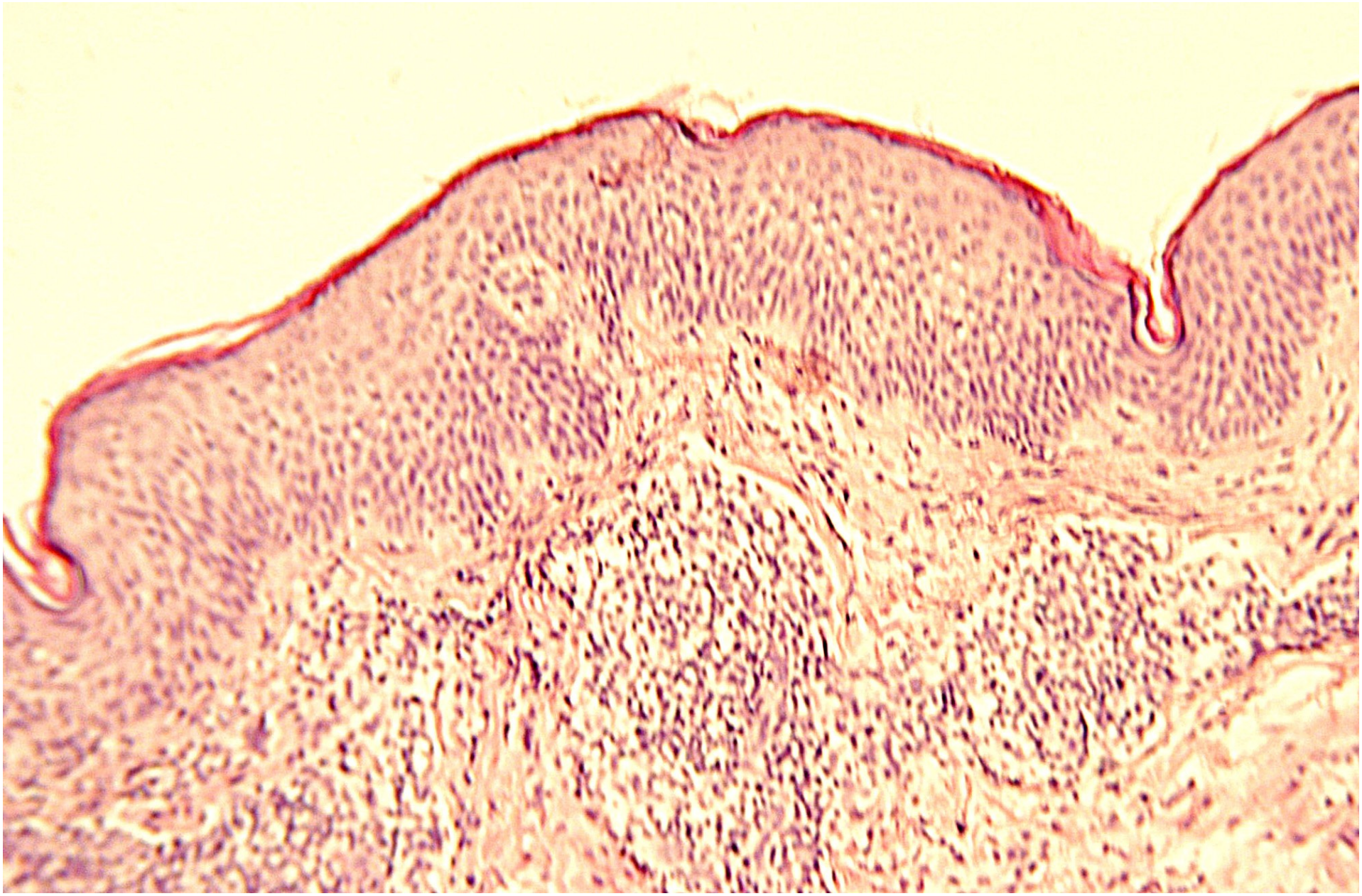


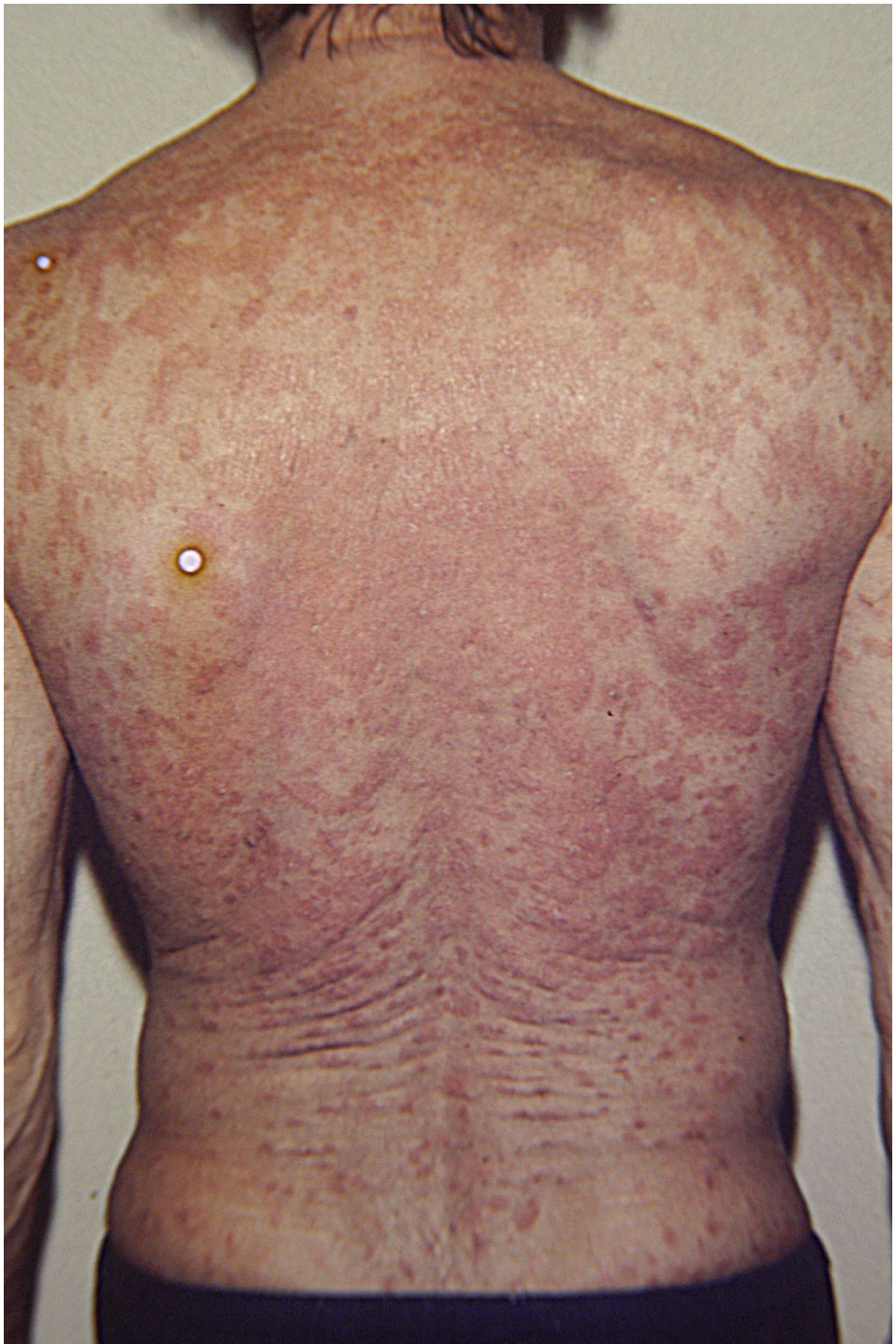


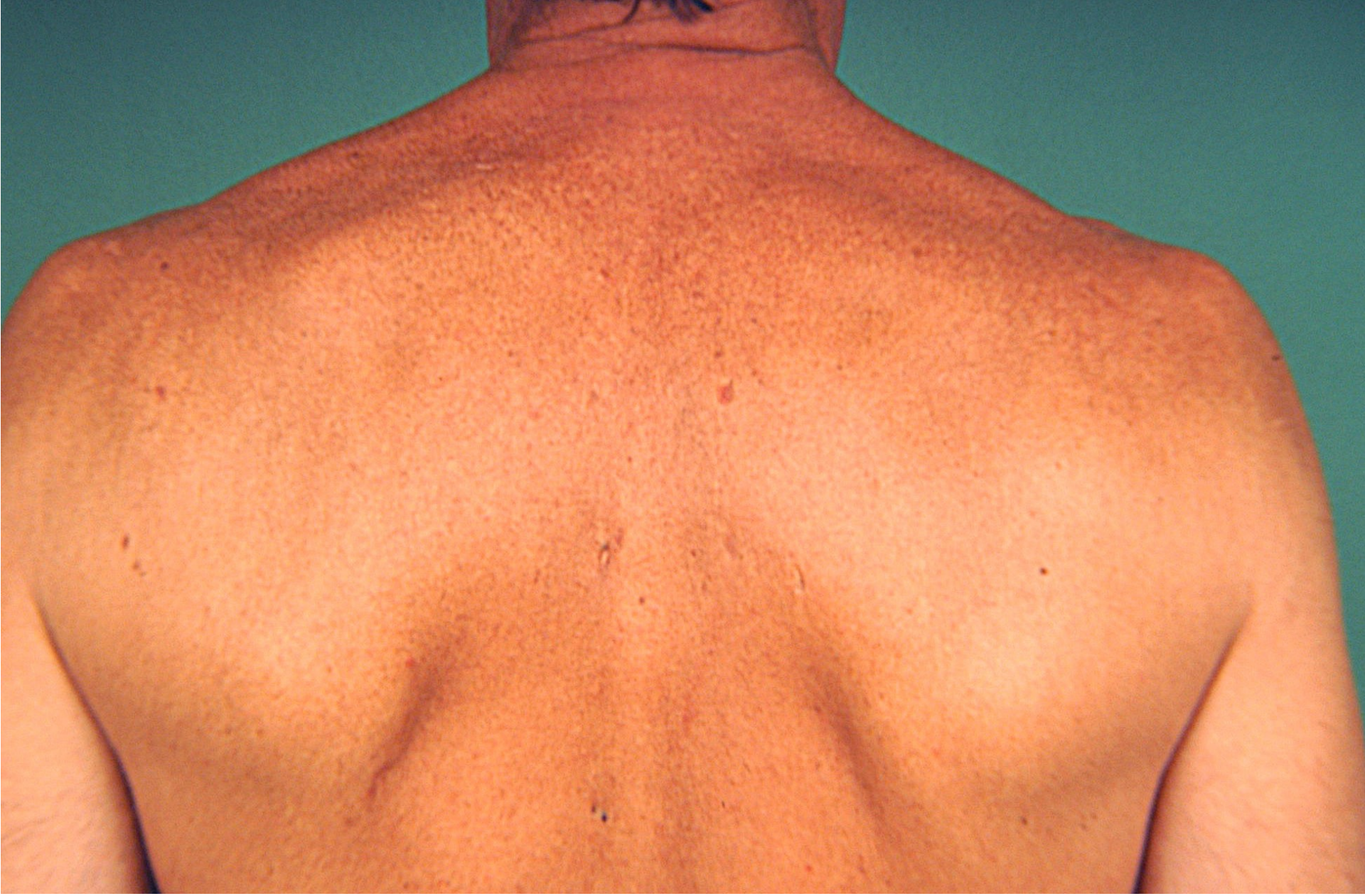
Sézary syndrome,
after rePUVA
1054 J/cm^2



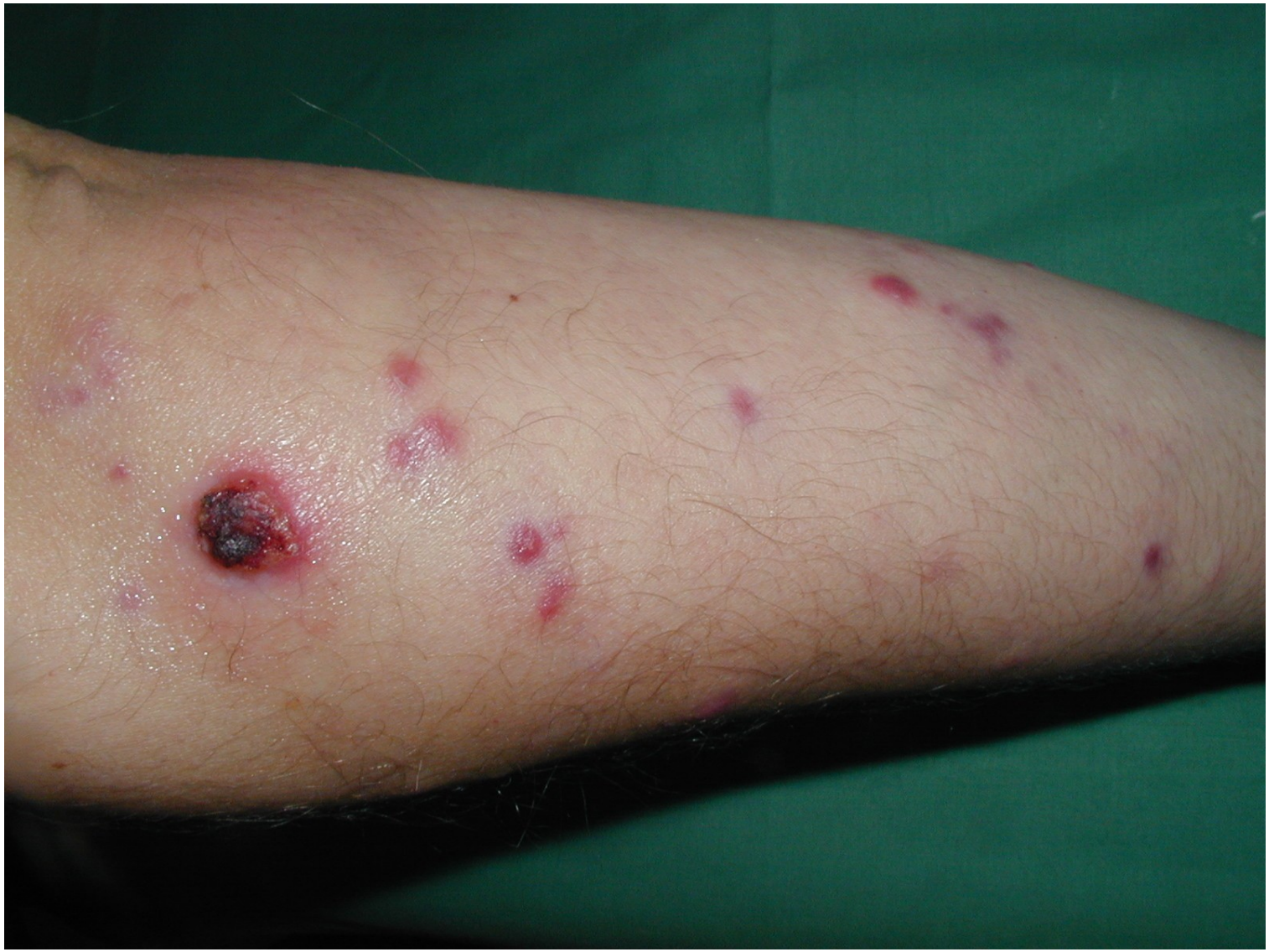
MF 1994





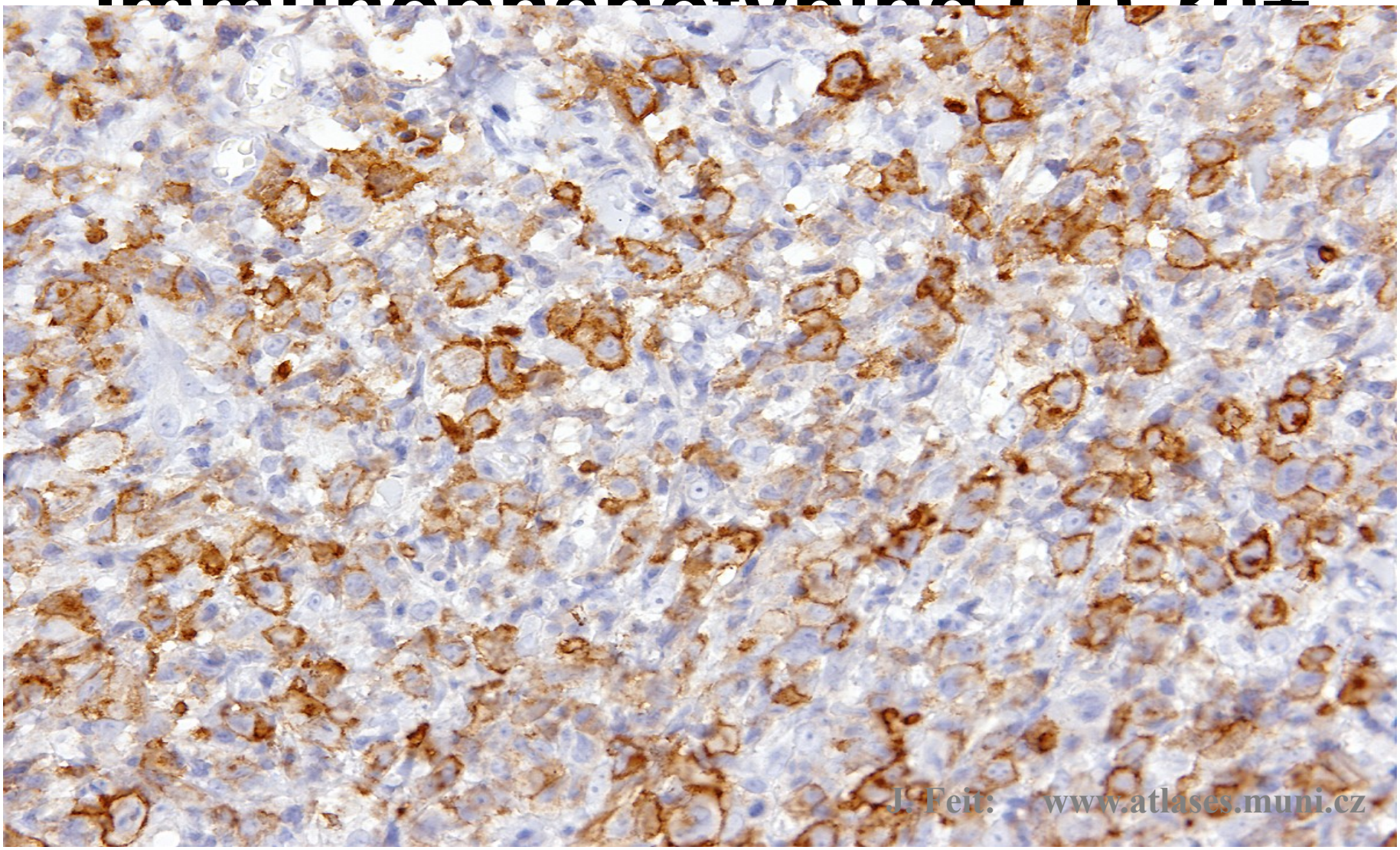


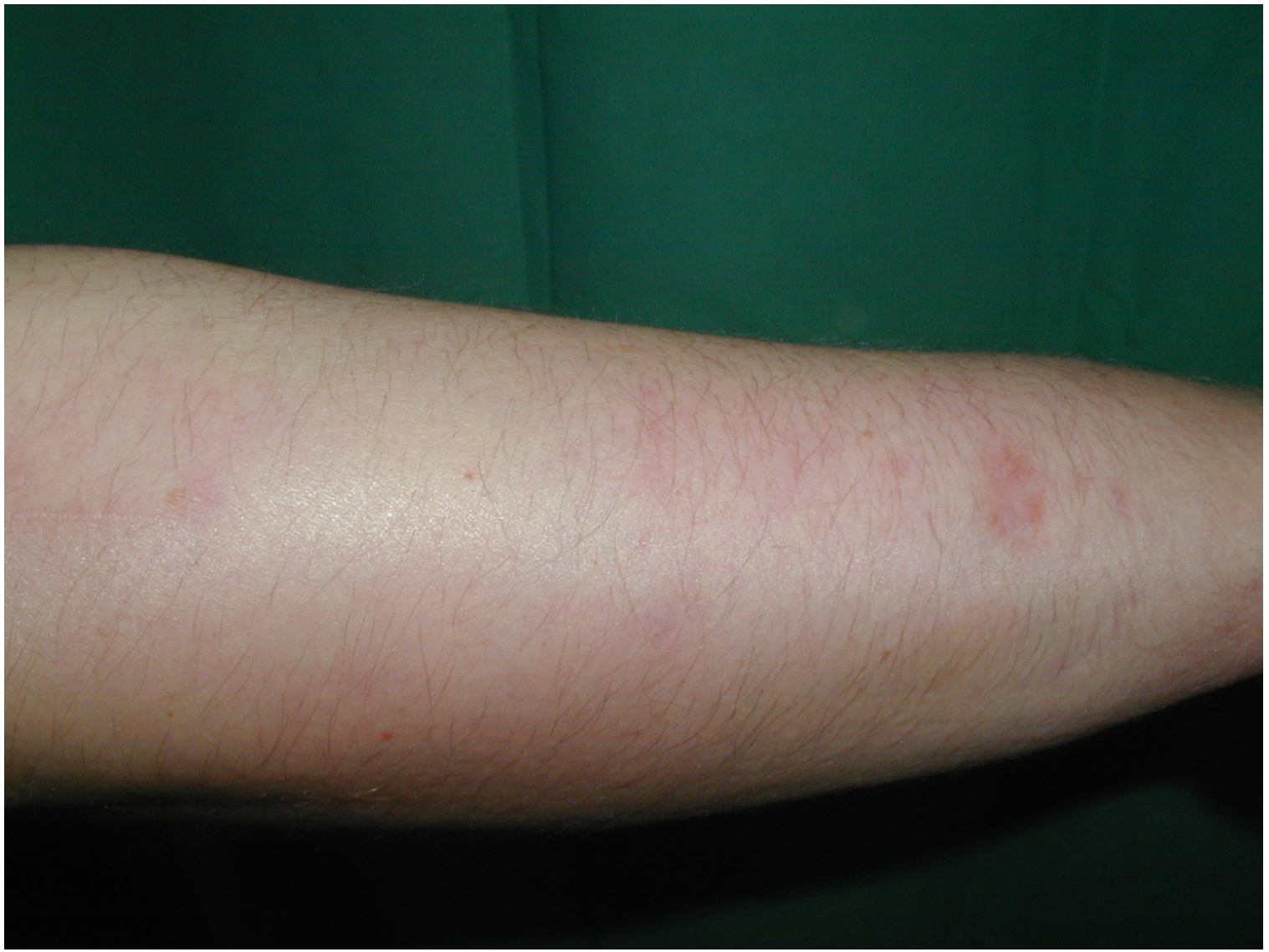
In remission after IFNα + acitretin until 2009



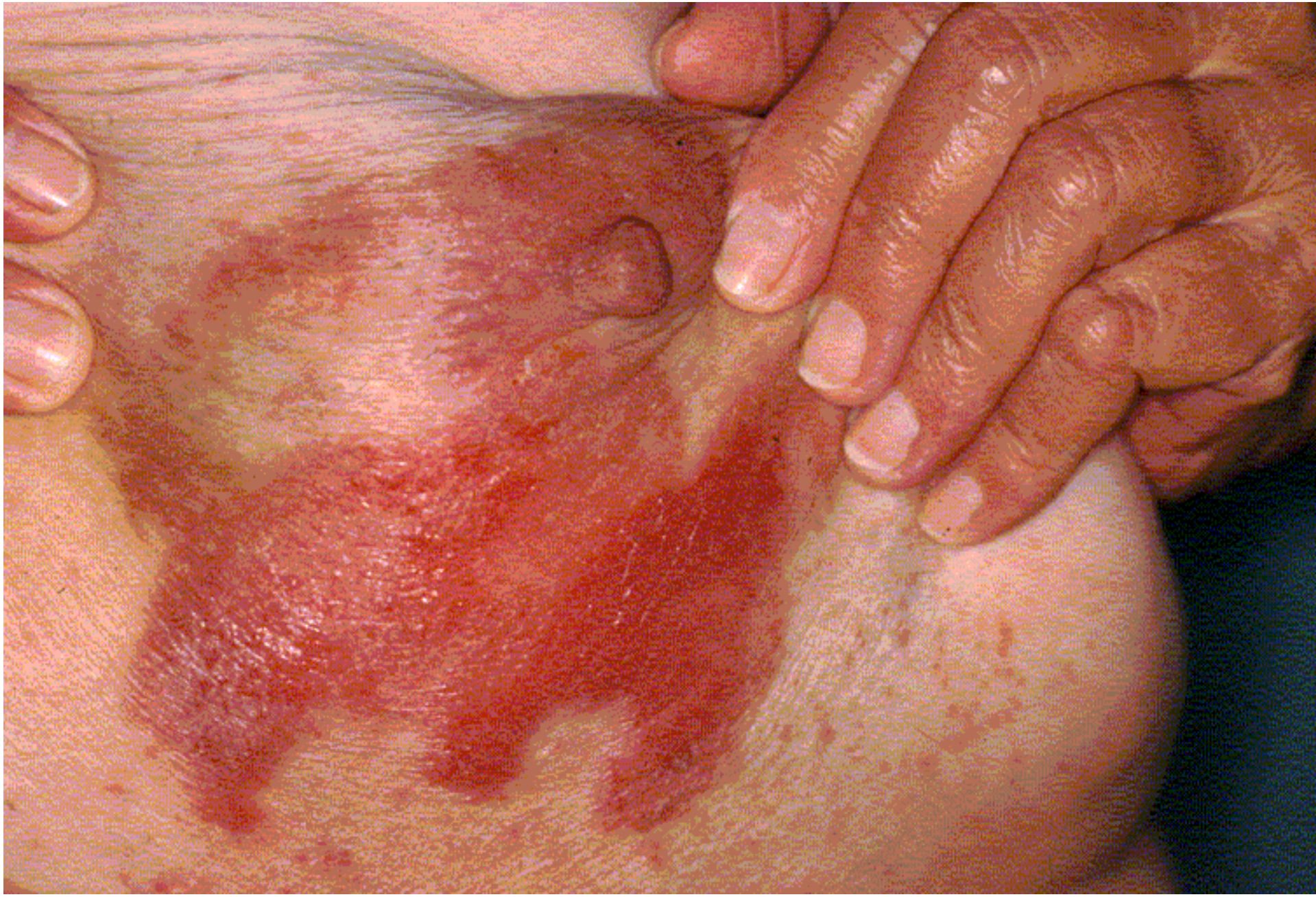
LyP

Immunophenotyping CD 30+

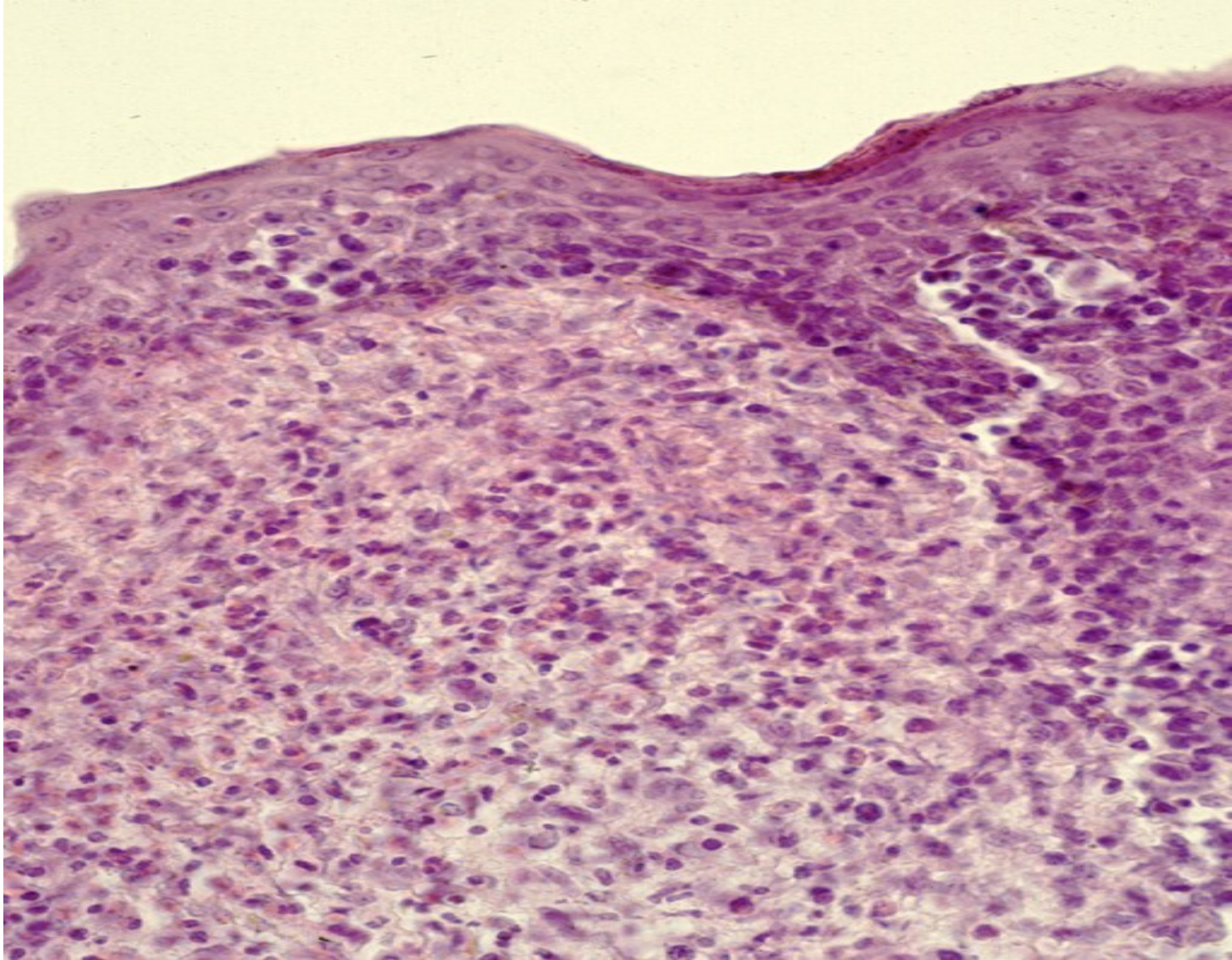


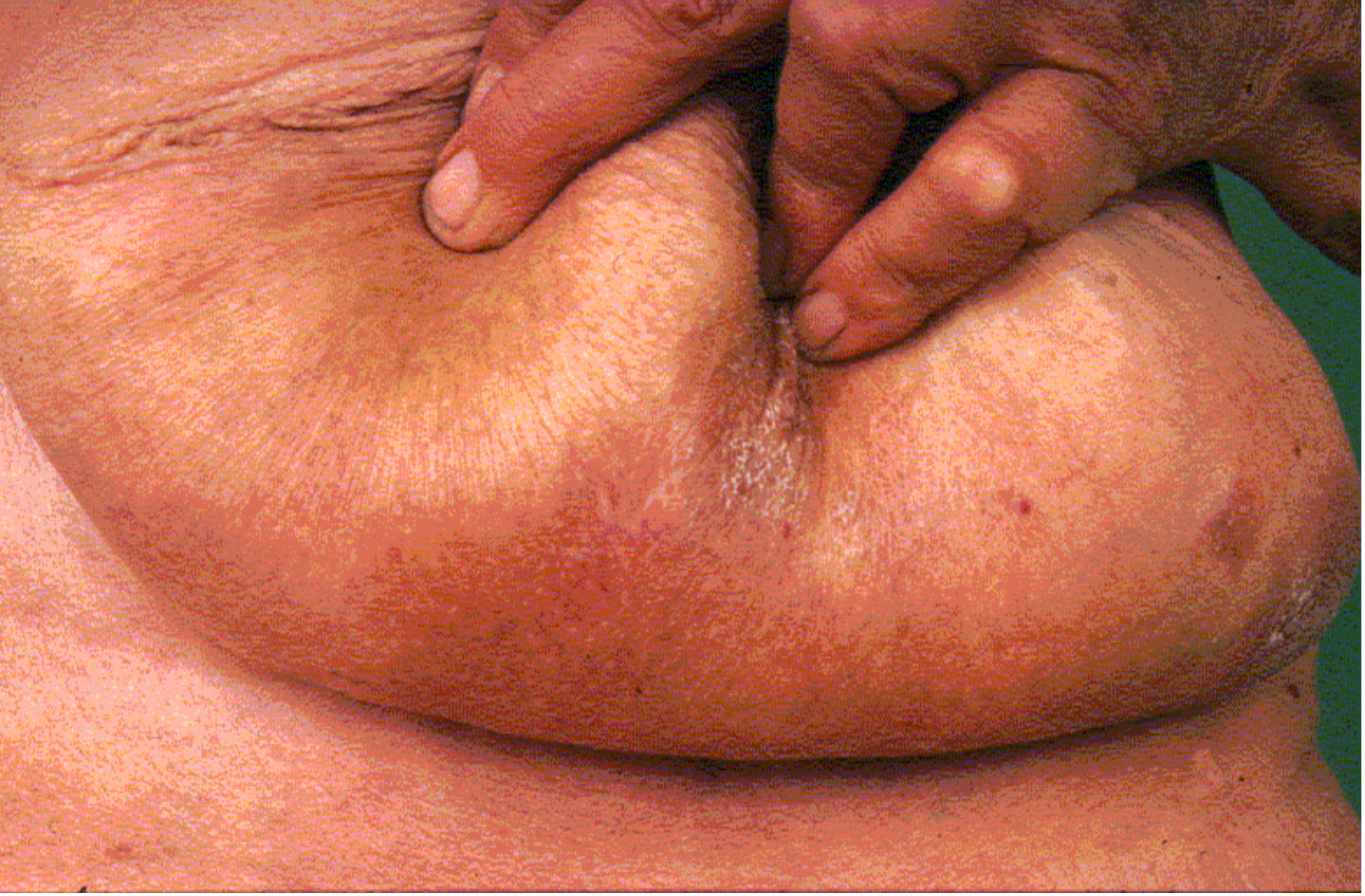


Remission after rePUVA treatment

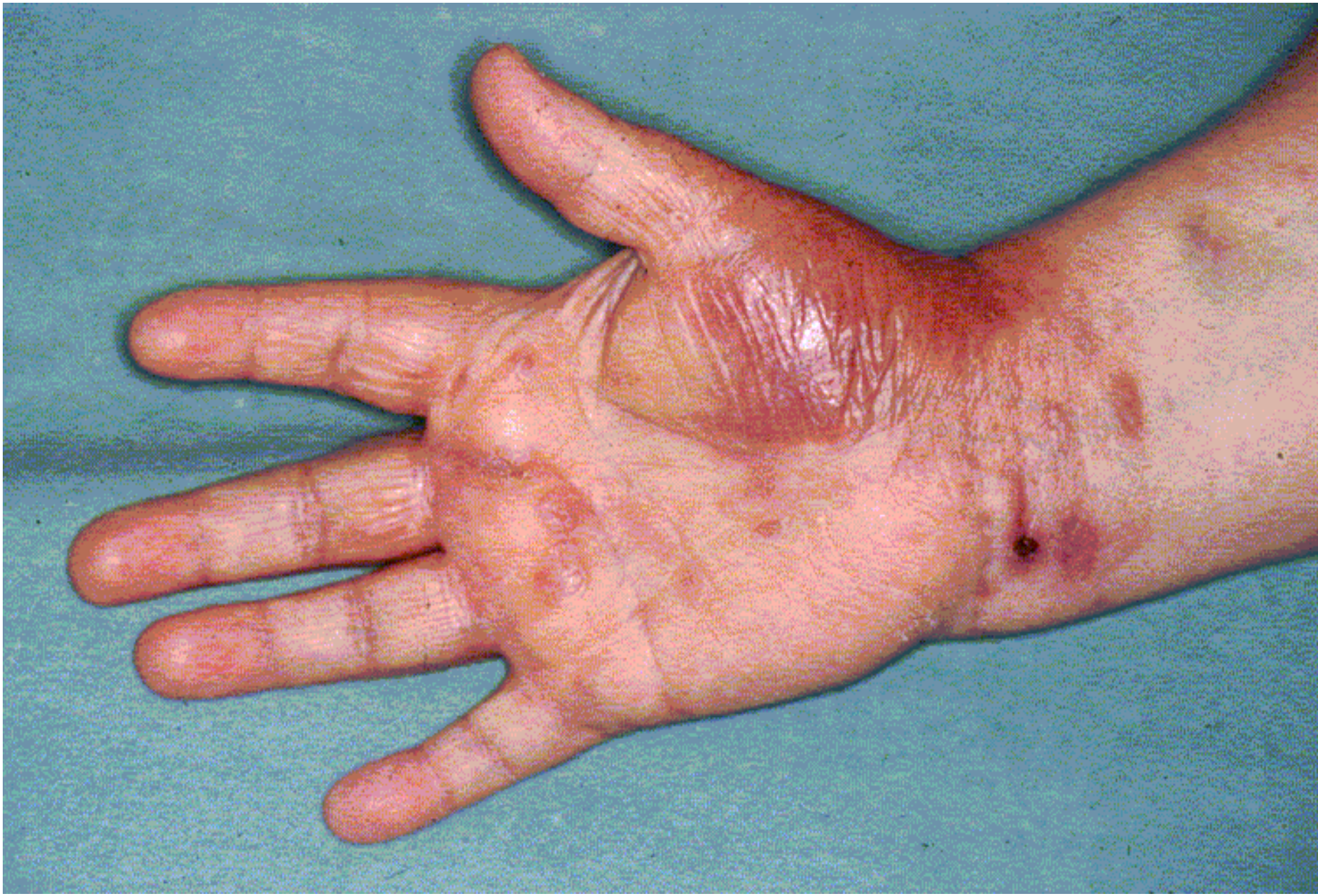


MF 1998

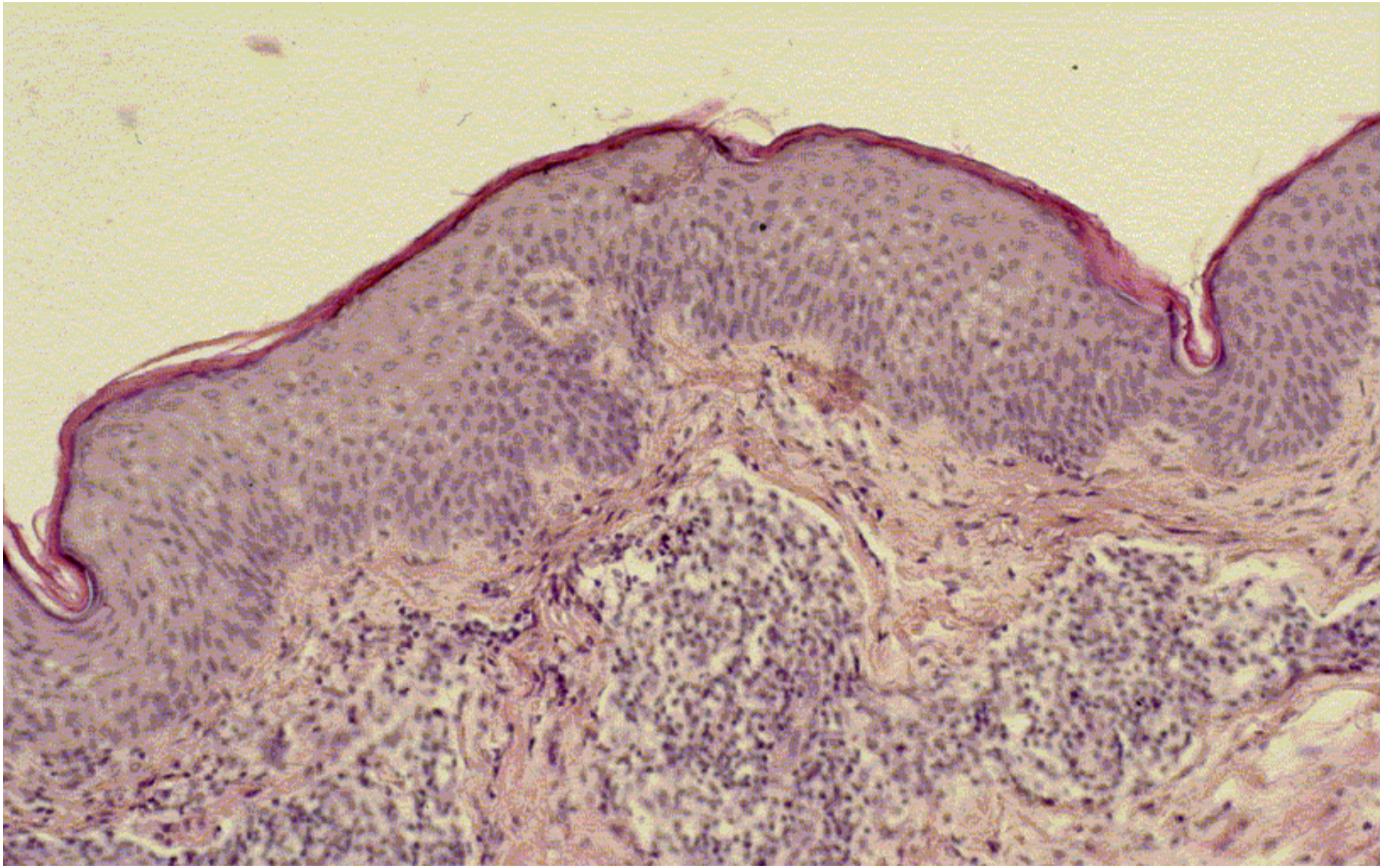


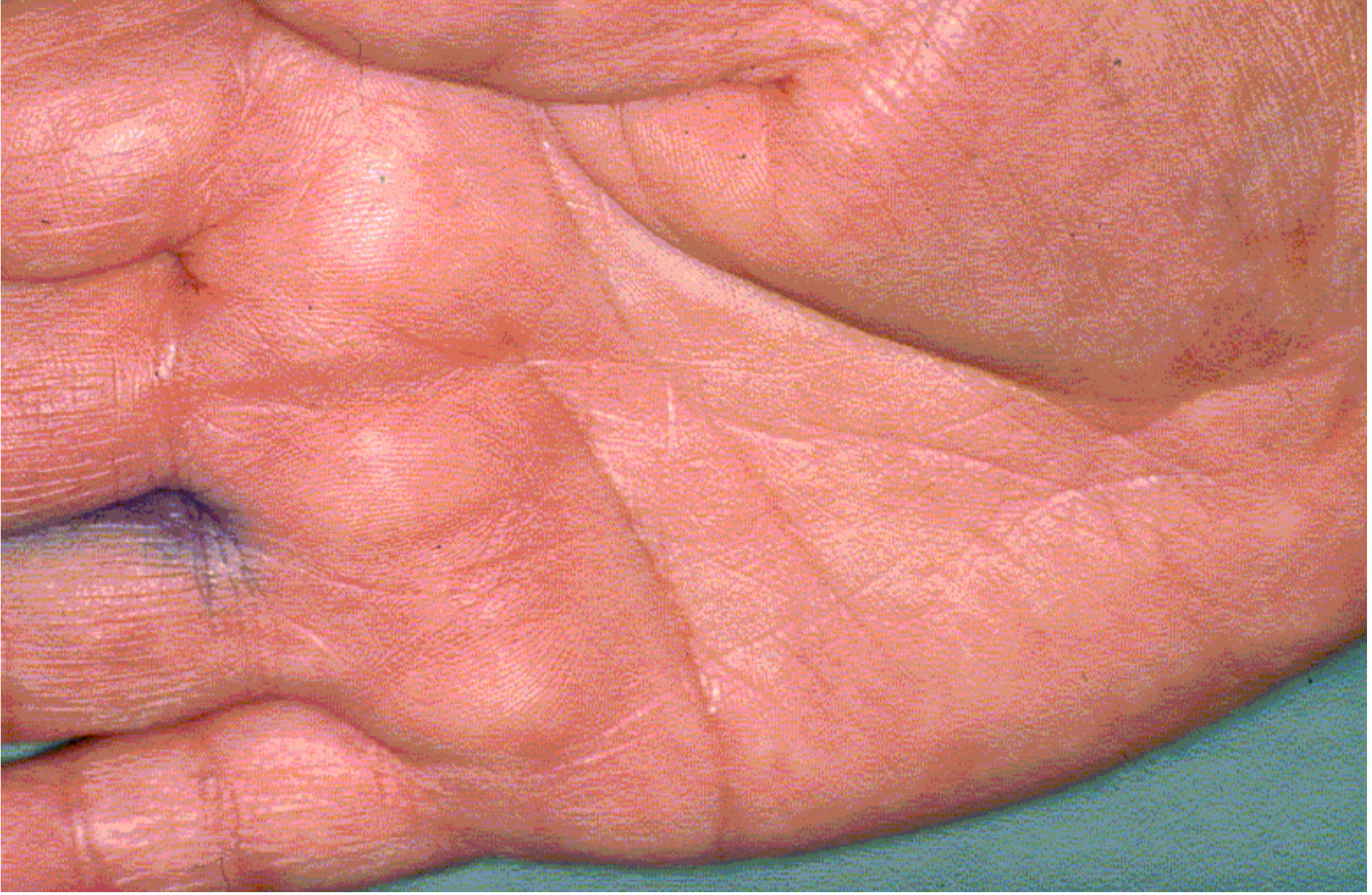


MF after 12 month of PUVA and Intron-A cumulative dose 210 J/cm^2, in remission with low dose of acitretin until now

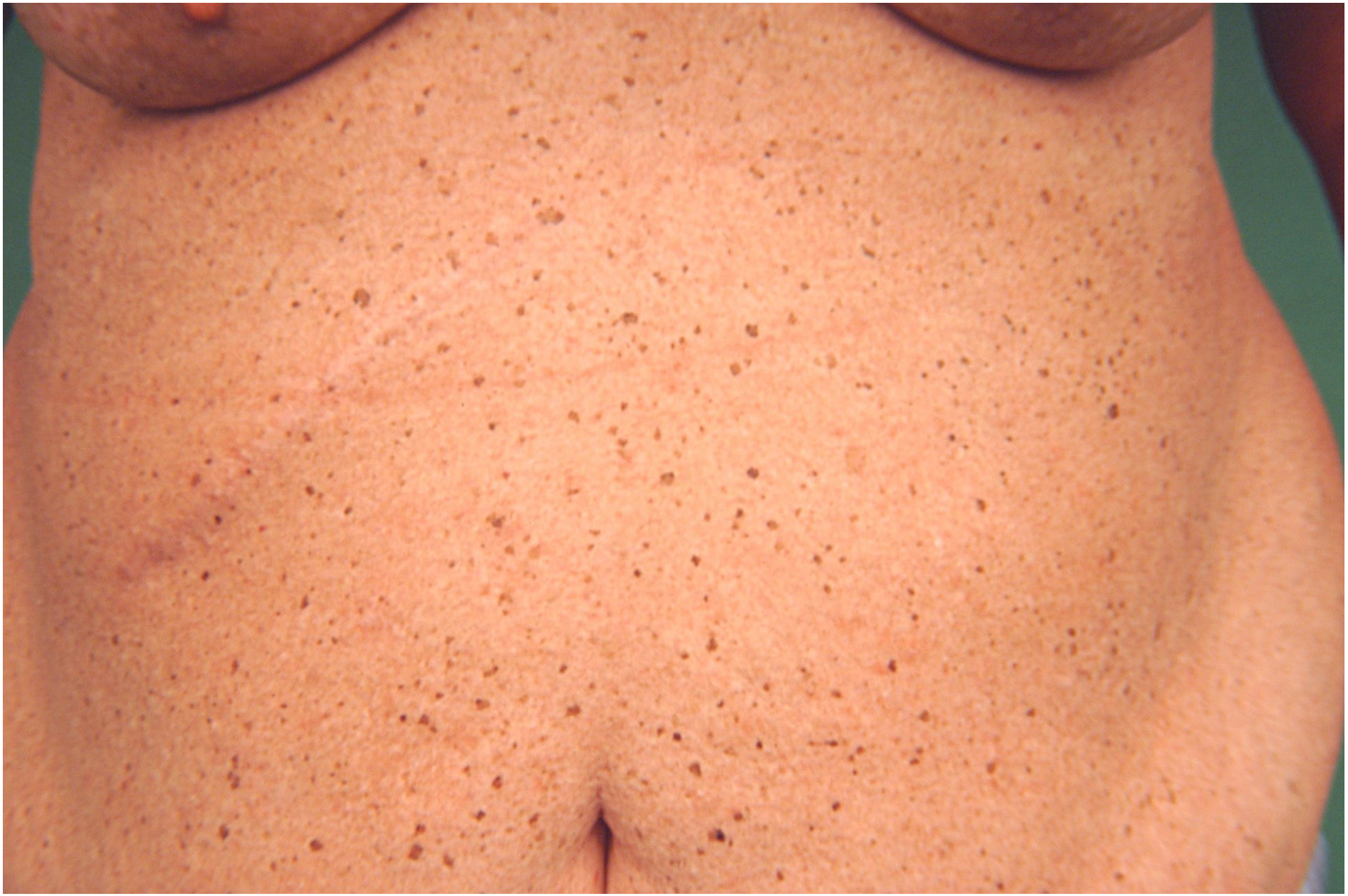


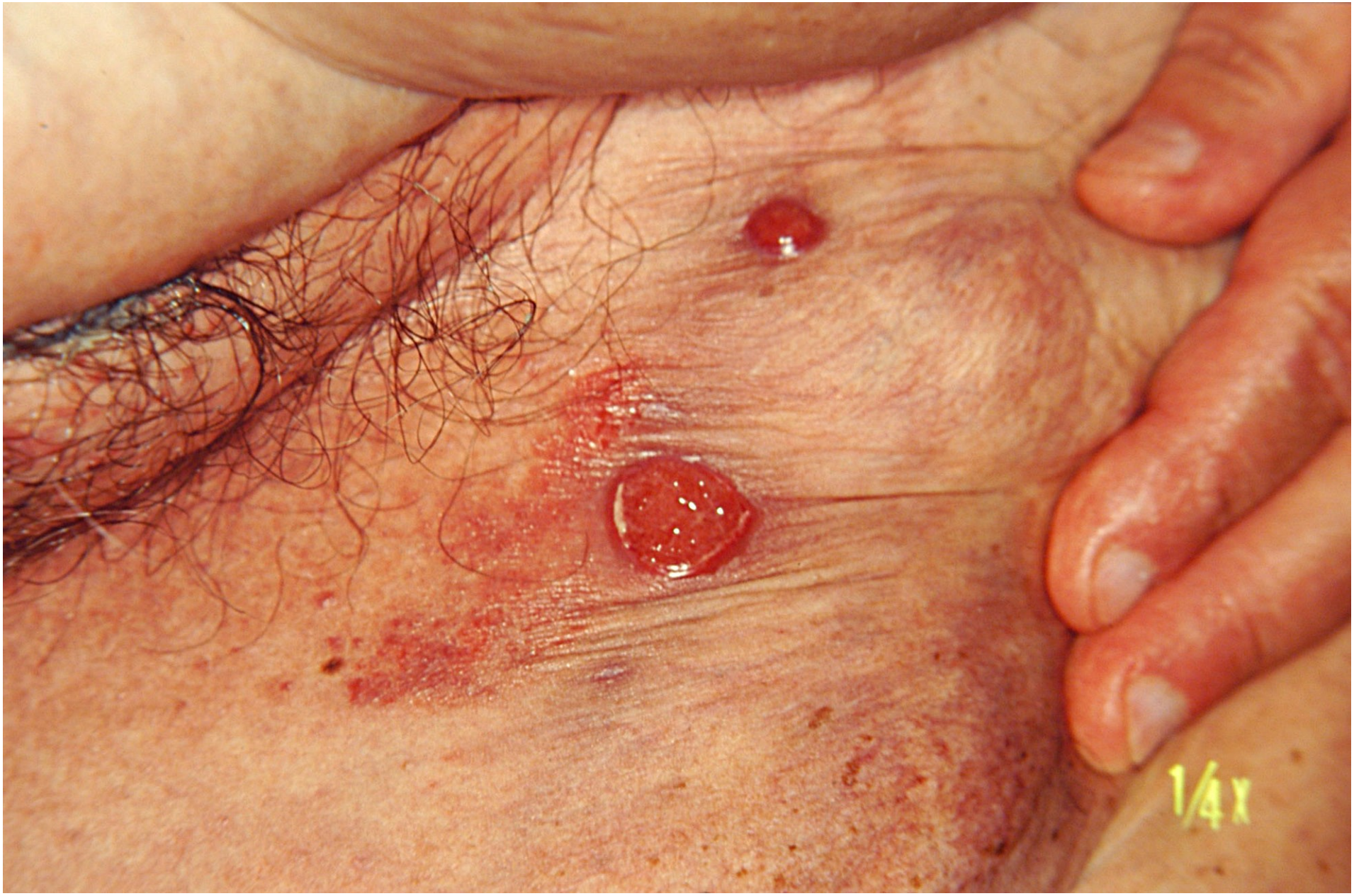
MF 1995





MF 1998, after rePUVA, cumulative dose 500 J/cm^2

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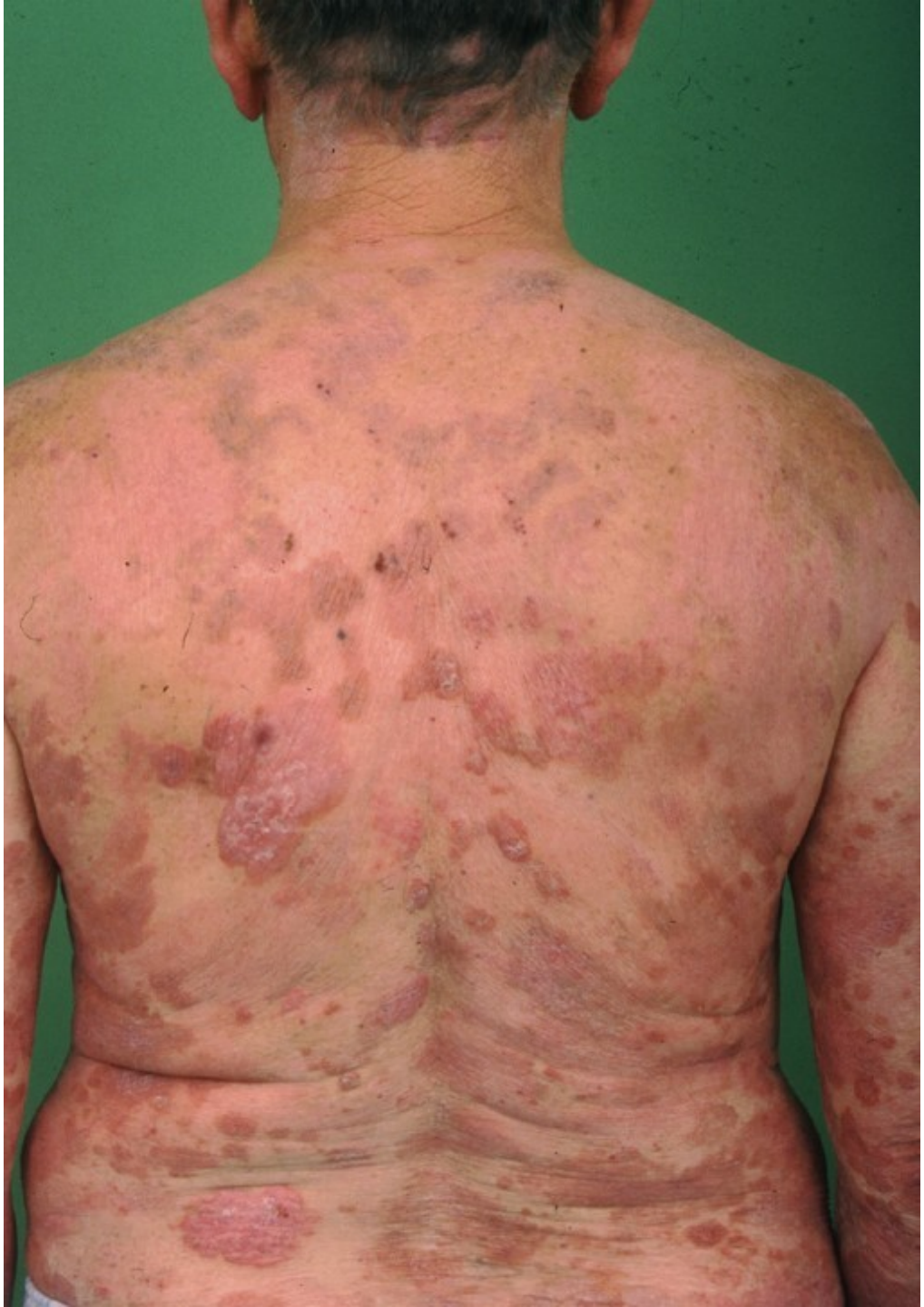
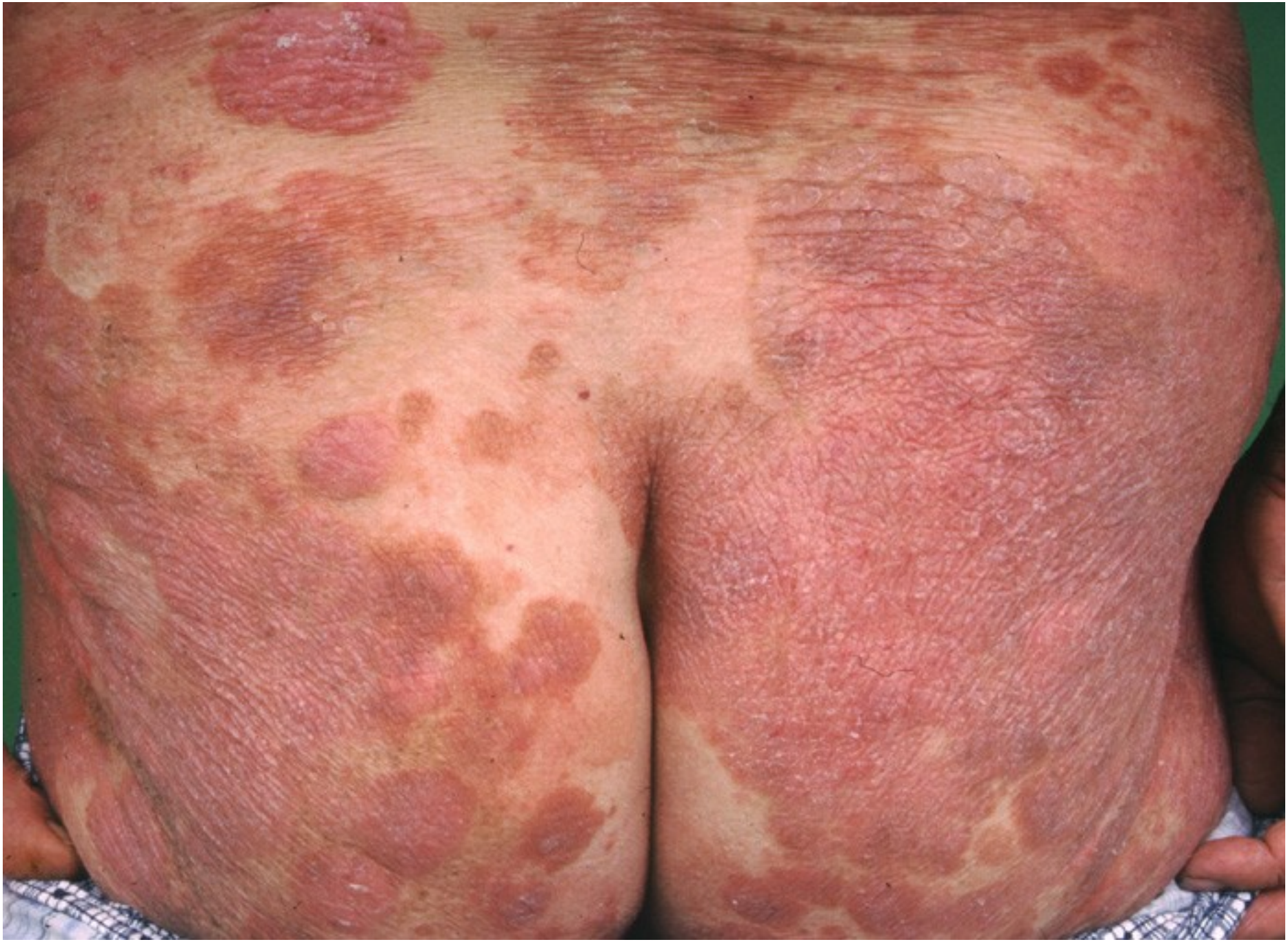
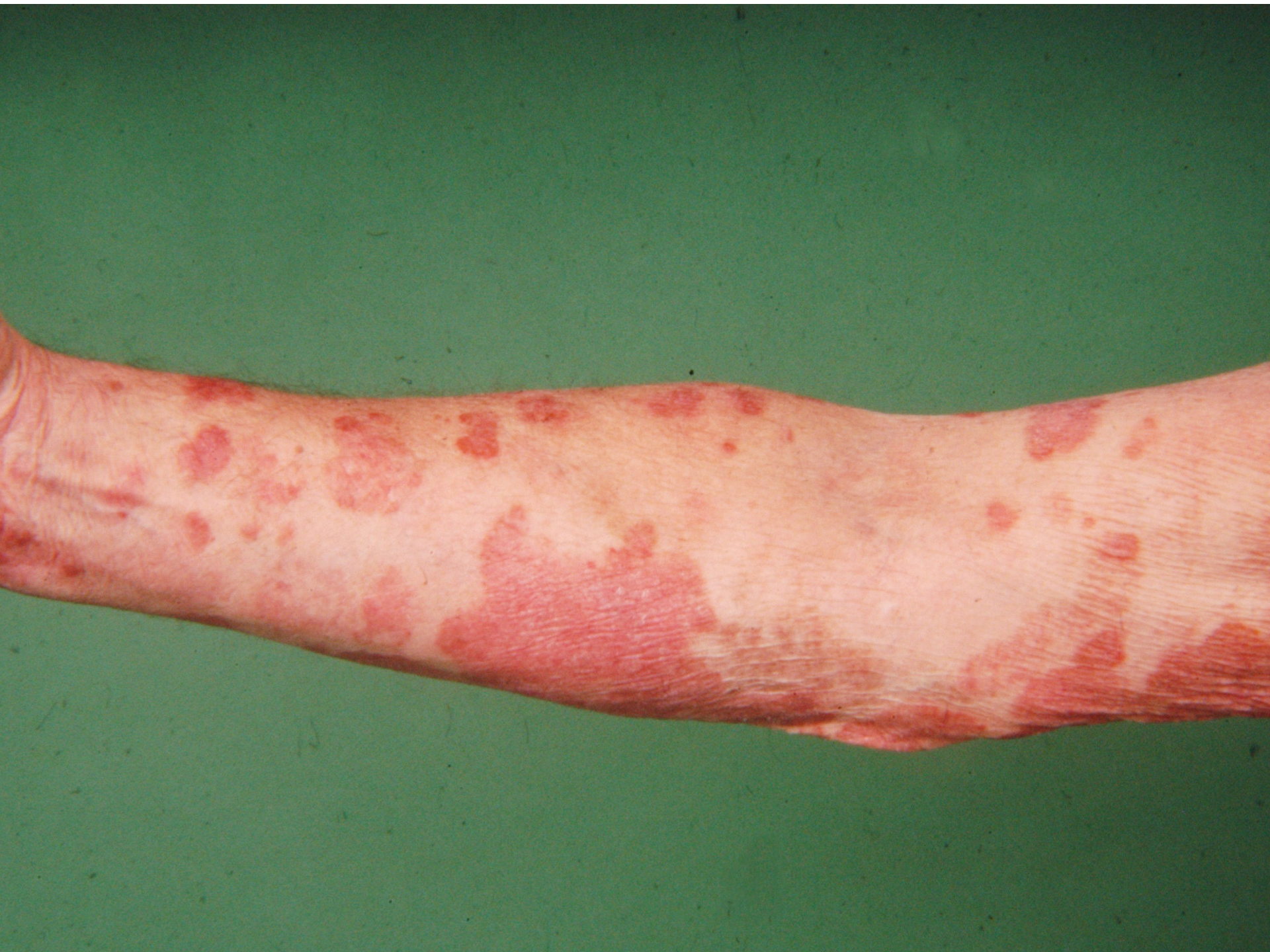
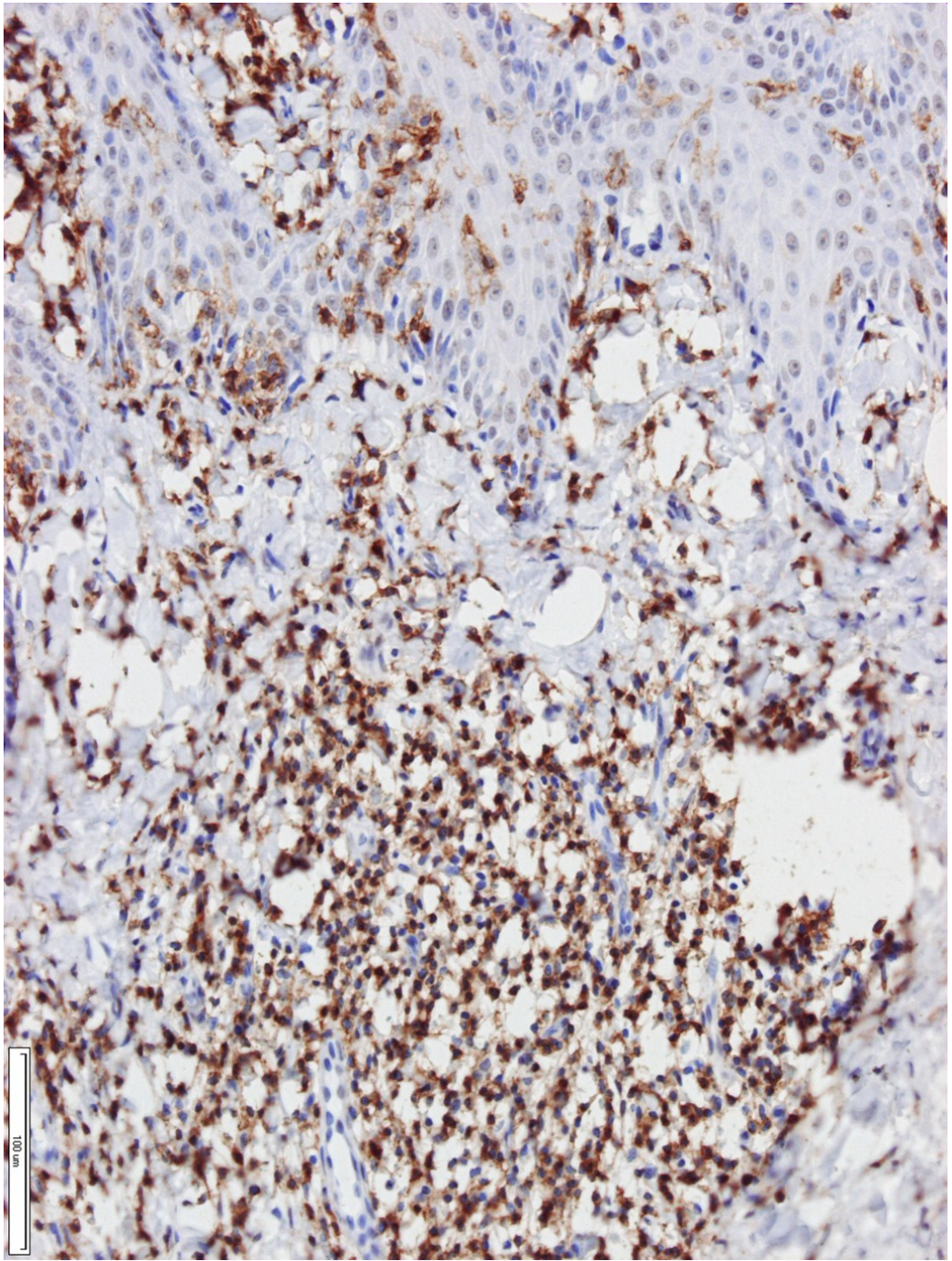
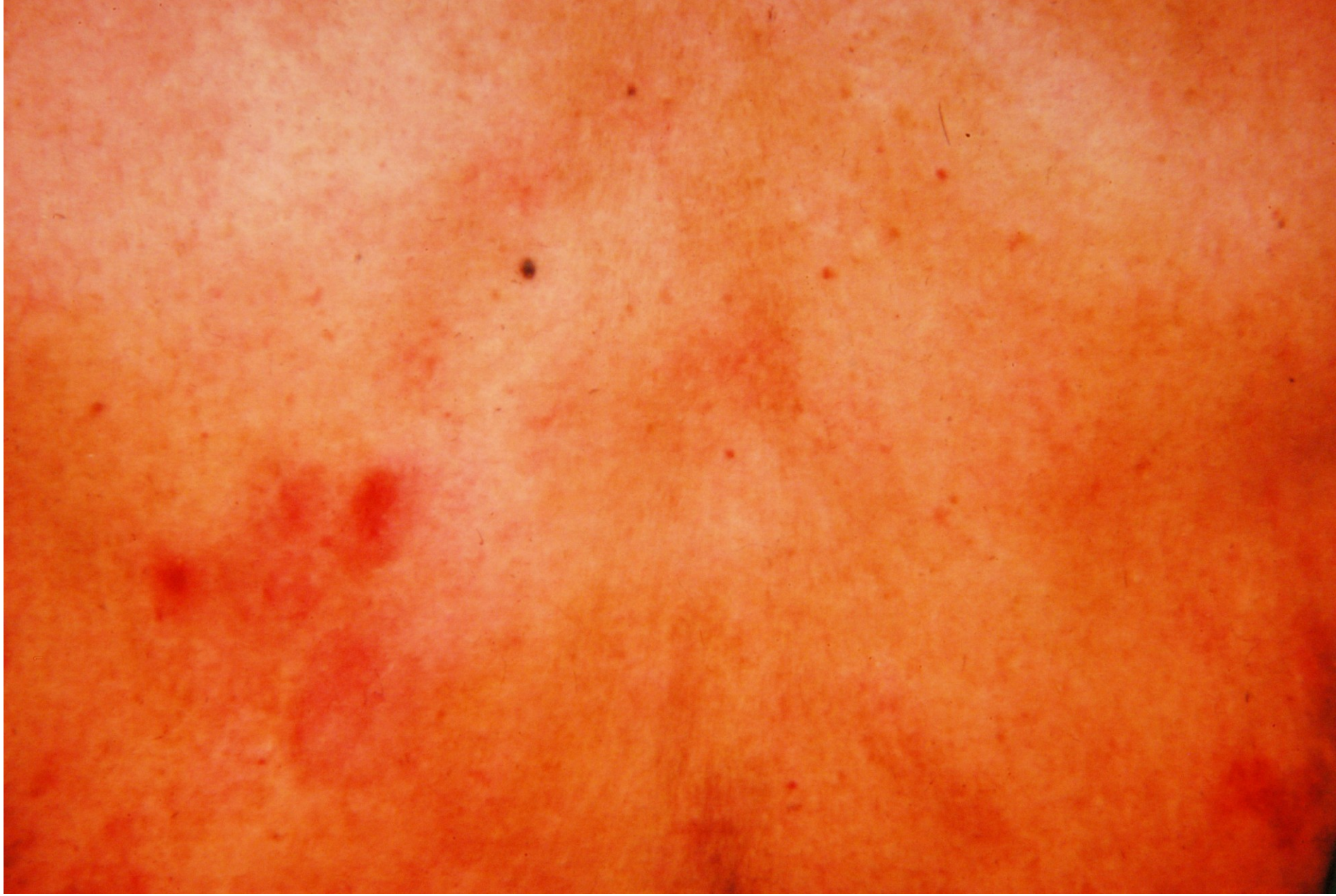


MF - before therapy

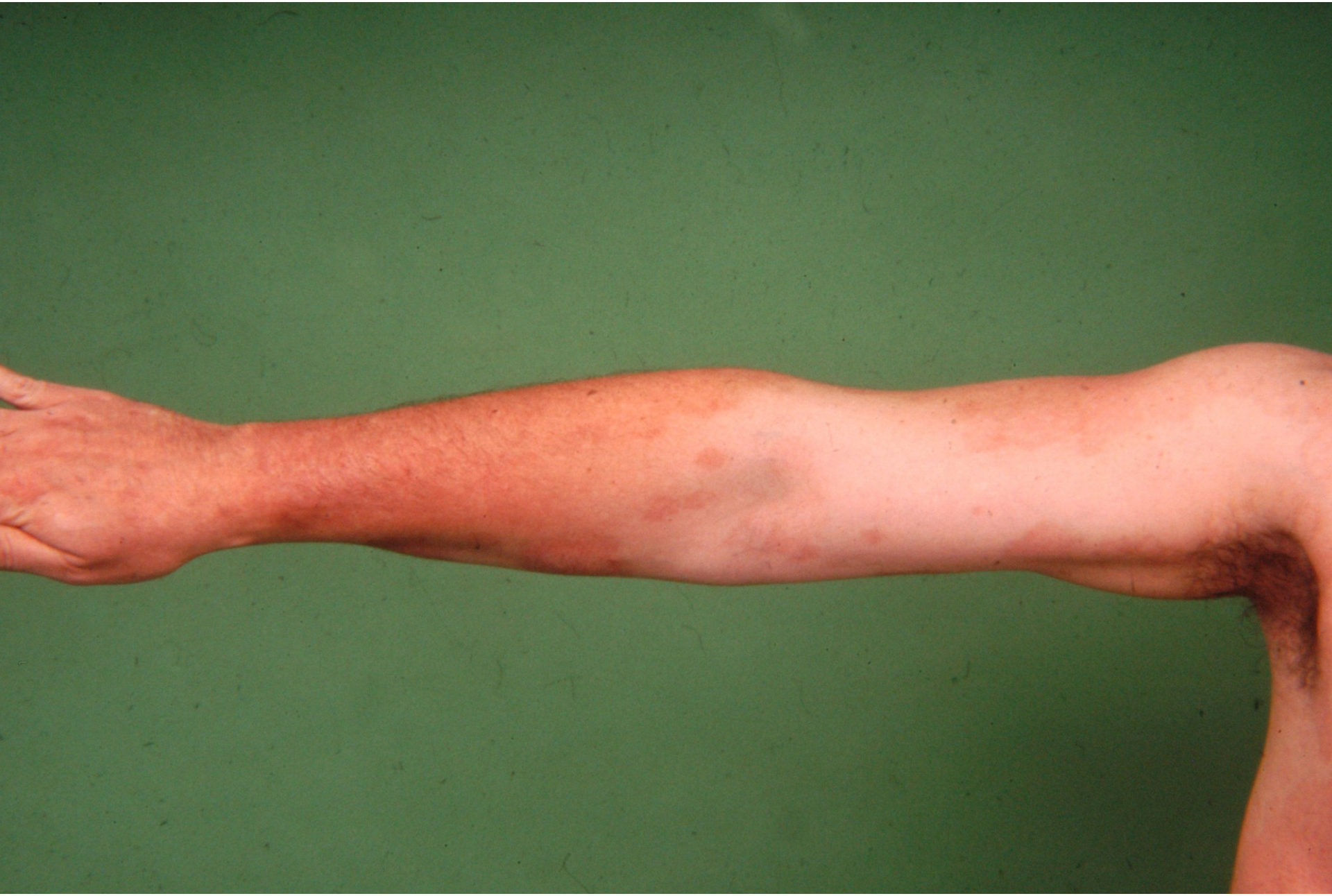


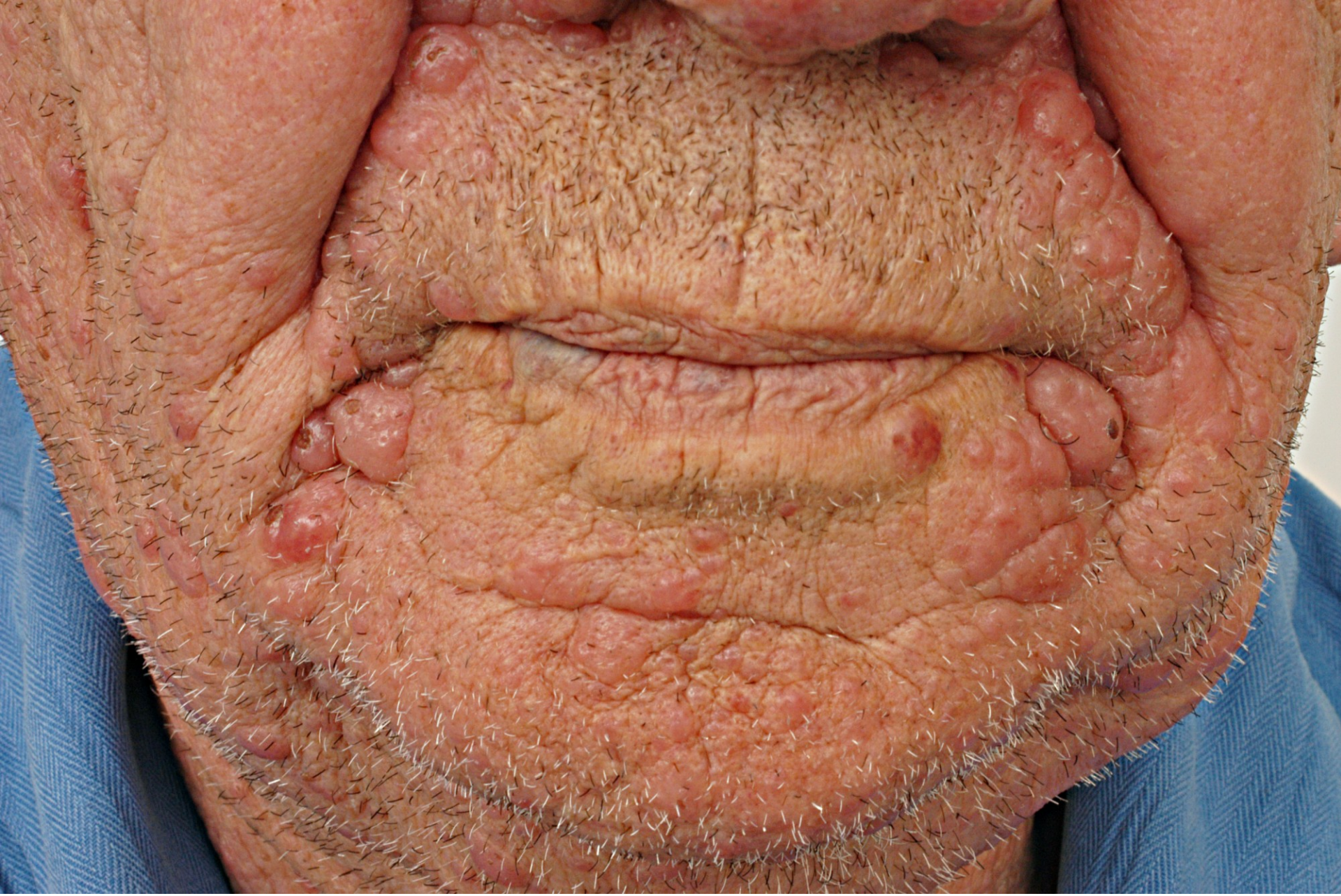



100 um

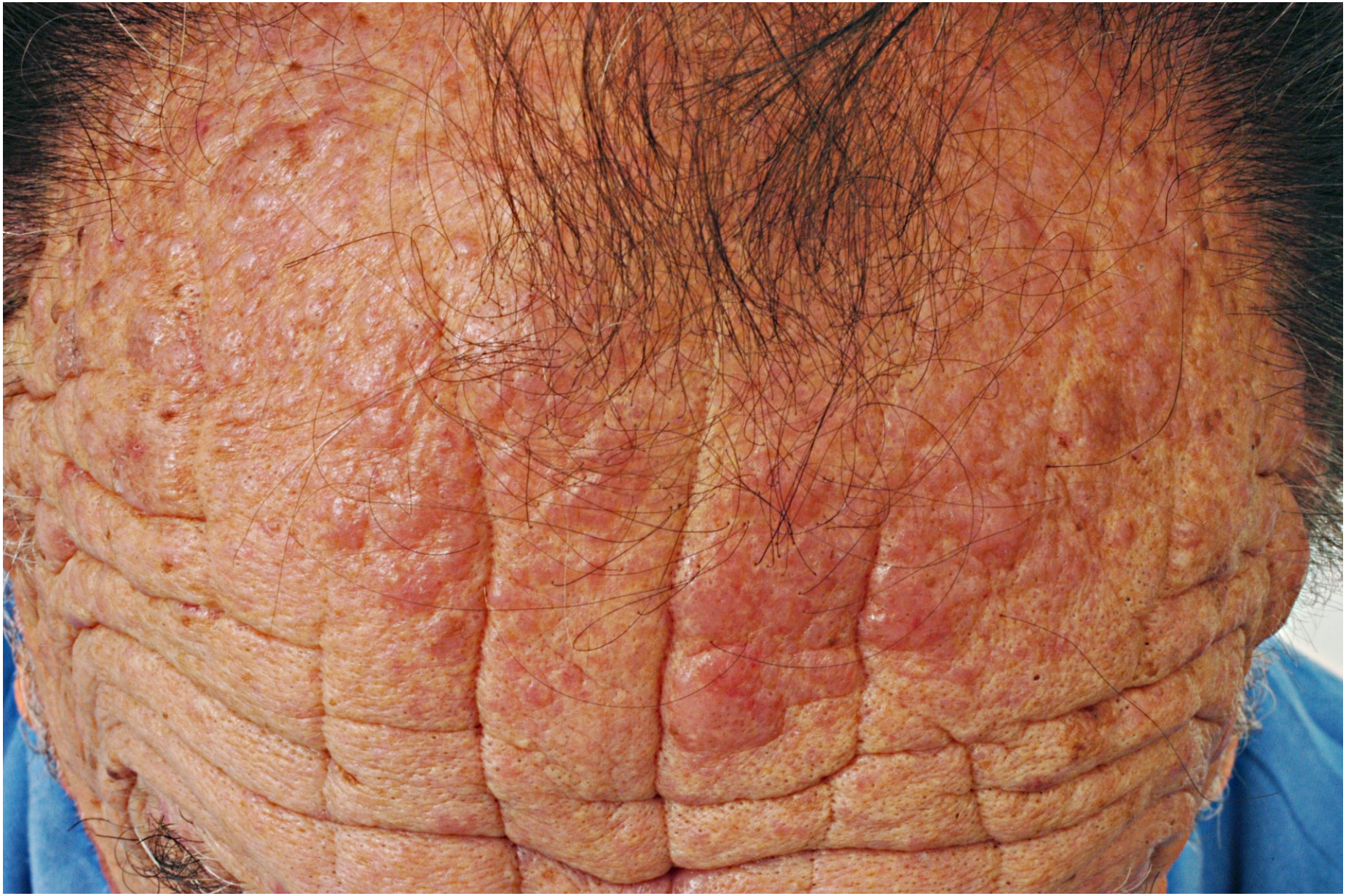


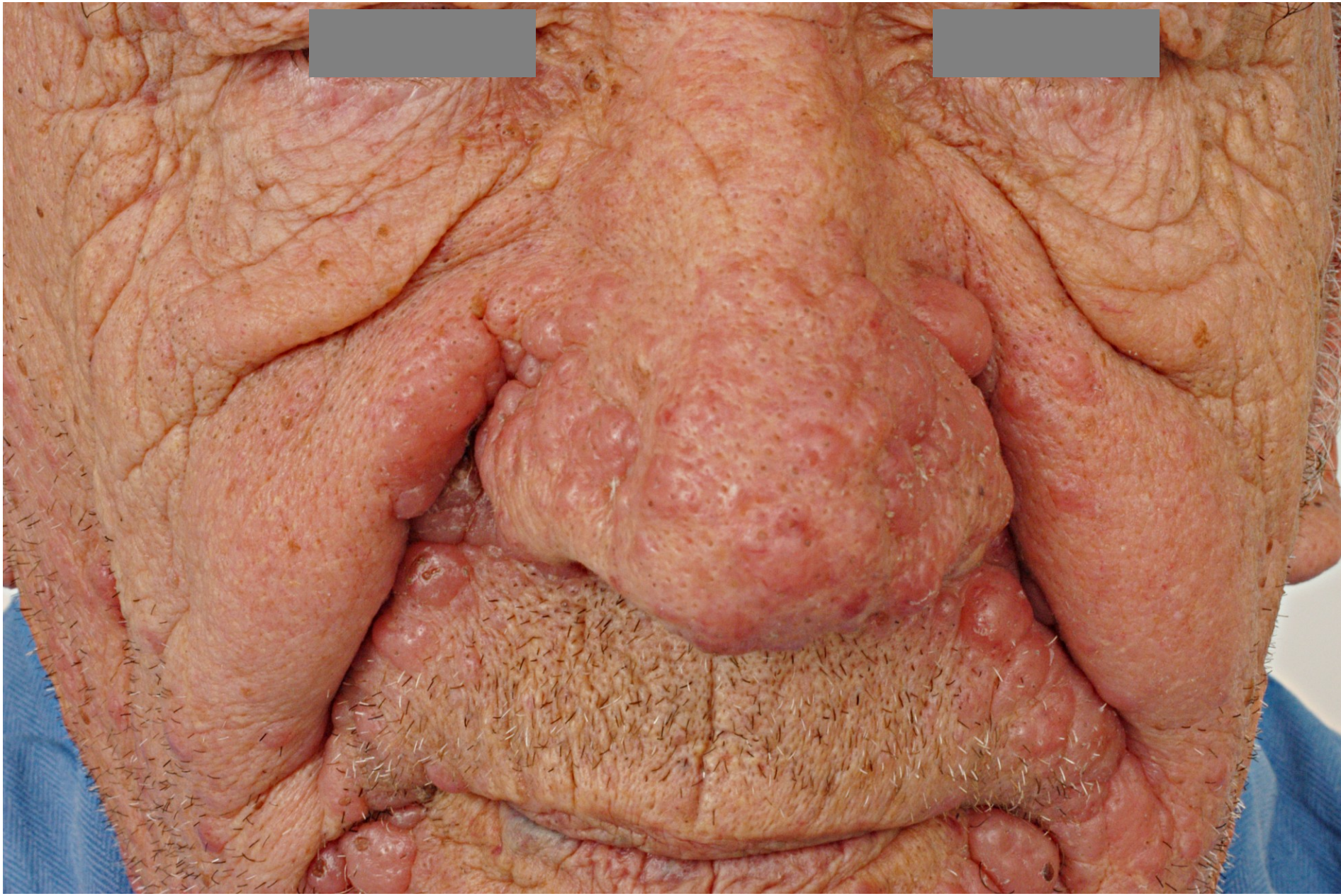
Remission after IFNα + acitretin

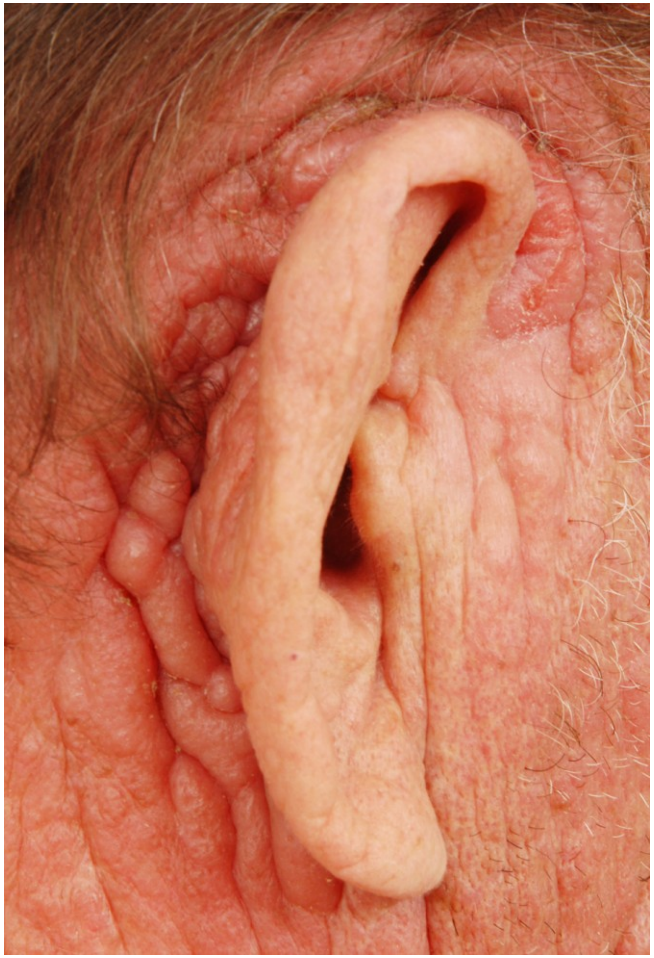


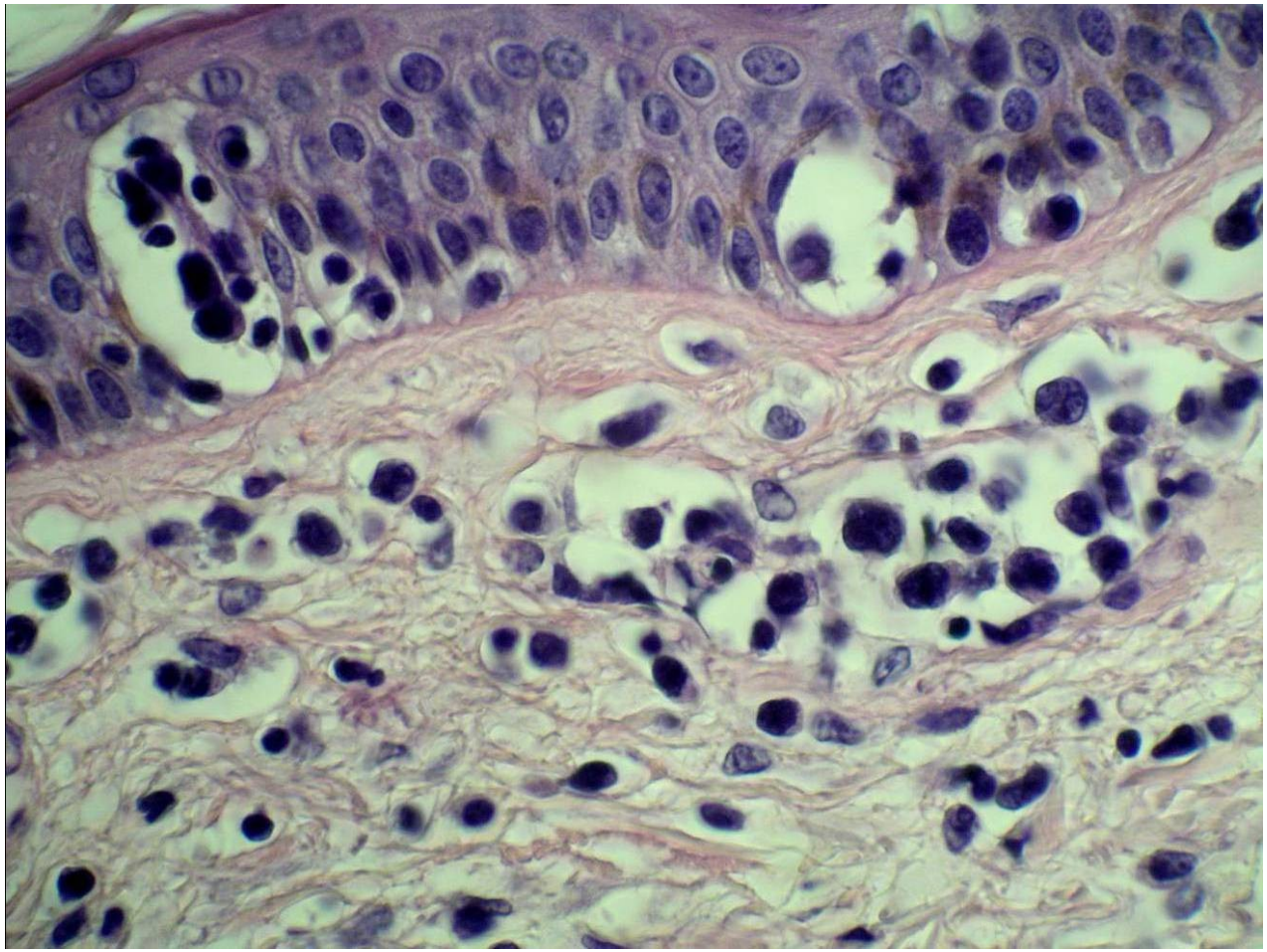


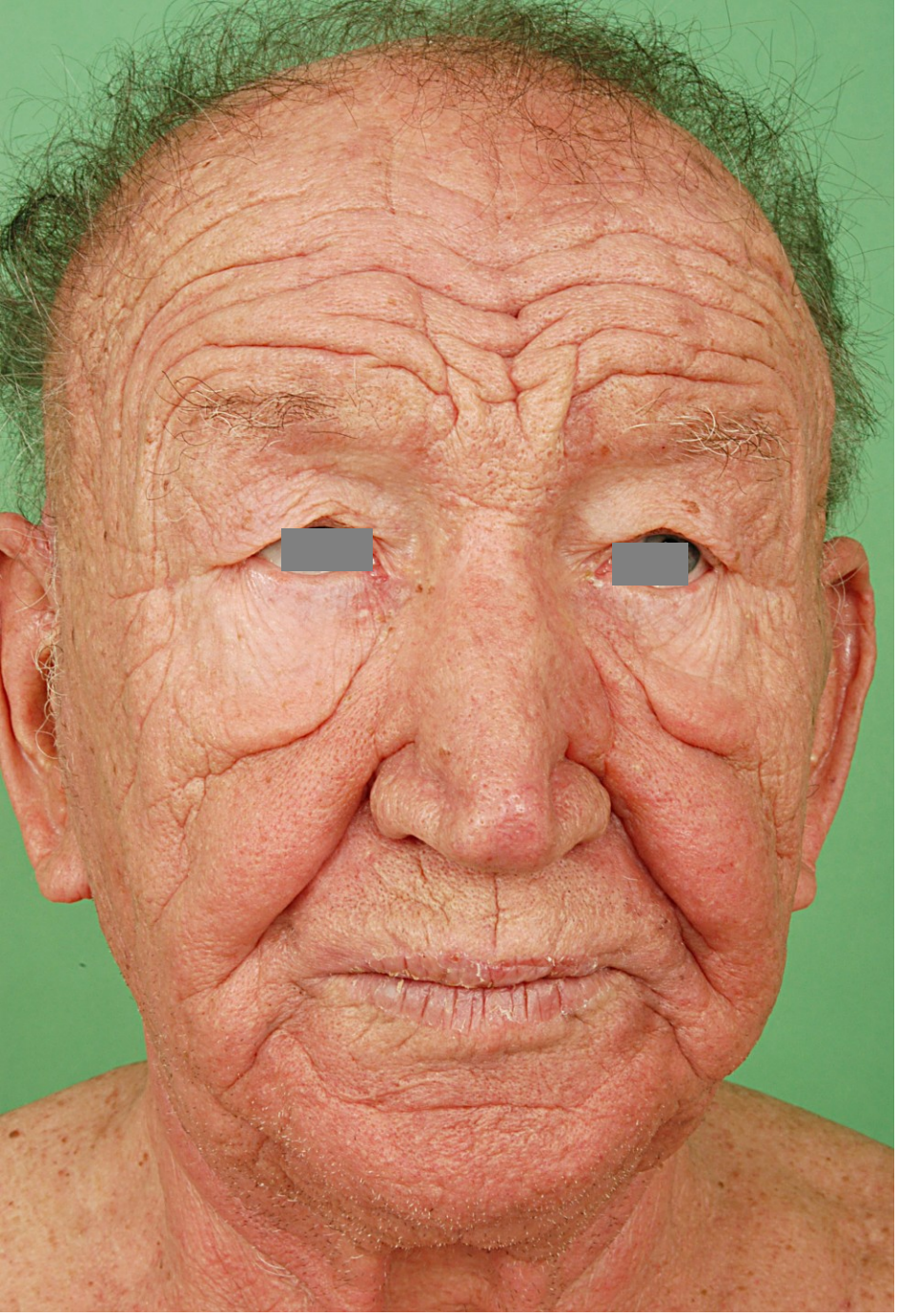
MF - before therapy, 2007



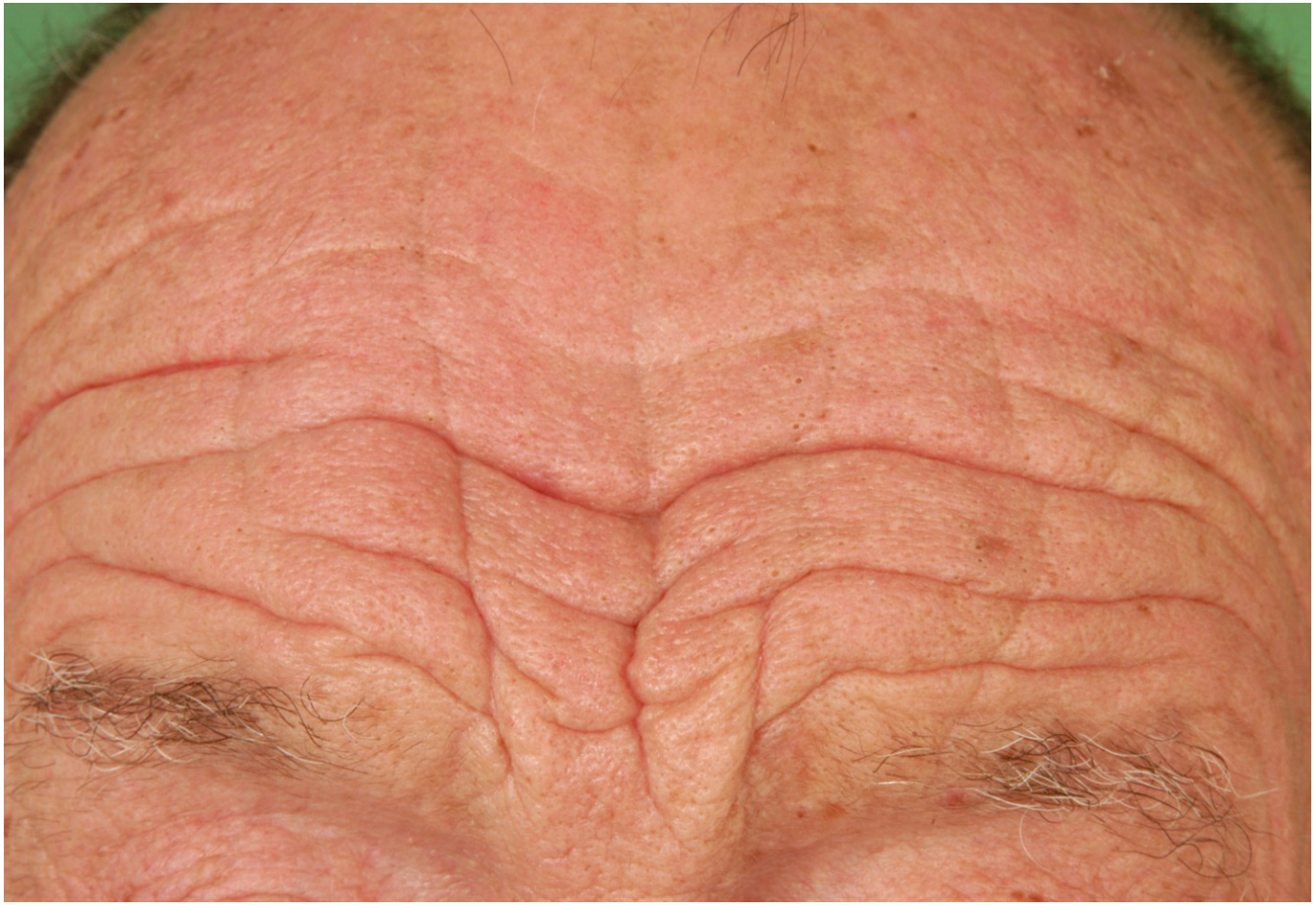


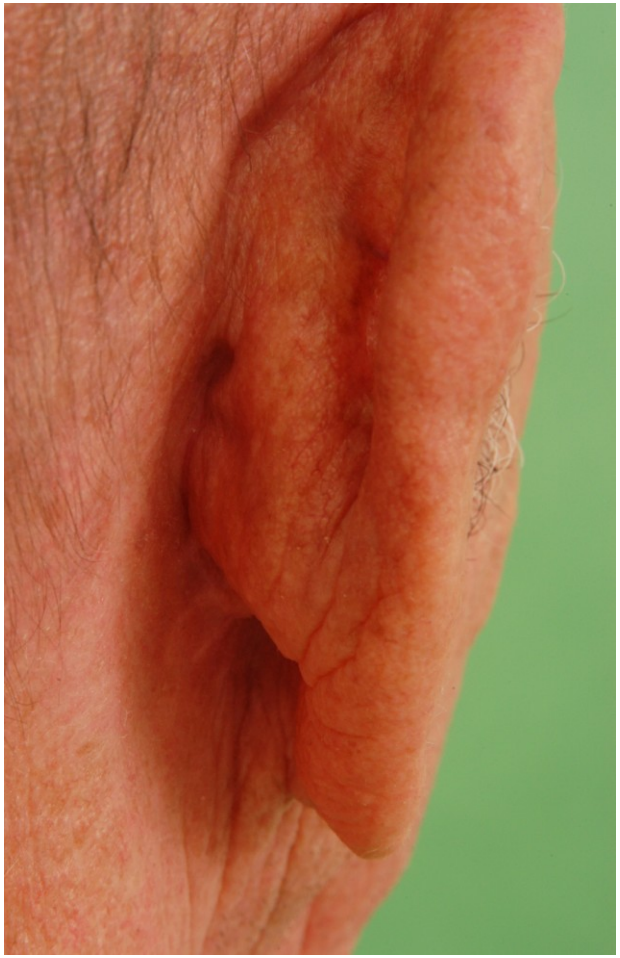




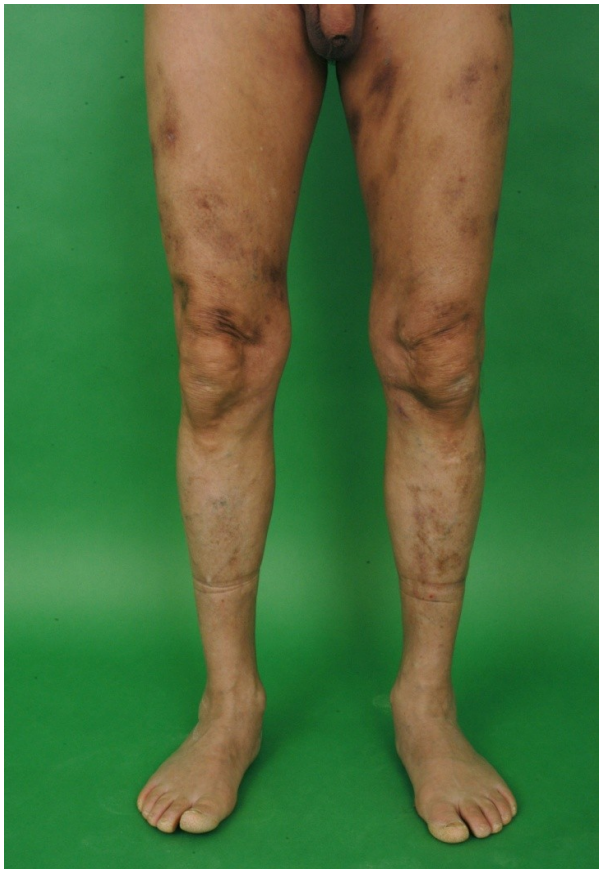


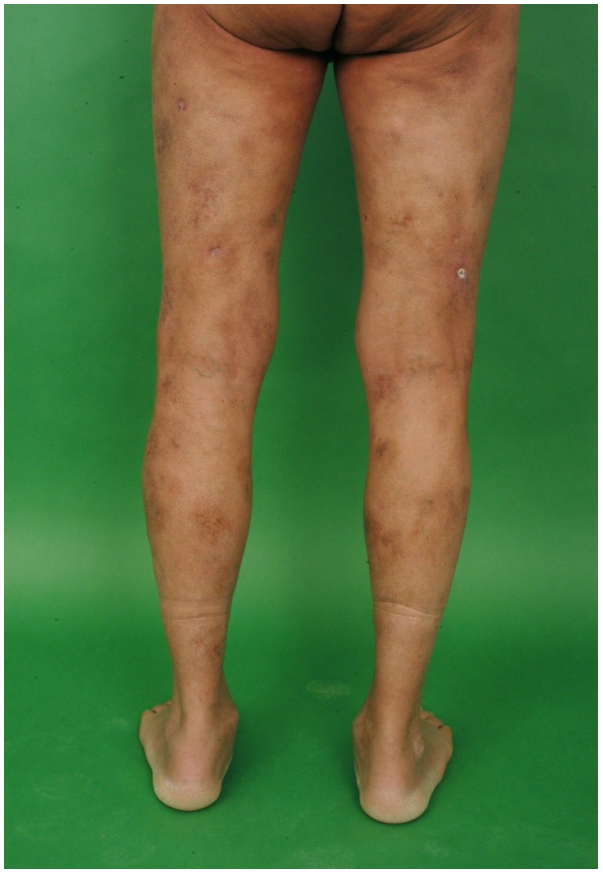
Complete remission after rePUVA + IFNα until now

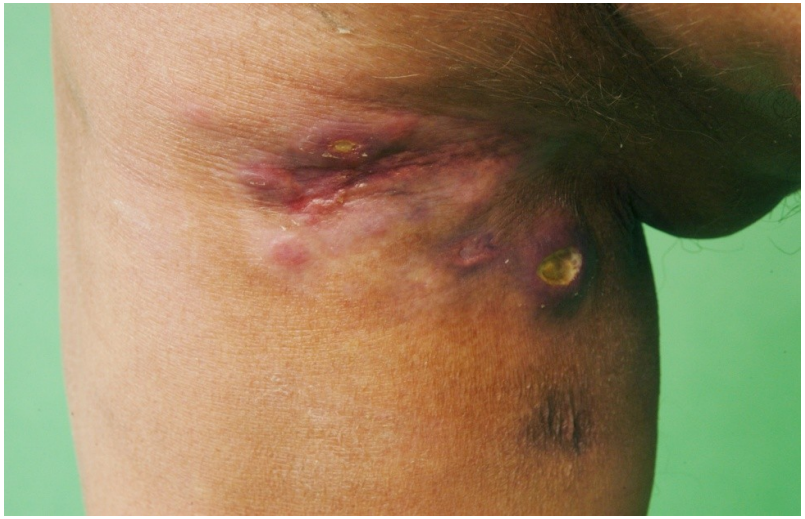


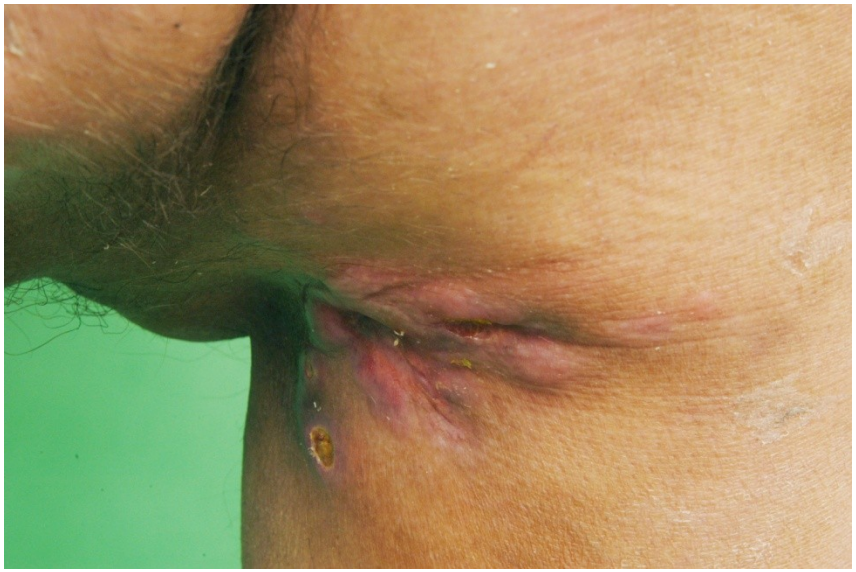


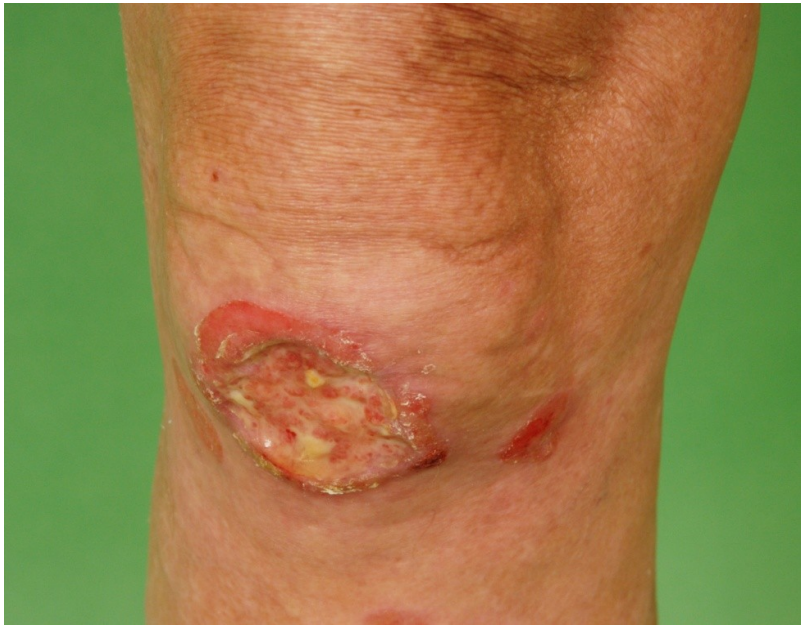
MF – before therapy, 2007

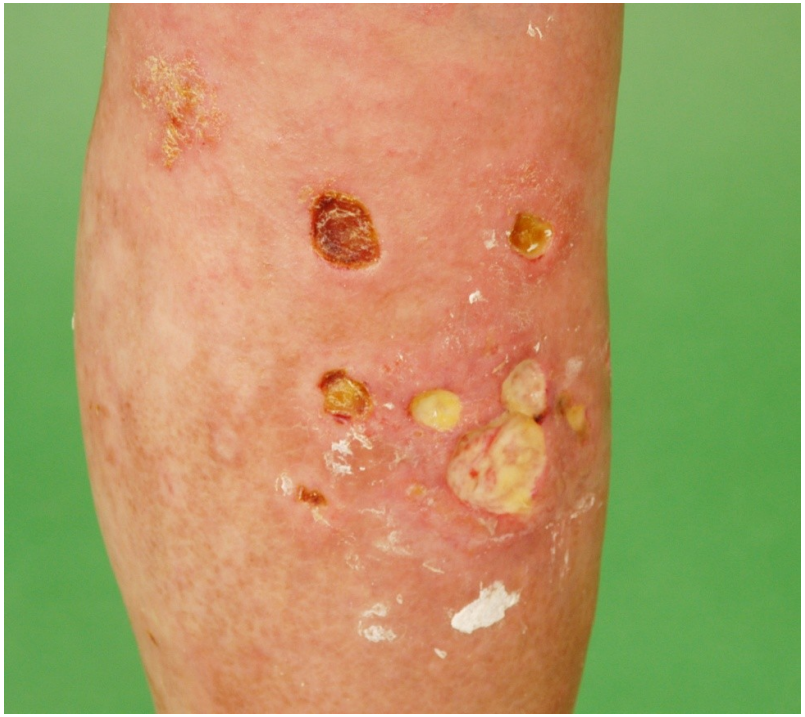


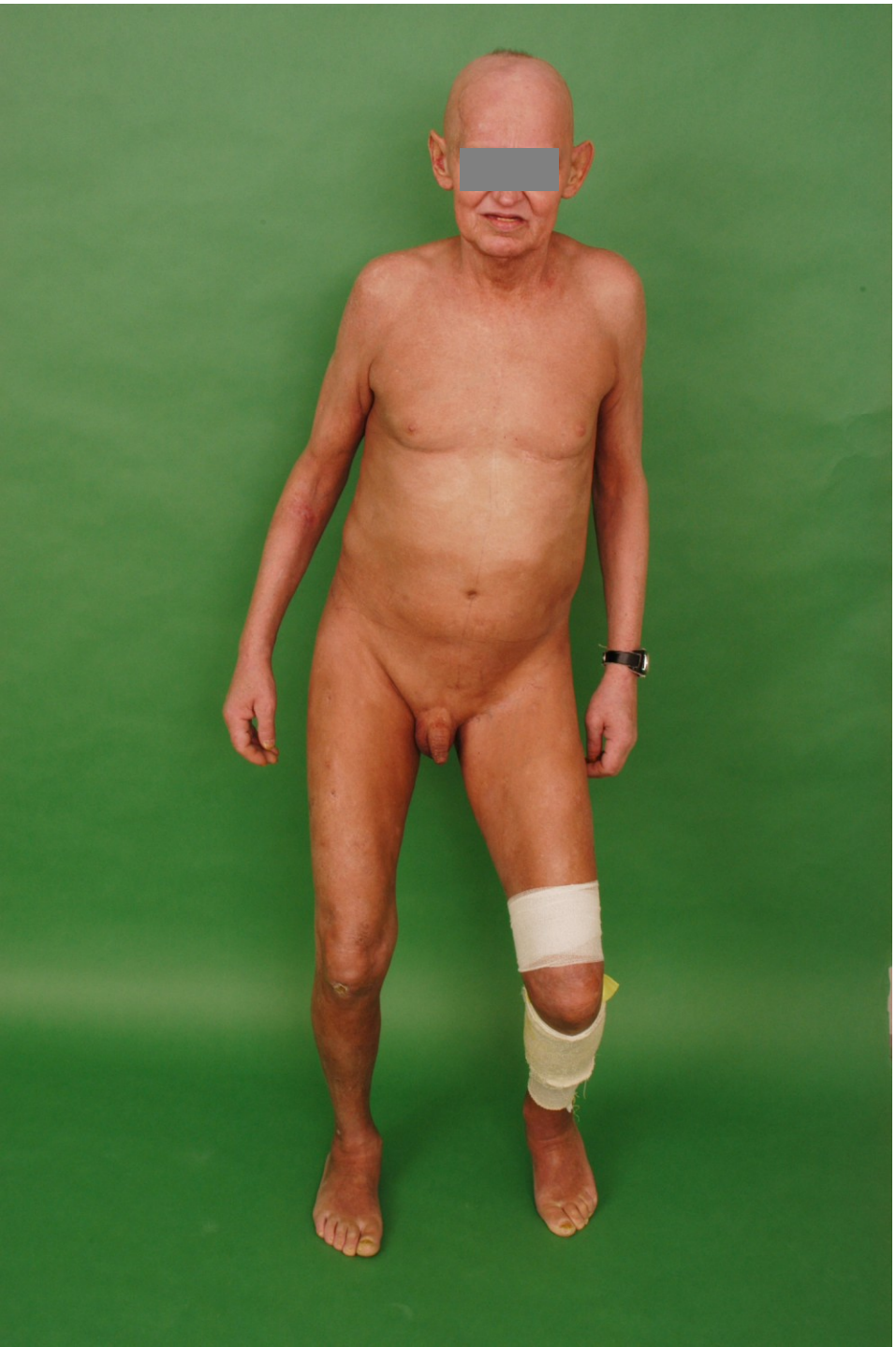




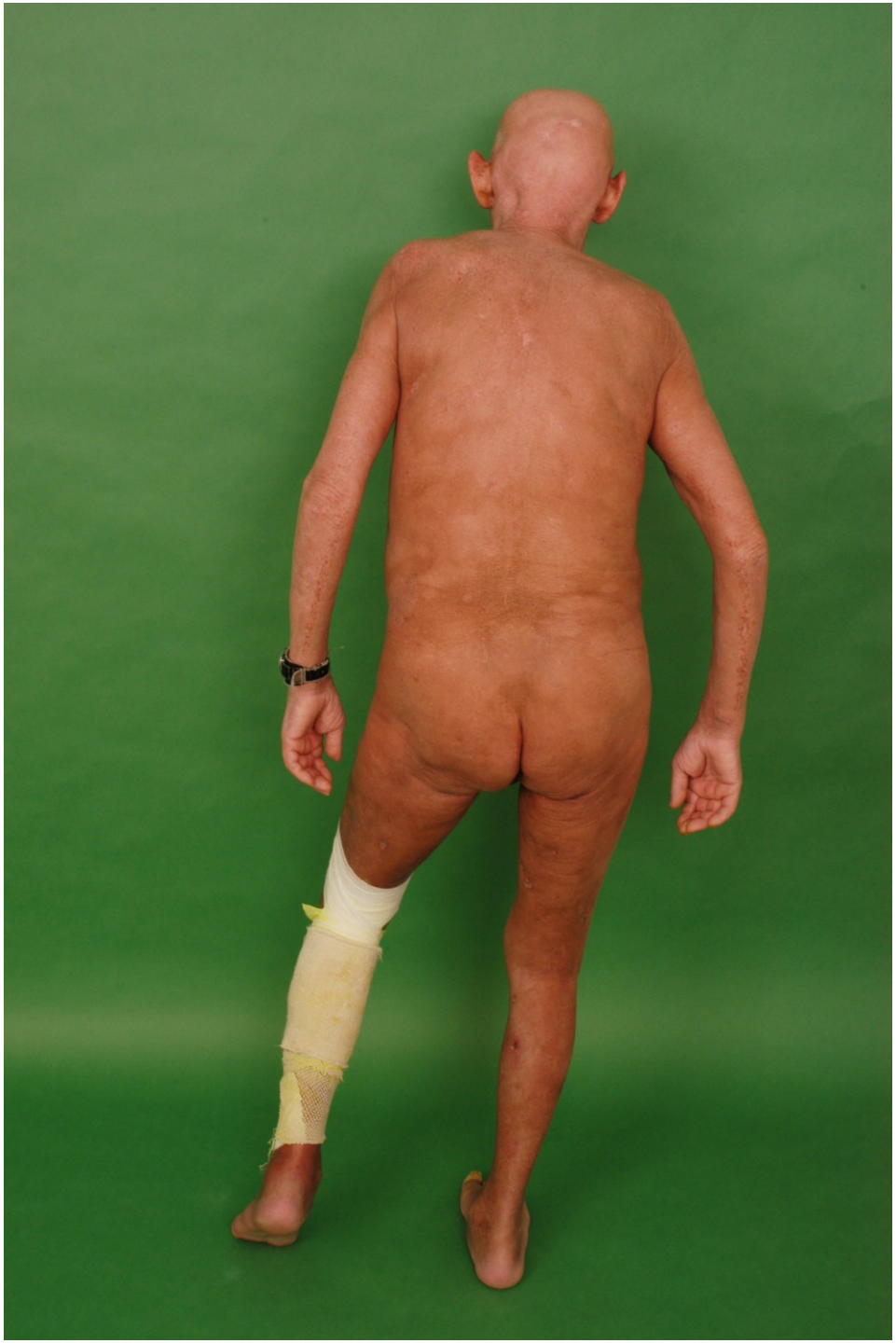




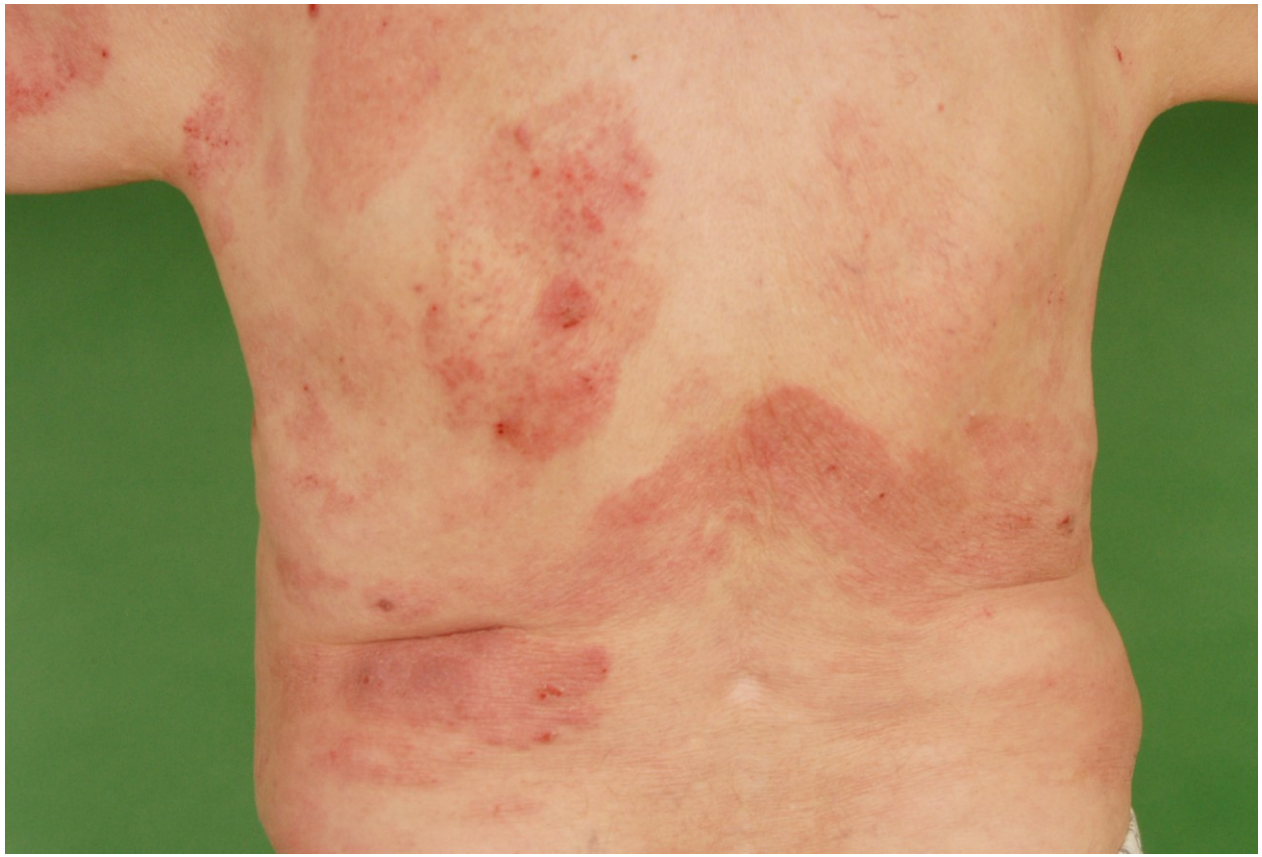




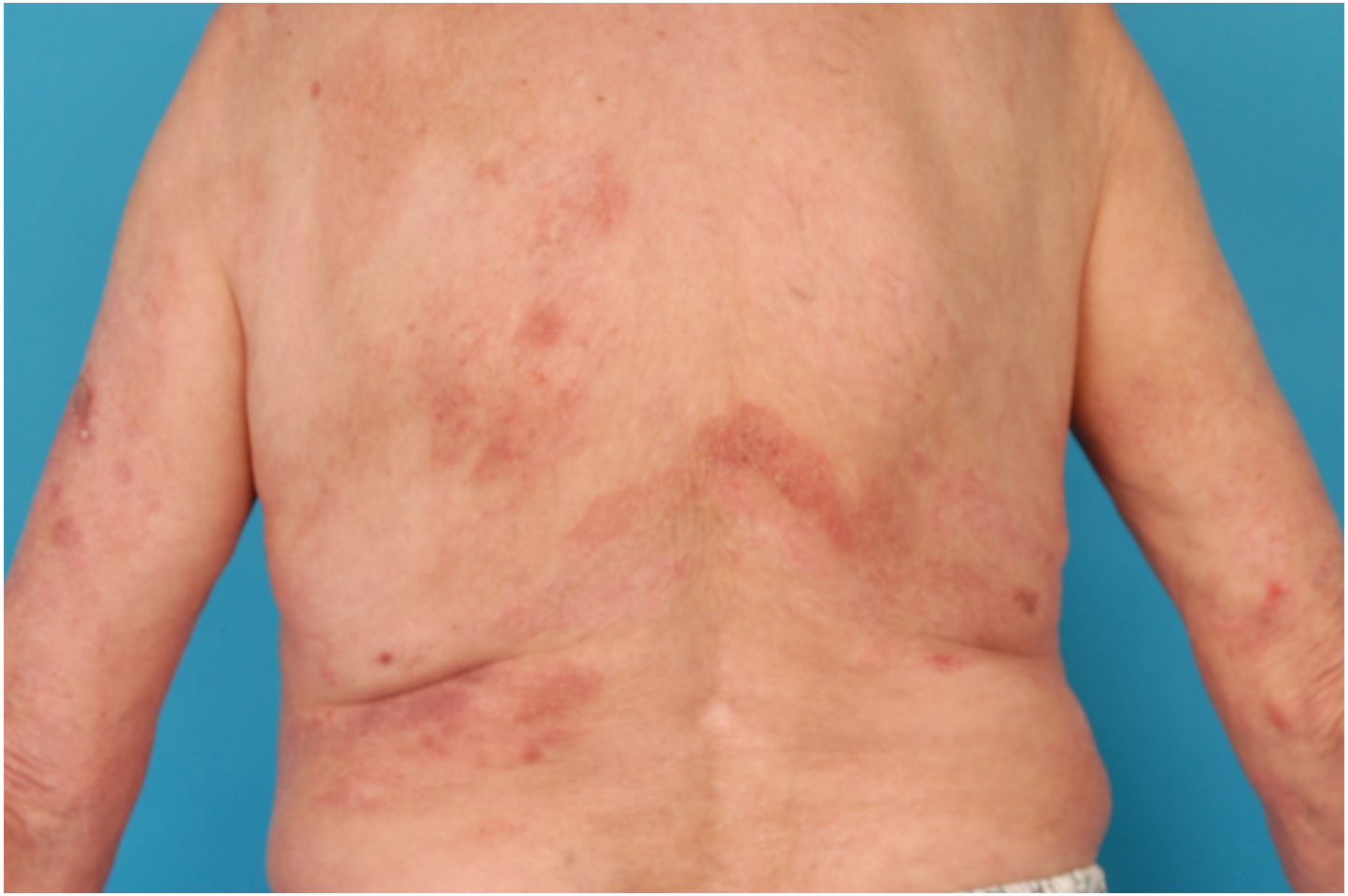
After 2 years of bexarotene therapy



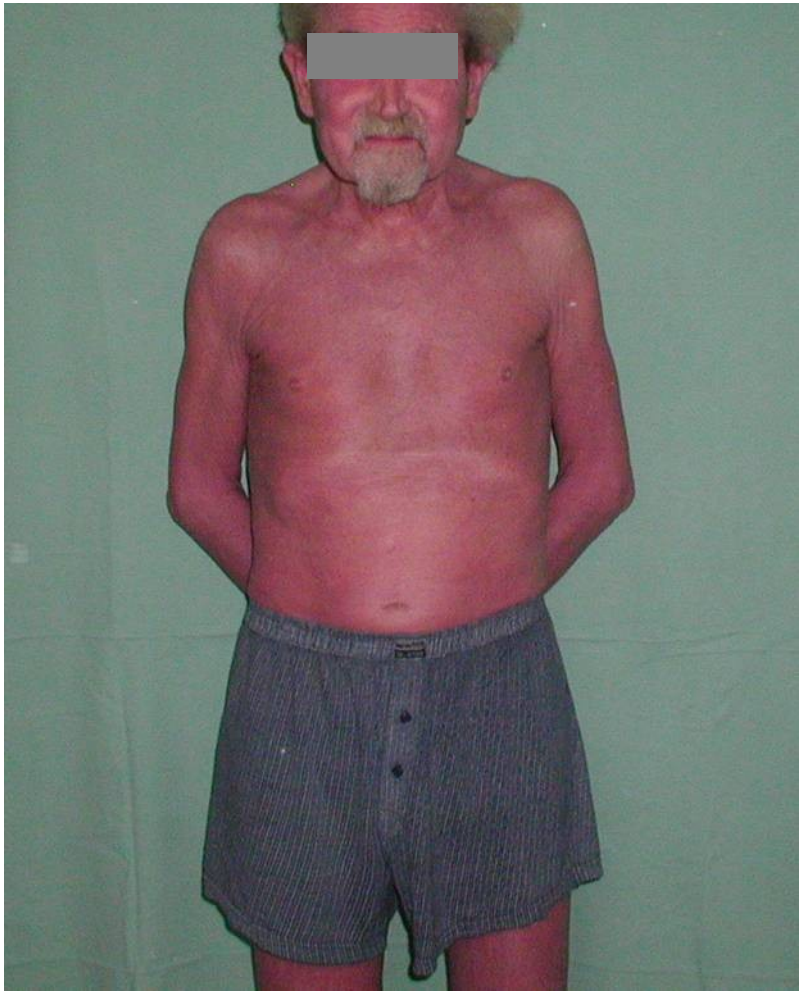
MF – before therapy

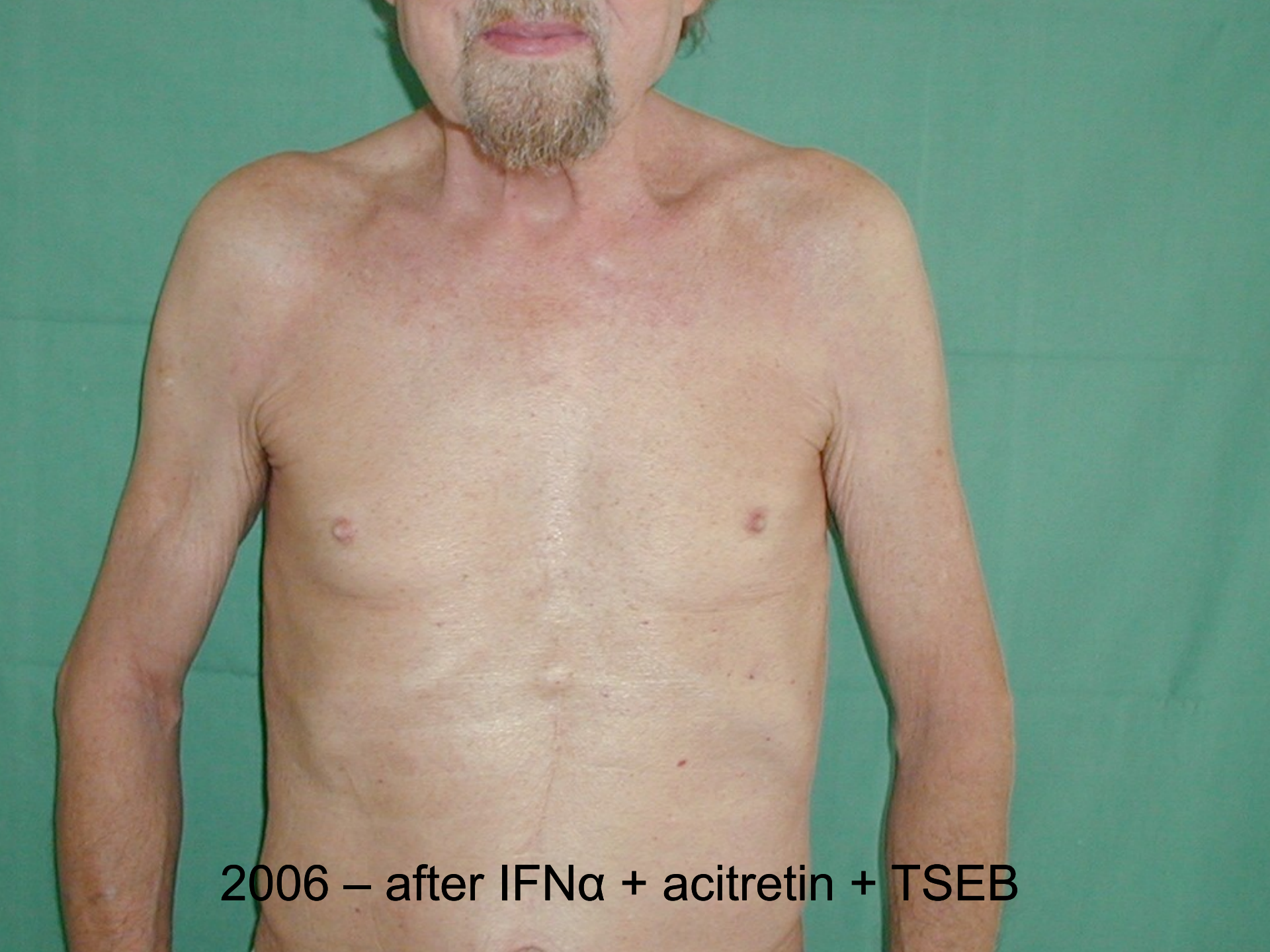


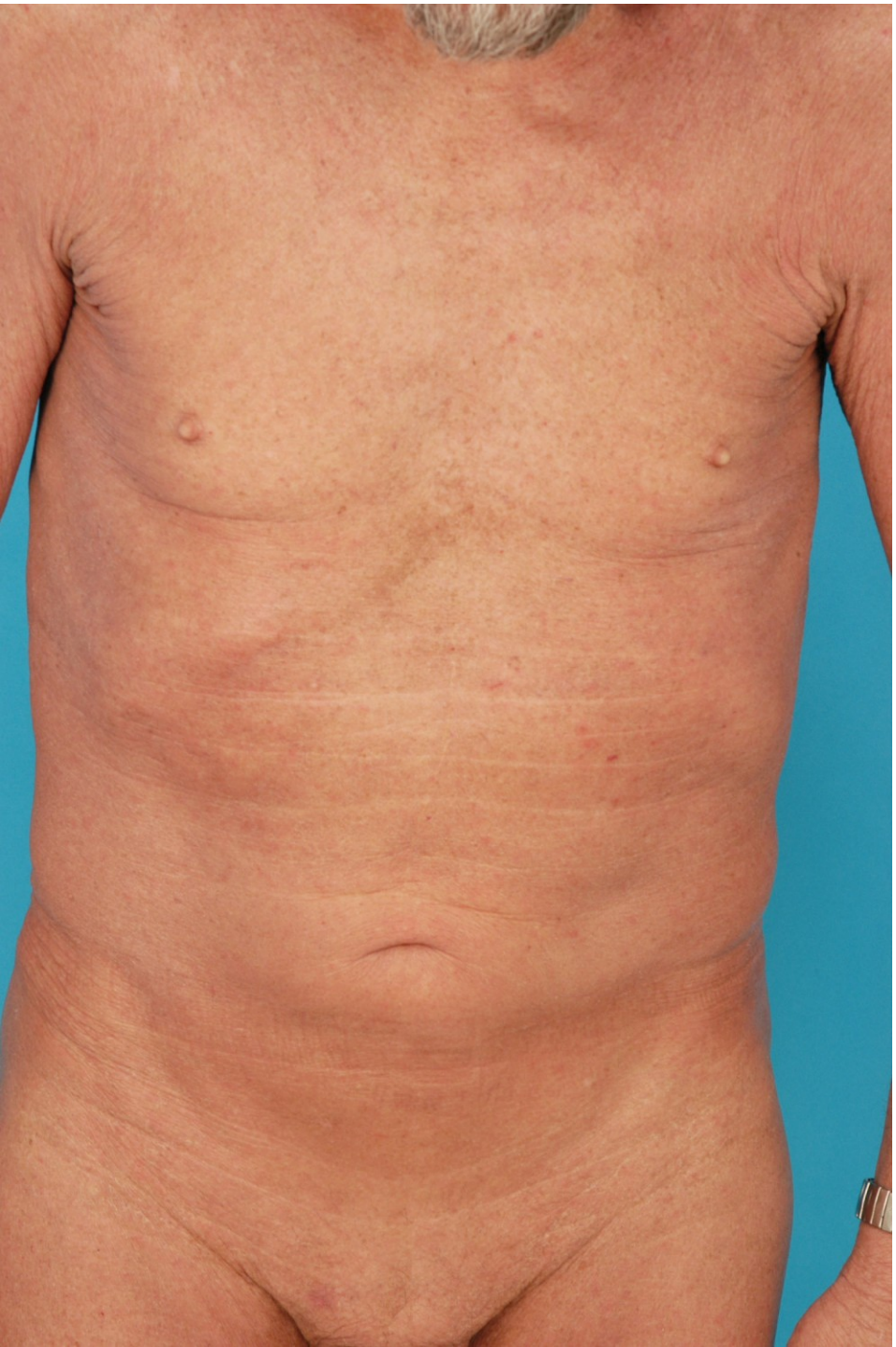
MF – after 2 months bexarotene therapy



Erythrodermic MF – before therapy 2003

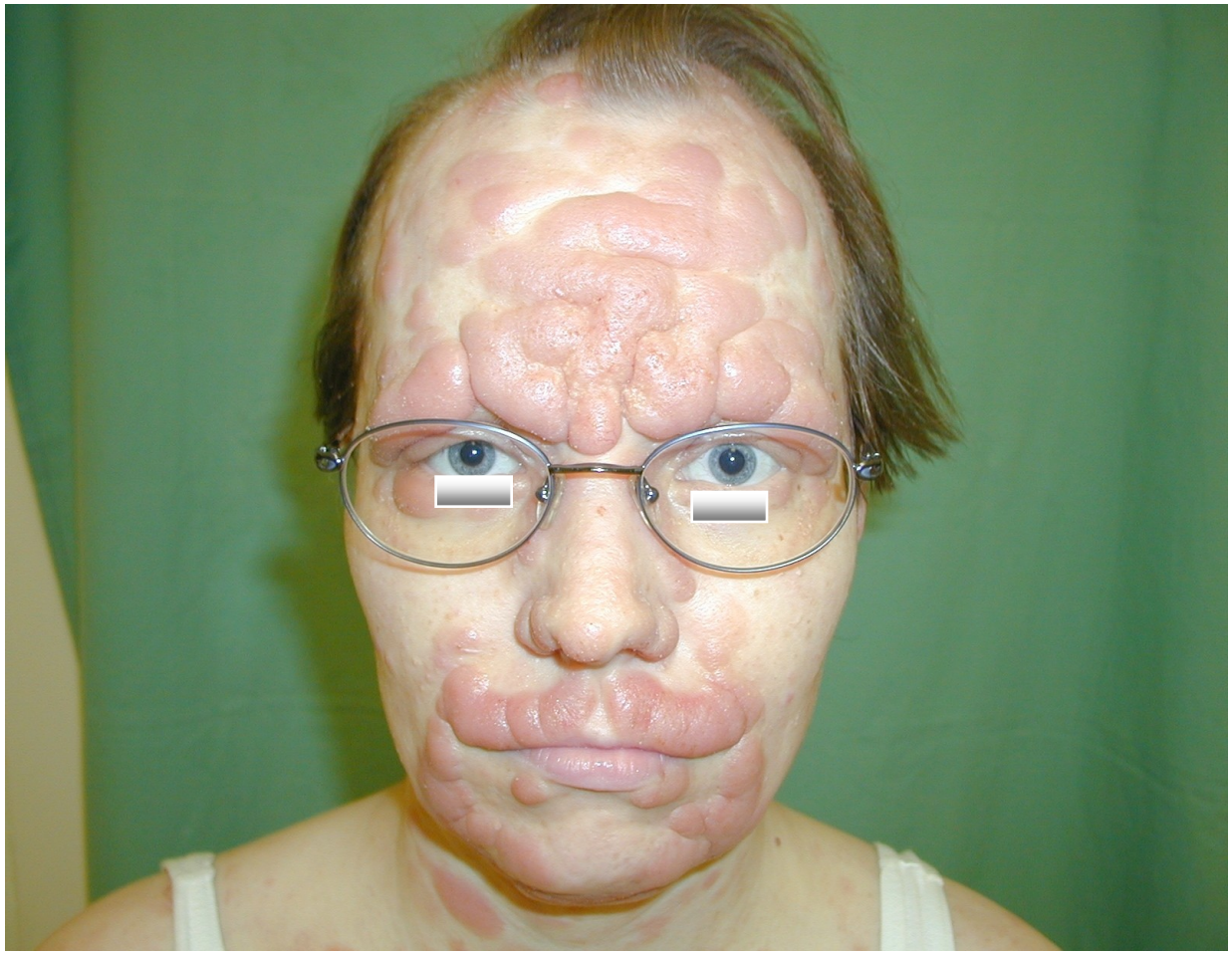



2006 – after IFNα + acitretin + TSEB

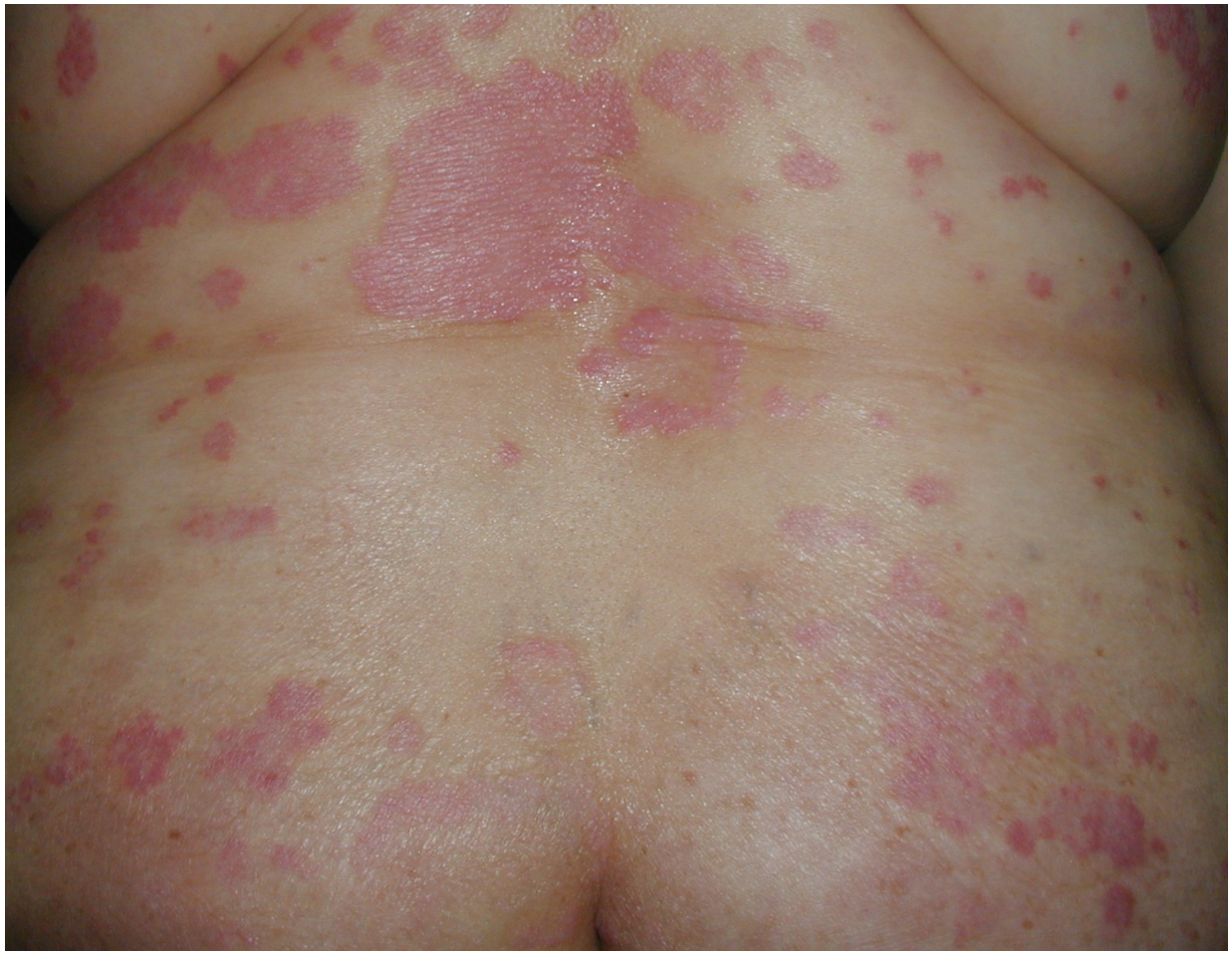


2009 – bexarotene therapy

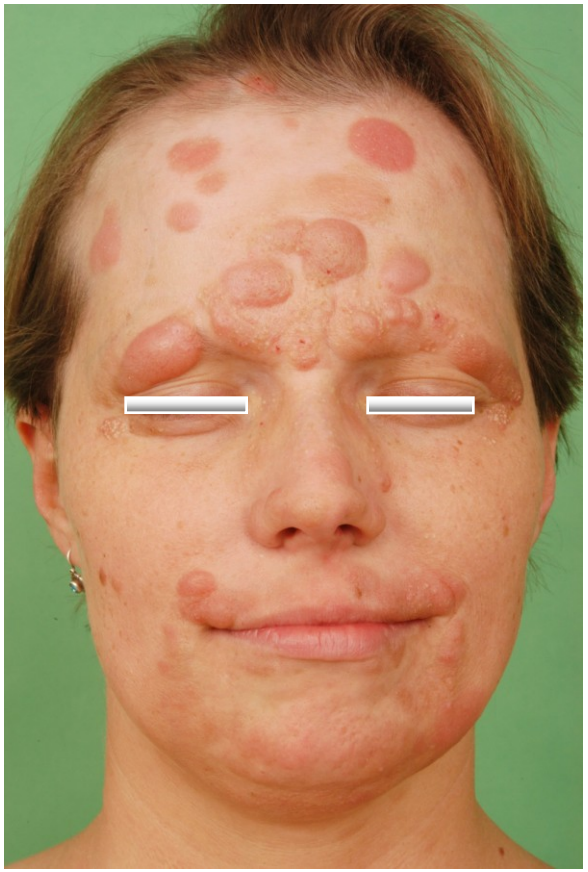
MF – before therapy

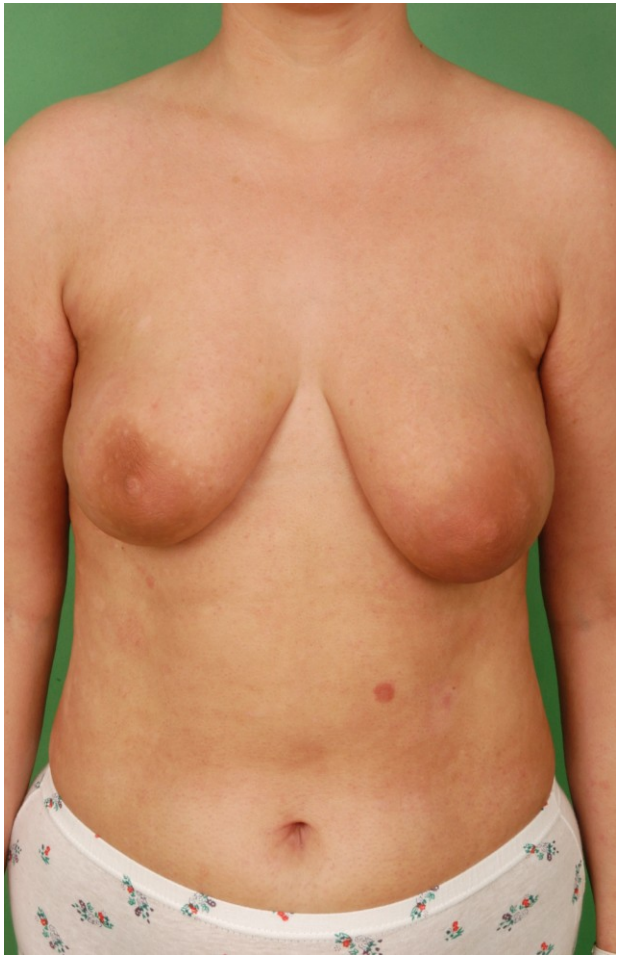


MF – before therapy

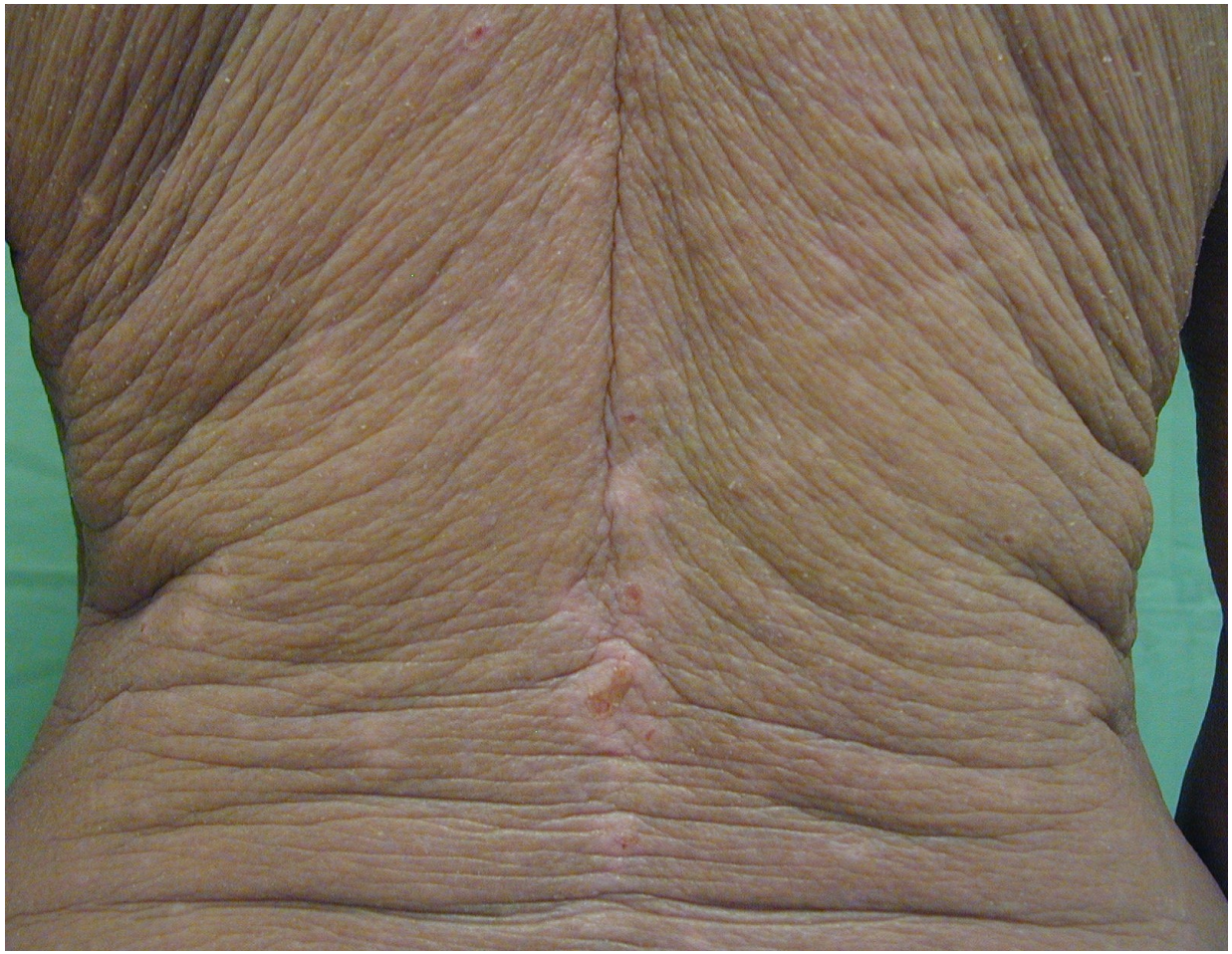


3 months bexarotene therapy + PUVA

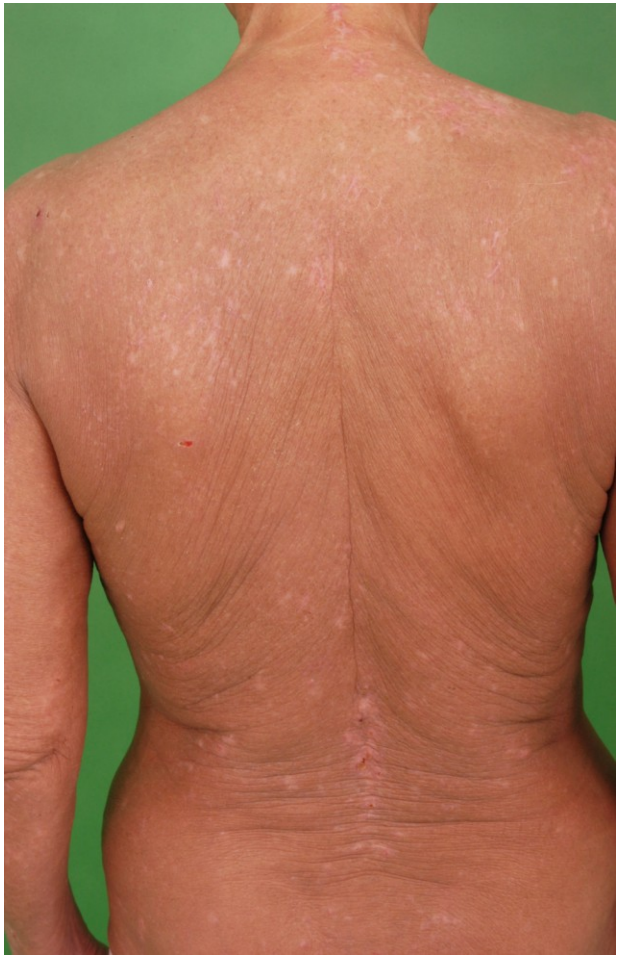


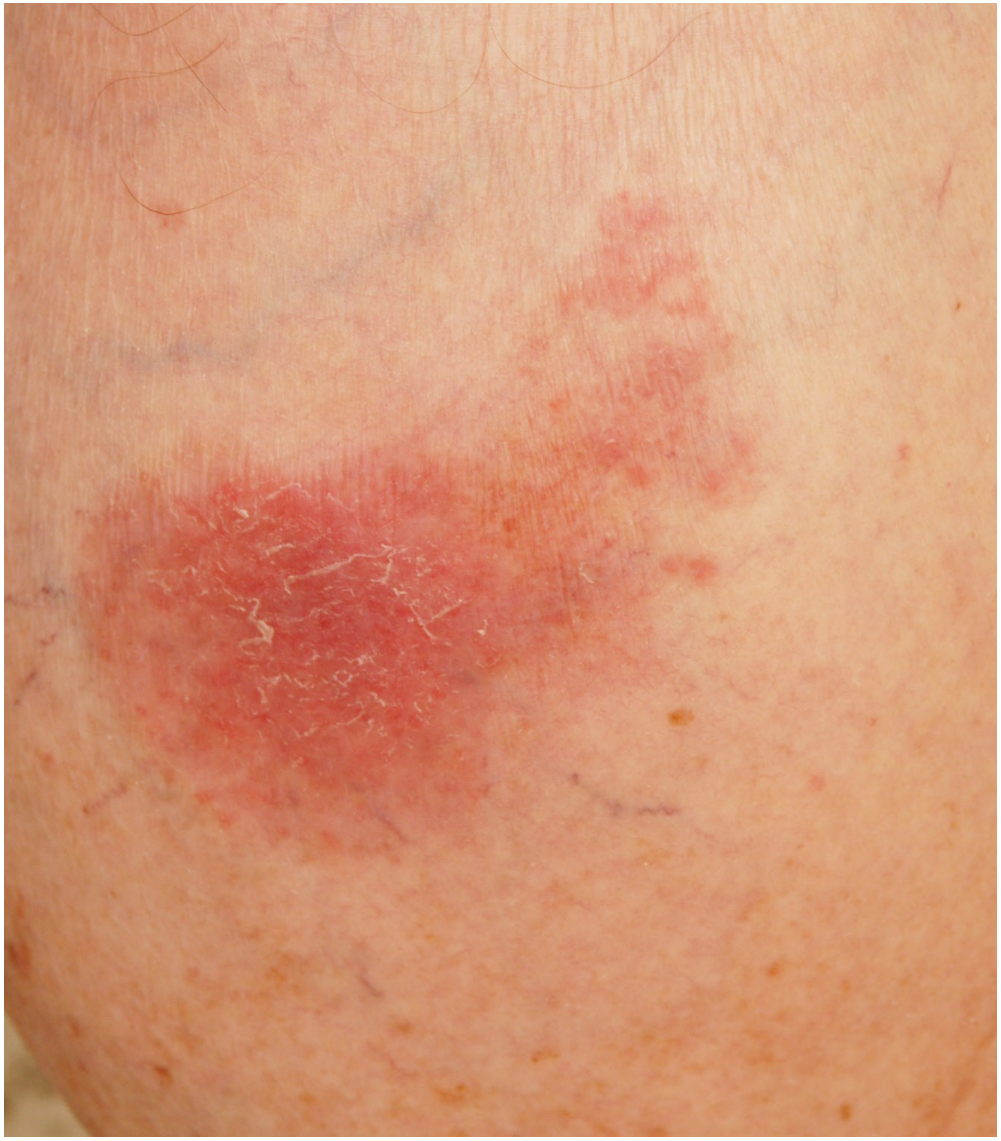


Sézary syndrome

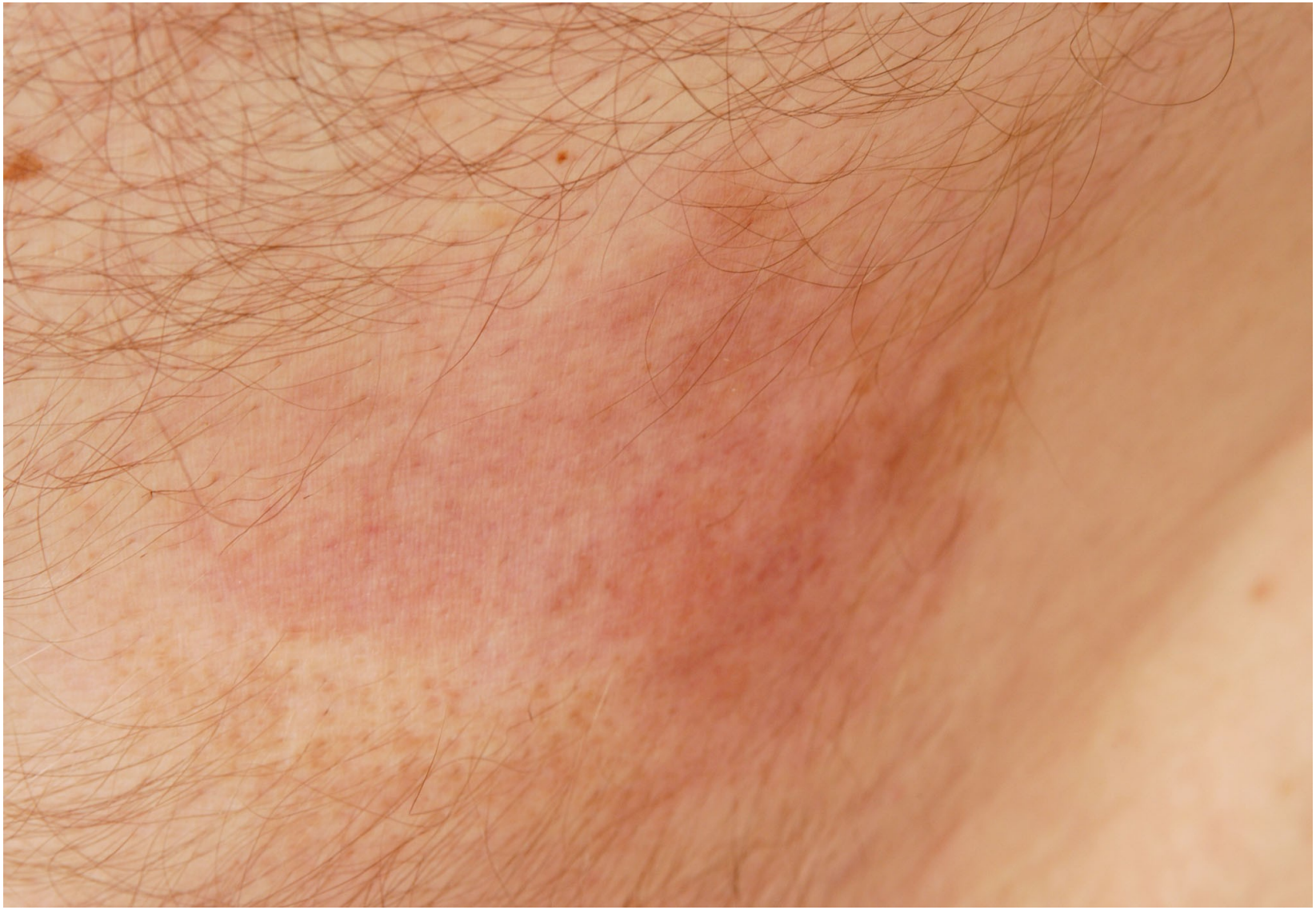


Sézary syndrome – 3 months bexarotene + PUVA therapy





MF before PDT



After PDT

Conclusion

- In dermatology we have possibilities to treat CTCL by many methods according to diagnose and staging.
- In initial stage of mycosis fungoides we are able to stop or to control it’s development
- In Sézary syndrome recent immunotherapy can attribute to longer remission