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Transformation of chronic atopic dermatitis to a cutaneous T- cell lymphoma: a case report

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Patient T.B., born in 1983

Family history: father hay fever , cardiac arrhythmia
mother: healthy
siblings: brother - asthma, atopic dermatitis, allergy to pollen
children: 0

Personal history: common childhood diseases
asthma until 10 years

FA: Symbicort 200 inh. Pulv., Xyzal 1-0-0, 0-0-1 Dithiaden

AA**: pollen, animal dander, dust mites**

Abuse: smoker, little alcohol, coffee once daily
PP: height 181 cm, weight 58 kg,
PSA: Logistics at Pelikan Hard Copy comp., Kyjov,
Lives with his wife in an apartment house. Animals: water turtle

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Course of the disease

Atopic dermatitis since early childhood / since 4 years of age/

Since 2009 **erythroderma** IgE 2300 IU/ml (2010)

since the end of 2010 reccurent herpetication of AD,

thererefore topical KS discontinued. Treaterd repeatedly with acyclovir

Severe itching - antihistamines, sedatives, with minimal effect

8/2010 LN biopsy /left axilla/ - benign lymphadenopathy within AD

Immunophenotyping of periferal blood T cells (flow cytometry) - normal

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Course of the disease

Treated with phototherapy: **UVB 311** in spring 2010

for two months and in spring 2011

Inguinal lymphadenopathy appeared in Aug 2011

Histology of the skin in the right groin : epidermotropic peripheral T-cell lymphoma - **mycosis fungoides, patch stage**

Lymh node biopsy /right groin/ histological picture compatible with dermatopatic lymphadenopathy within MF / SS, LN involvement is proportional to category I.

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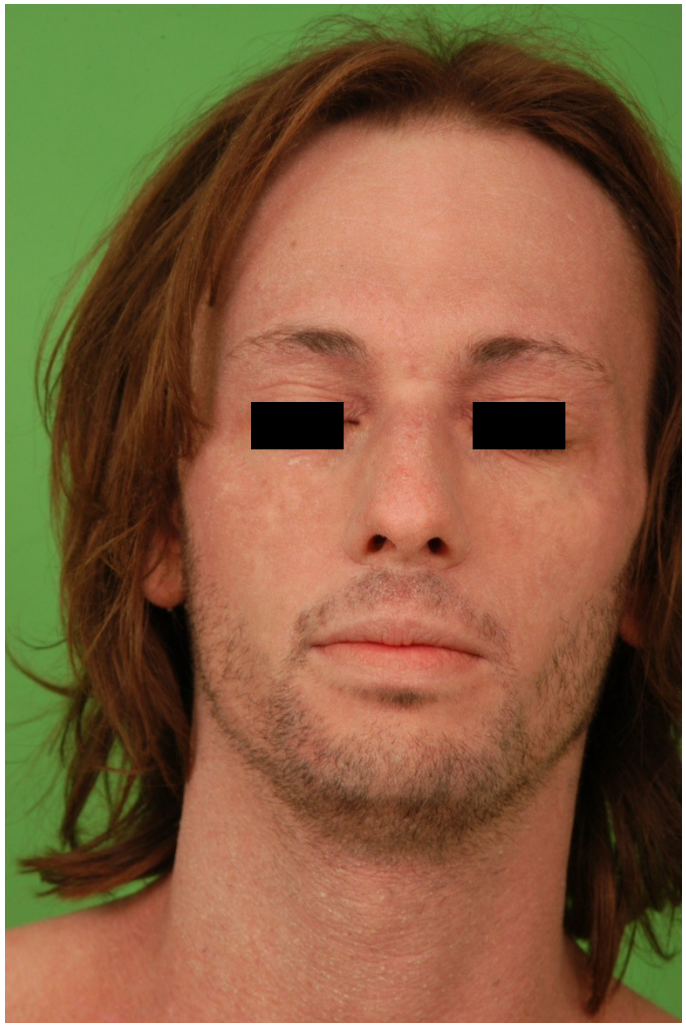
Aug 2011



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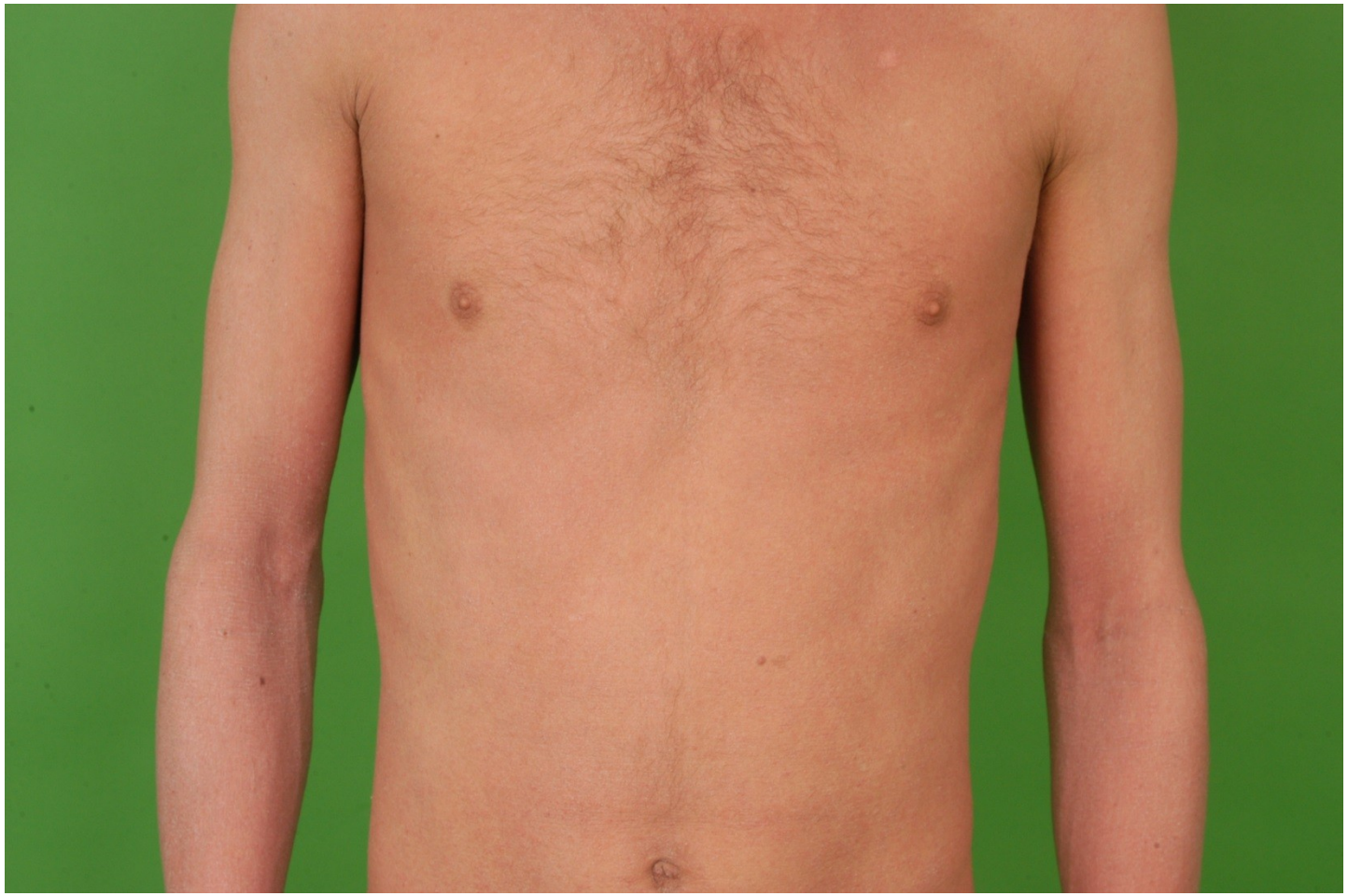
Aug 2011



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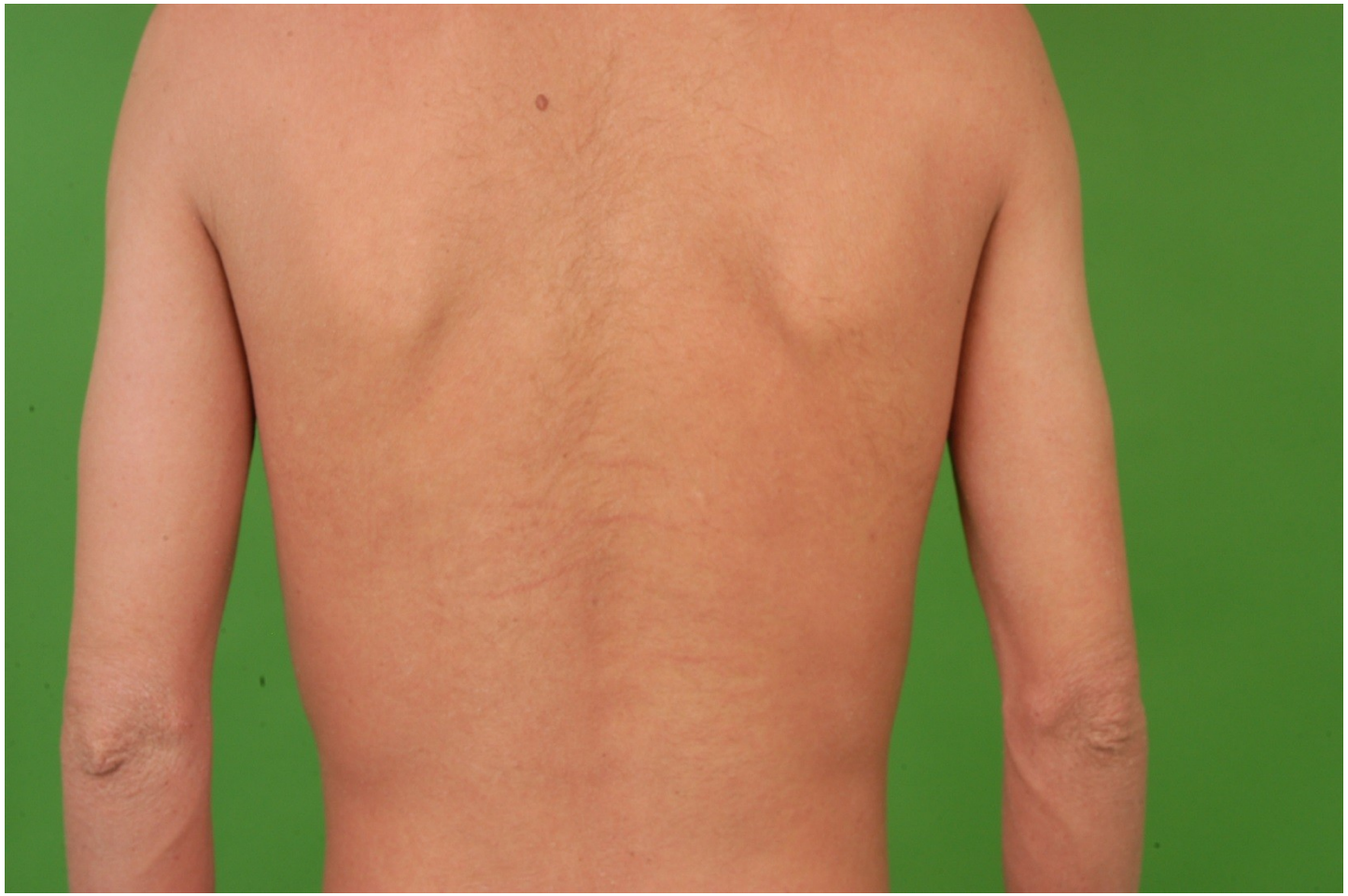

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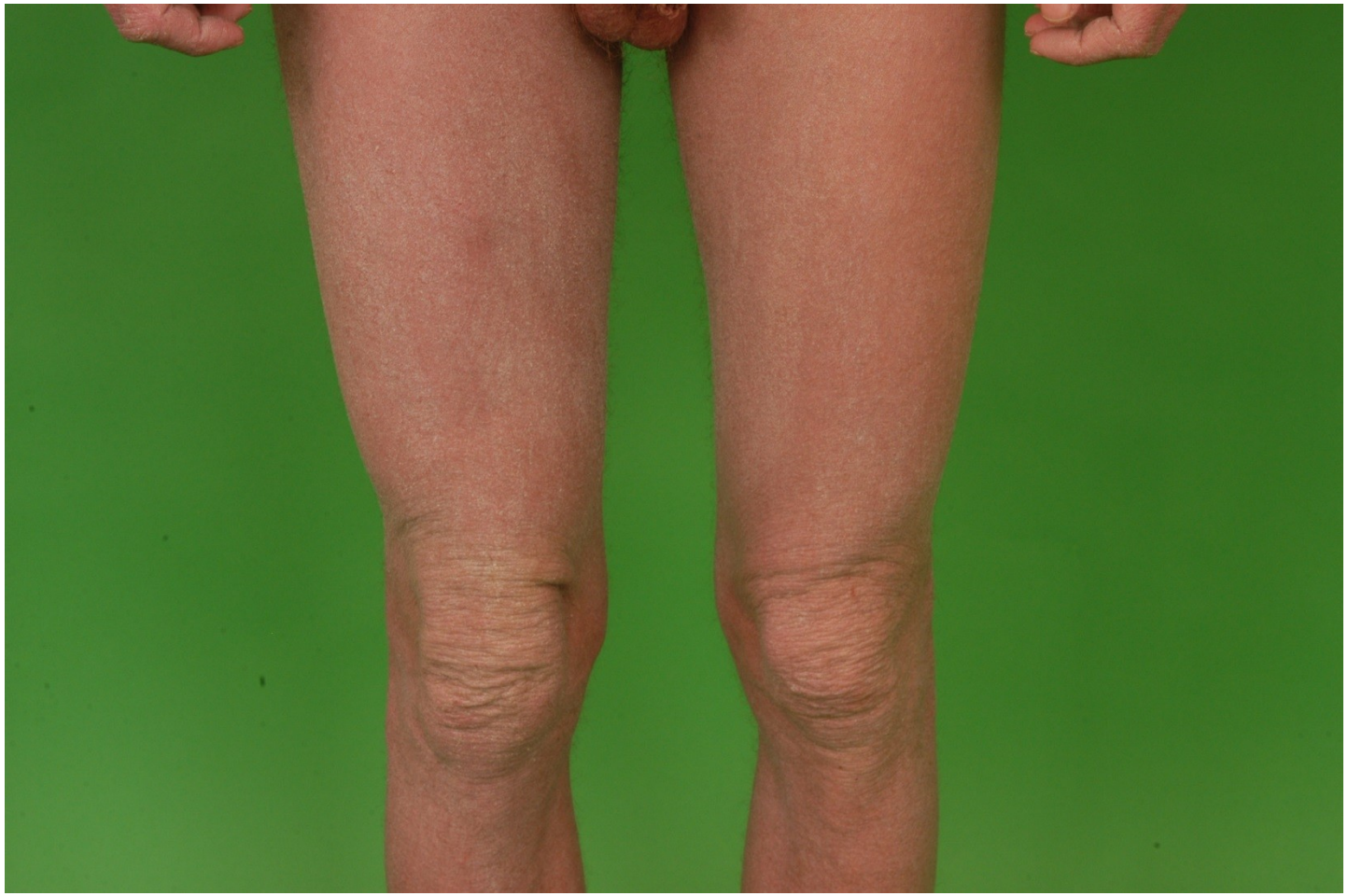

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Sept-Oct /2011

Total IGE 11 942 IU/ml

Immunophenotyping of periferal blood T cells /Flowcytometry/:
CD 3-+4+7 (MF) cells make 7,82 % of lymphocytes
Index CD4/CD8 2,157

Biopsy from right thigh: **chronic dermatitis of AD type**. Signs suggestive of mycosis fungoides are insufficient in this preparation. Material submitted for a second reading and examination of clonality

Clonality test result was unassessable.

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Oct-Dec/2011

PUVA : end of 10/2011 to half 12/2011 - terminated because of irritation

5/2012 erysipelas of the right thigh, treated with procaine penicillin G for 10 days, at the end benzathin PNC 1,5 MIU applicated.
Later 5 or 6 more erysipelas at the same site happened, probably because of removed LN in the right groin, treatment with benzathin PNC was introduced - pendeponization

Total IgE 8 030 IU/ml

flowcytometry - CD3 + 4 + 7 – MF cells make 6.35 % of lymphocytes
index CD4 / CD8 2,612.

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July-Sept/2012

July/2012 **PET/CT**: slightly increased metabolism in both axillary and inguinal lymphnodes compatible with suspected low grade lymphoma

Total IgE 5 837 IU/ ml

9/2012 biopsy from the left trunk : The finding corresponds with subacute **atopic eczema.** For the diagnosis of mycosis fungoides there are not enough signs. Yet sorting of the cells near basement membrane may preceed the development of lymphoma. **Clonality assessment not possible**

Sept/2012 biopsy from left axillary LN : negative for MF

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Jan-May/2013

Phototherapy UVA- 1 from Jan 2013 to end of May 2013

Total IgE 6 564 IU/ ml

Immunophenotyping of periferal blood T cells /flowcytometry/:
CD3+4+7- cells make 7,67% of lymphocytes
Index CD4/CD8 3,324

PET / CT shows stationary finding of a higher FDG activity in LN of both axillary and groin LN, it might be an activity accompanying a low grade lymphoma

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Sept/2013

Biopsy from the skin lesions in the right forearm

Skin excision with psoriasiform hyperplasia of the epidermis covered by slightly extended hyperkeratotic slats with small areas of parakeratosis. Papillary dermis slightly expanded, with a vaguely nodular molded medium-dense infiltrates of small and medium-sized lymphoid cells somewhere with irregular contours of nuclei, inconspicuous focal pigment incontinence. Sporadically, the admixture of eosinophilic granulocytes. In the epidermis rare isolated cells of lymphoid appearance with cerebriform appearance of nuclei.

There is no sorting of lymphoid cells on the dermo-epidermal junction, no intraepidermal aggregates of lymphoid cells. Reticular dermis without alteration.

Conclusion: **rather chronic eczema/dermatitis**. Not all features which would allow an unambiguous diagnosis fulfilled. Progression to MF should be monitored.

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Histology

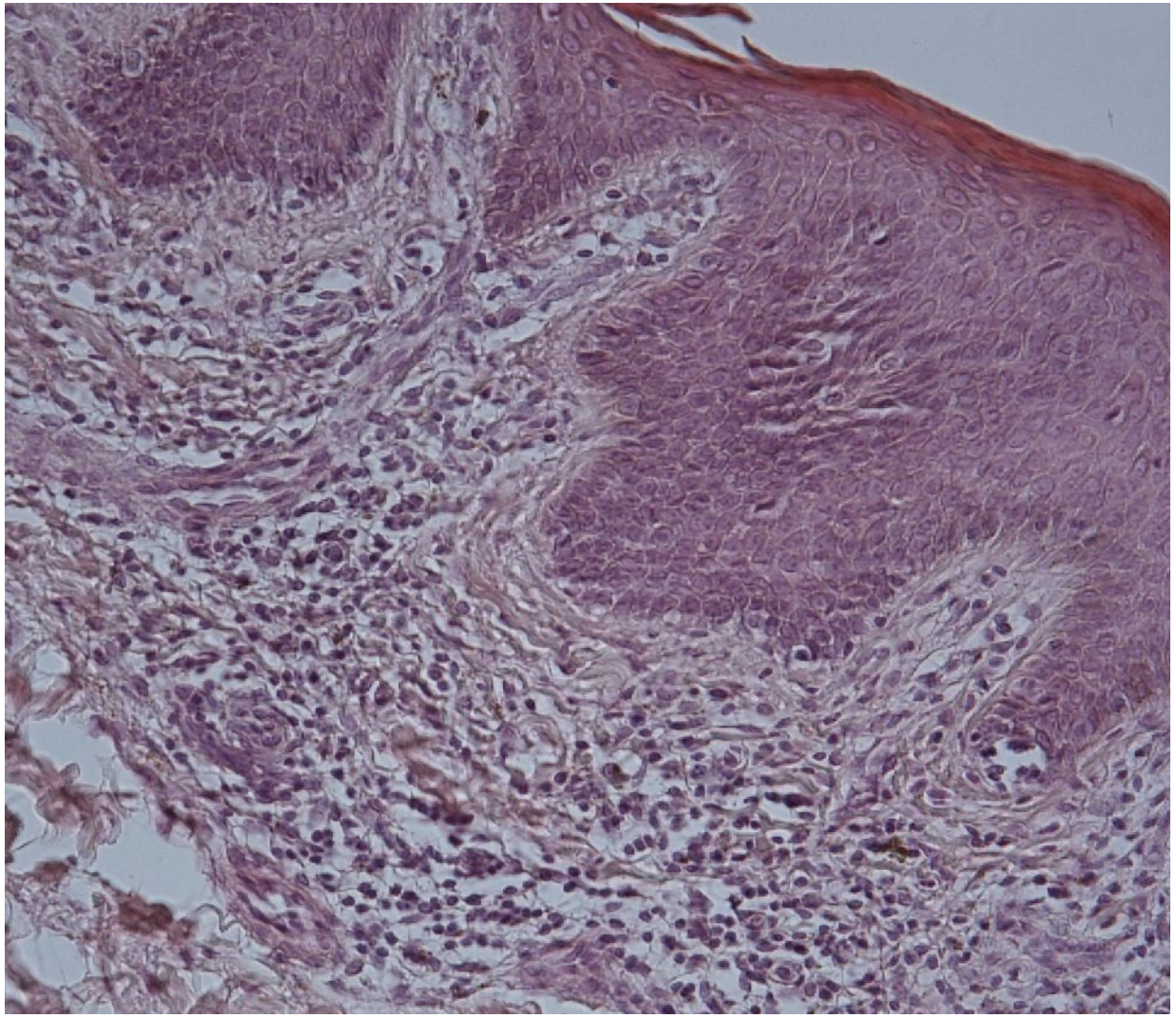

Photo: ass. prof. Jedličková, Ph.D.

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Nov/2013-Jun/2014

UVA -1 from Nov/2013 to June/2014

IgE 9 164,0 kU/l

9/2014 Flow cytometry CD4+8+7- cells 8% index. 2,594

9/2014 biopsy from the forehead skin

Epidermis with reduced straum corneum, distinct acanthosic pins. Beneath the epidermis there are dense spherical lymphohistiocytic infiltrates with deposits of pigment. Lymphocytes focally enter epidermis

RES: Density of the infiltrates and the character of the invasion of lymphocytes into the epidermis is very suggestive of mycosis fungoides, material sent for immunostaining.

Clonality test: Isolated DNA of poor quality. Clonality can not be assessed. Consider retesting for clonality and consultation in another laboratory.

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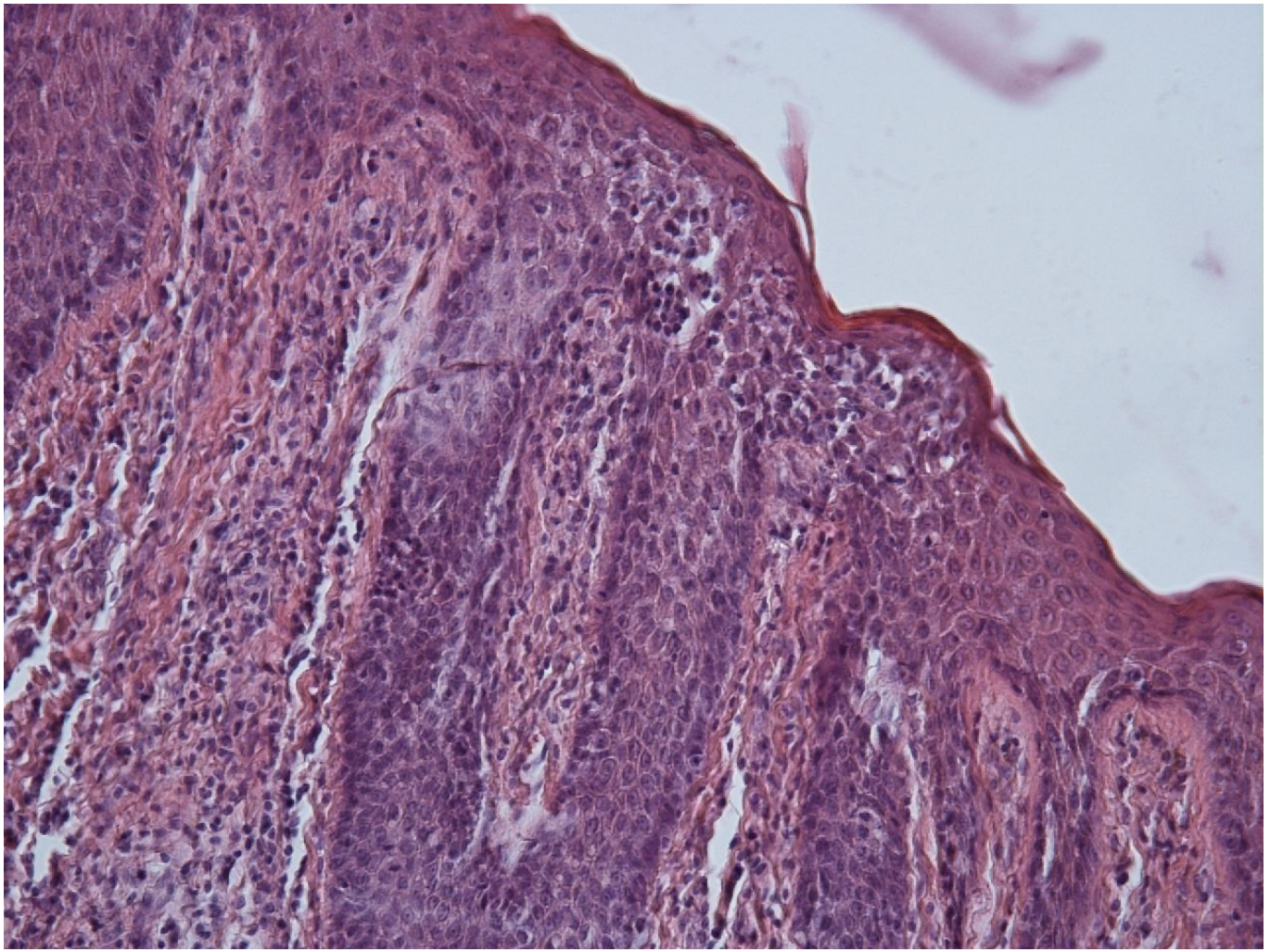
Histology



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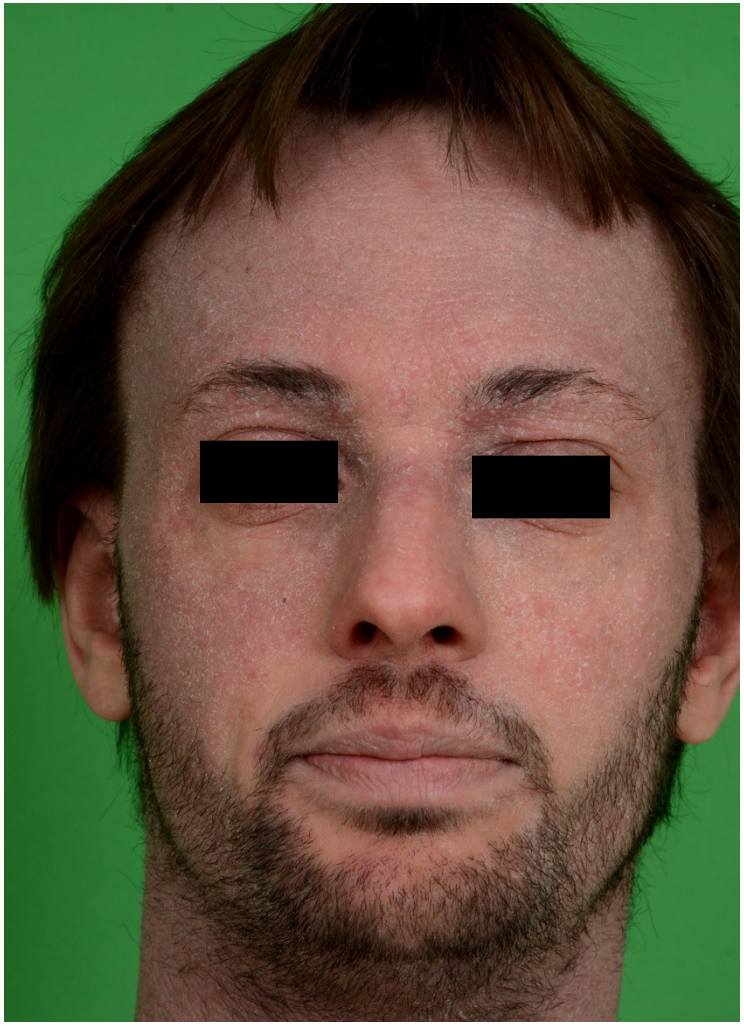
Sep/2014



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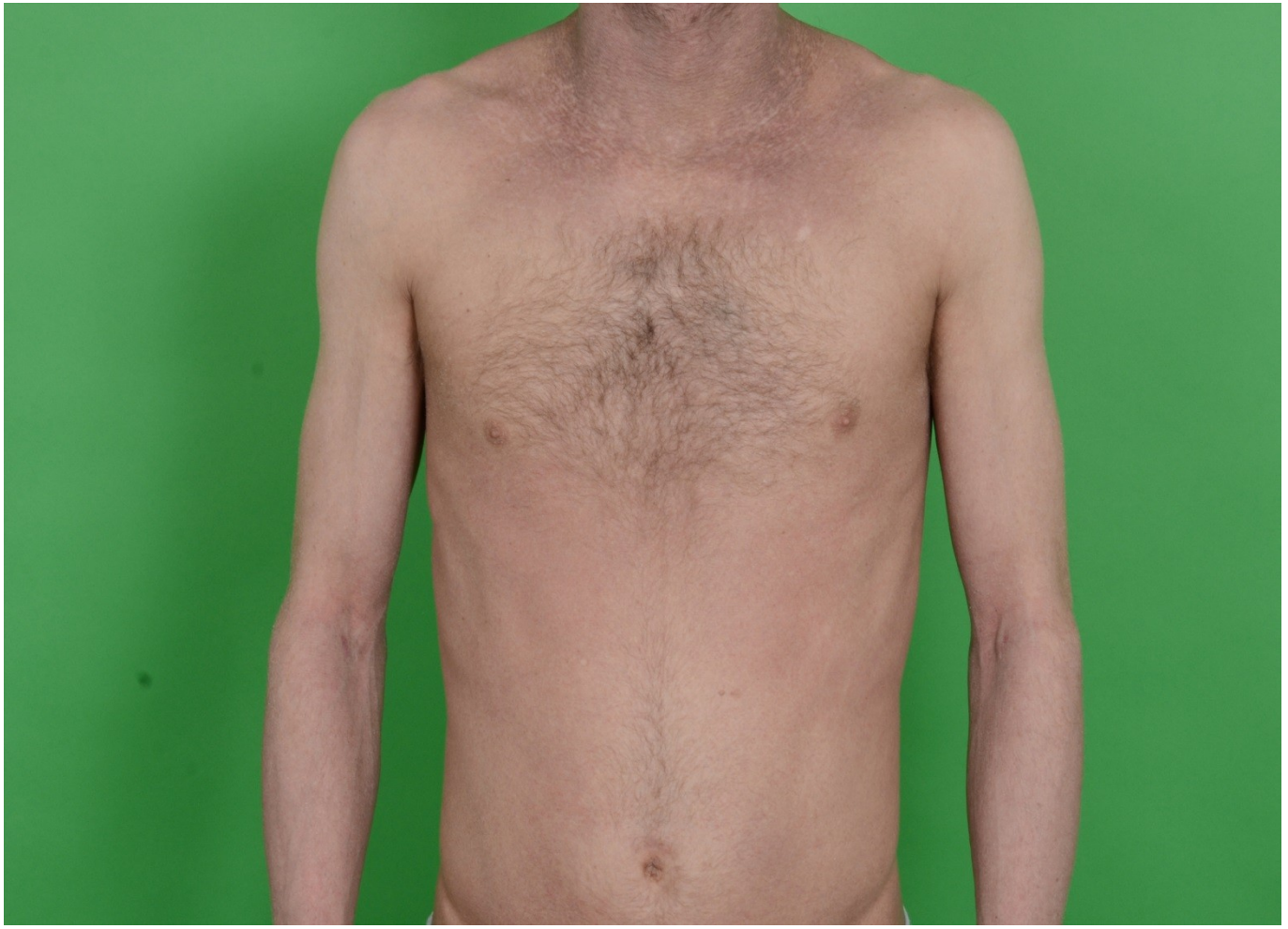

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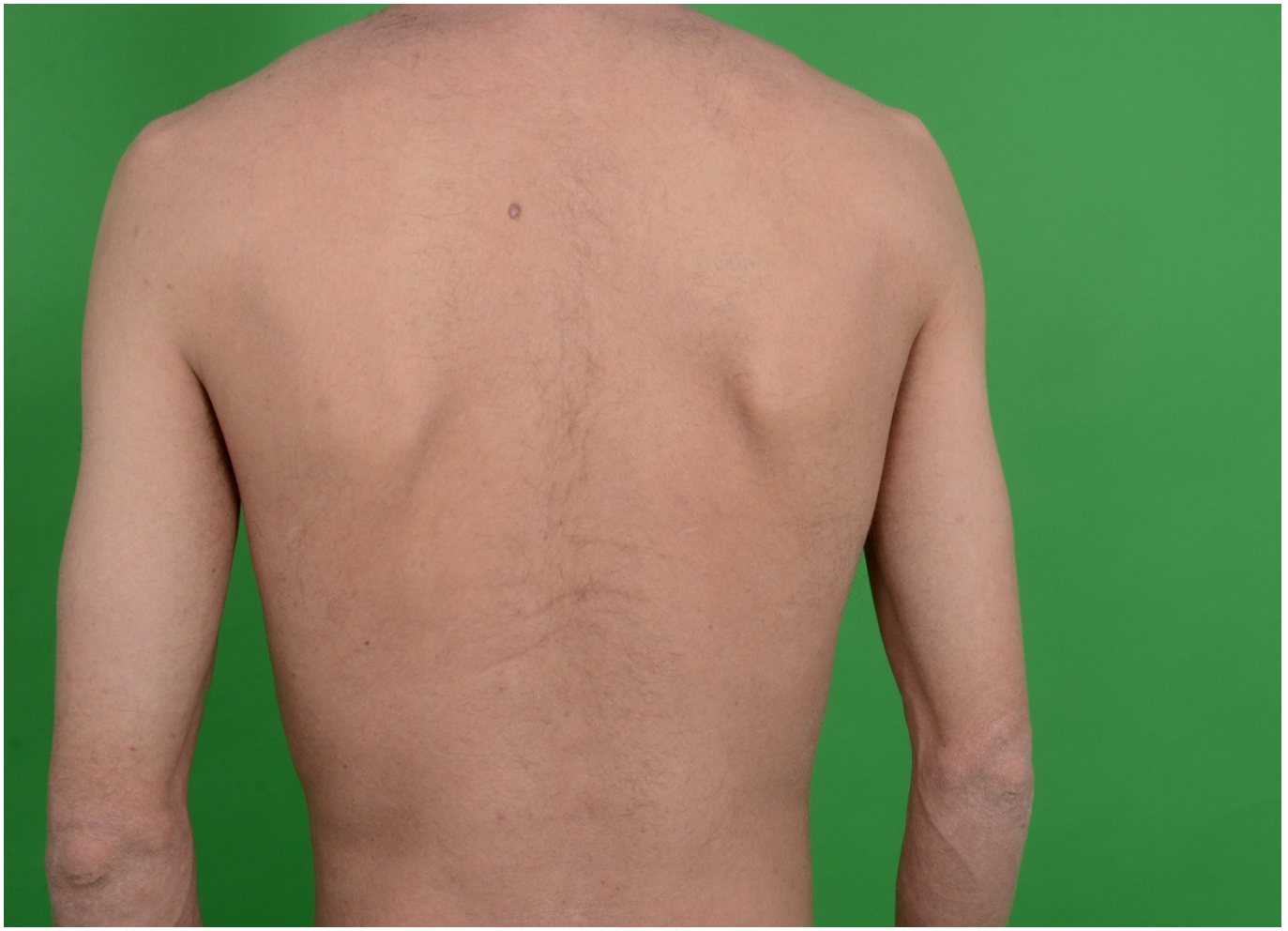

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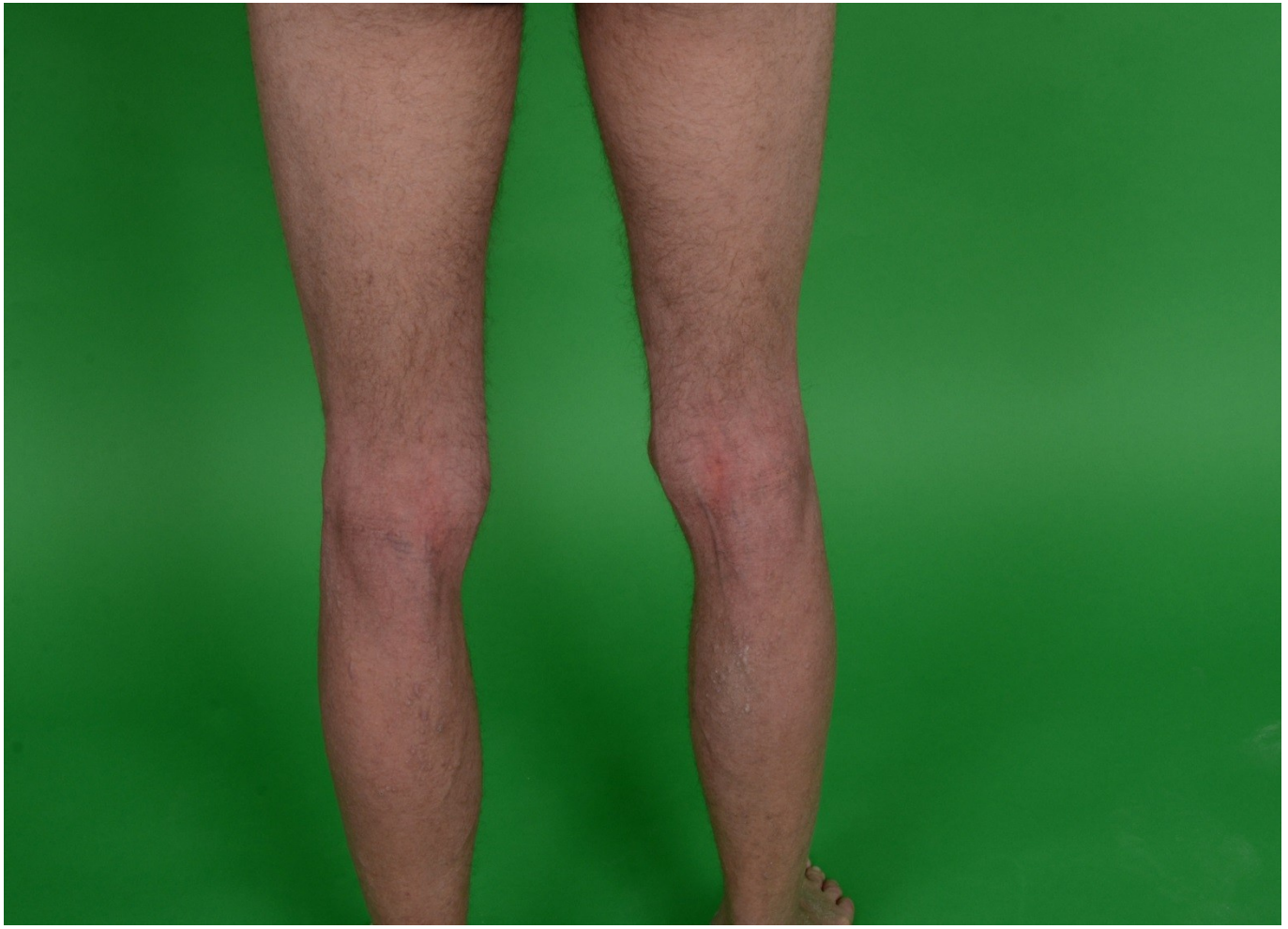

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Nov/2014

Nov/2014 Treatment with **acitretin** 40 mg daily

+ **interferon** α gradually increased to 6 MIU 3 times a week s.c.

Jan/2015 skin finding except the face satisfactory, significant reduction of lymphatic nodes

Tolerance of the treatment - very good

Laboratory findings satisfactory - slight elevation of LT and lipids

acitretin reduced to 30 mg daily, interferon α to 4.5 MIU 3 times a week

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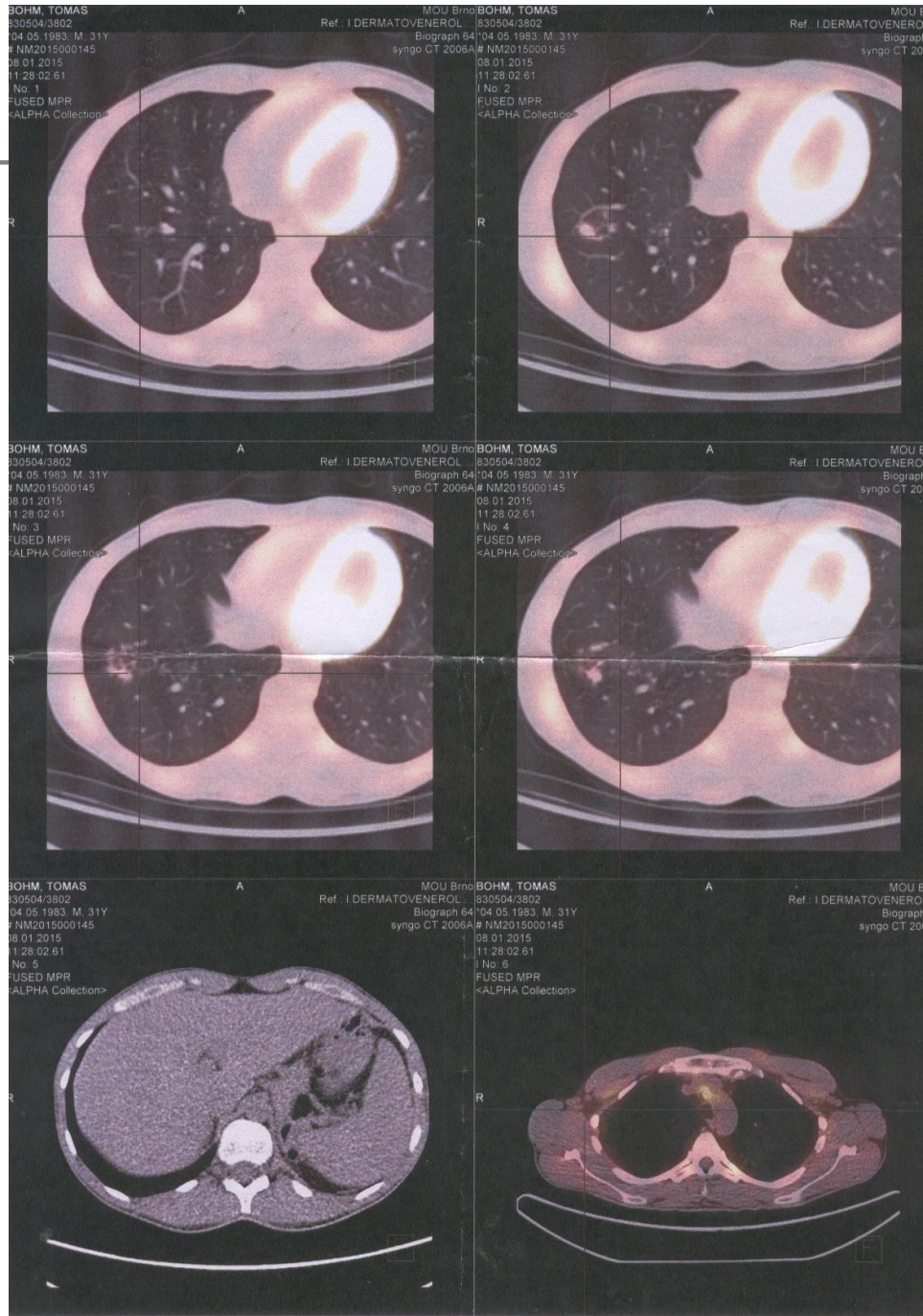
Jan/2015 PET CT:

- significant metabolic and size **regression of axillary and inguinal LN**
- higher metabolism of bone **marrow especially** in the **pelvic bone** and of the spine of unclear etiology.
- Several minor active areas in the S8 / 9 segment of the **lungs** – probably a postinflammatory change
- light progression of the spleen size



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Feb/2015-May/2015

2/2015: **bone marrow aspiration** was performed from the left hip

result: histologically in the bone marrow without an evidence of the infiltration of the bone marrow with a lymphoma

flowcytometry - normal

in myelogram rare atypical lymphocytes

res: no ivolvement of bone marrow by a lymphoma

5/2015 **acitretin reduced to 20 mg daily**, interferon α left on dose of 4.5 MIU 3 times a week

Laboratory: LT and cholesterol normalized

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Jun/2015-Sept/2016

6/2015 flowcytometry : CD4+8+7- 13% of lymphpocytes

index CD4/CD8 3,538

10/2015 total IgE 5 770 IU/ml

5/2016 total IgE 6 305 IU/ml

Lab: slight **leucopenia** (minim. 3,4 10^9/l) between 9/2015 and 11/2015

Interferon α reduced to 3 MIU and then to 1,5 MIU 3 times a week

7/2016 flowcytometry : CD4+8+7- 7,4 % of lymphocytes

index CD4/CD8 2,647

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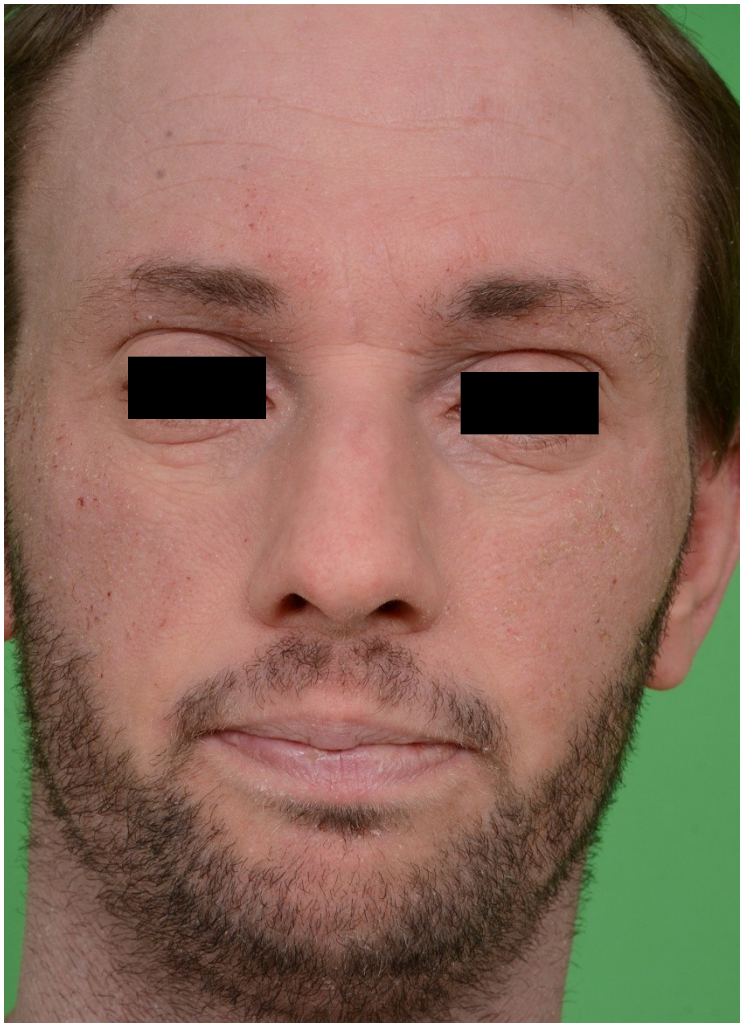
Sept/2016



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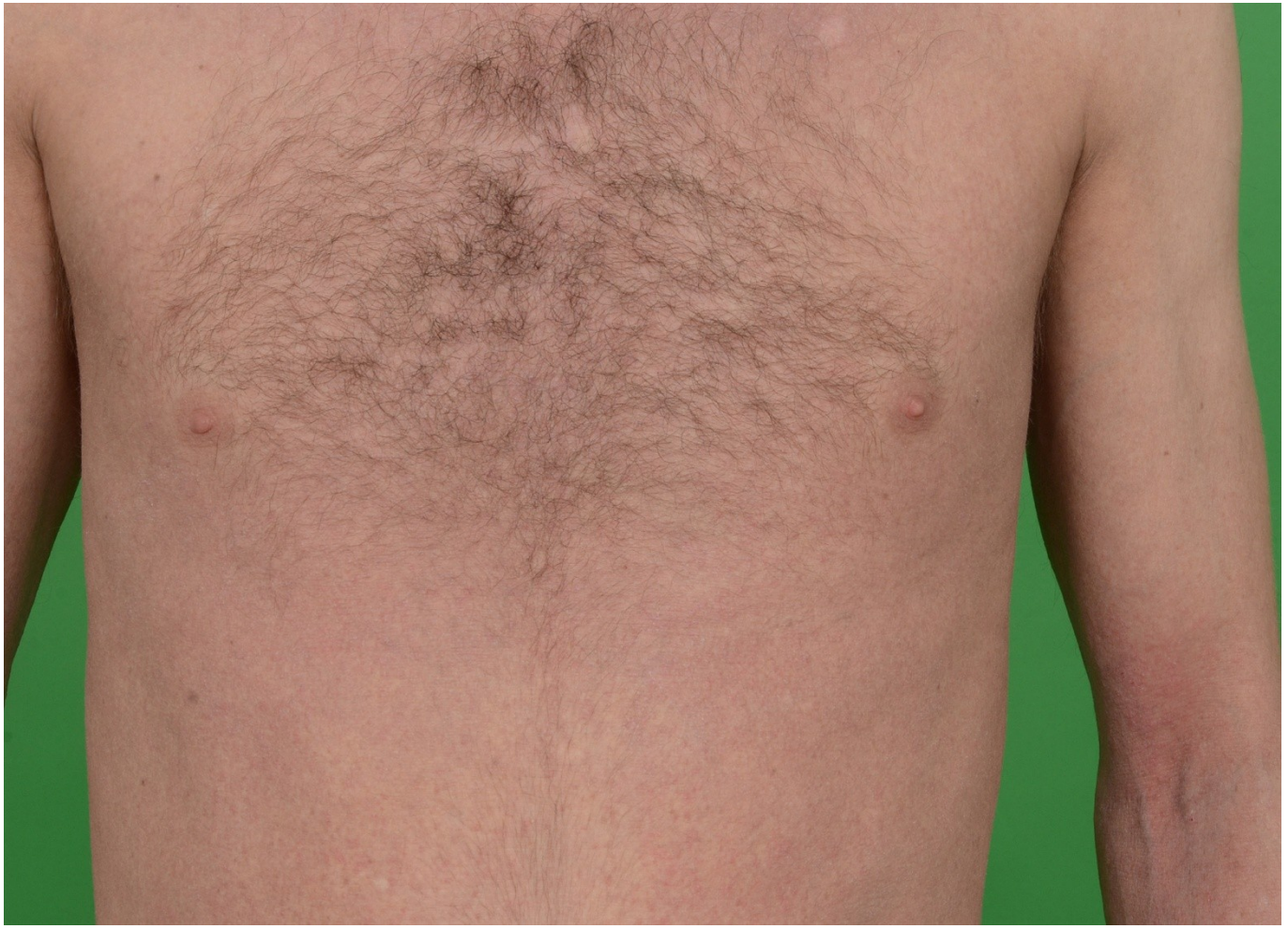

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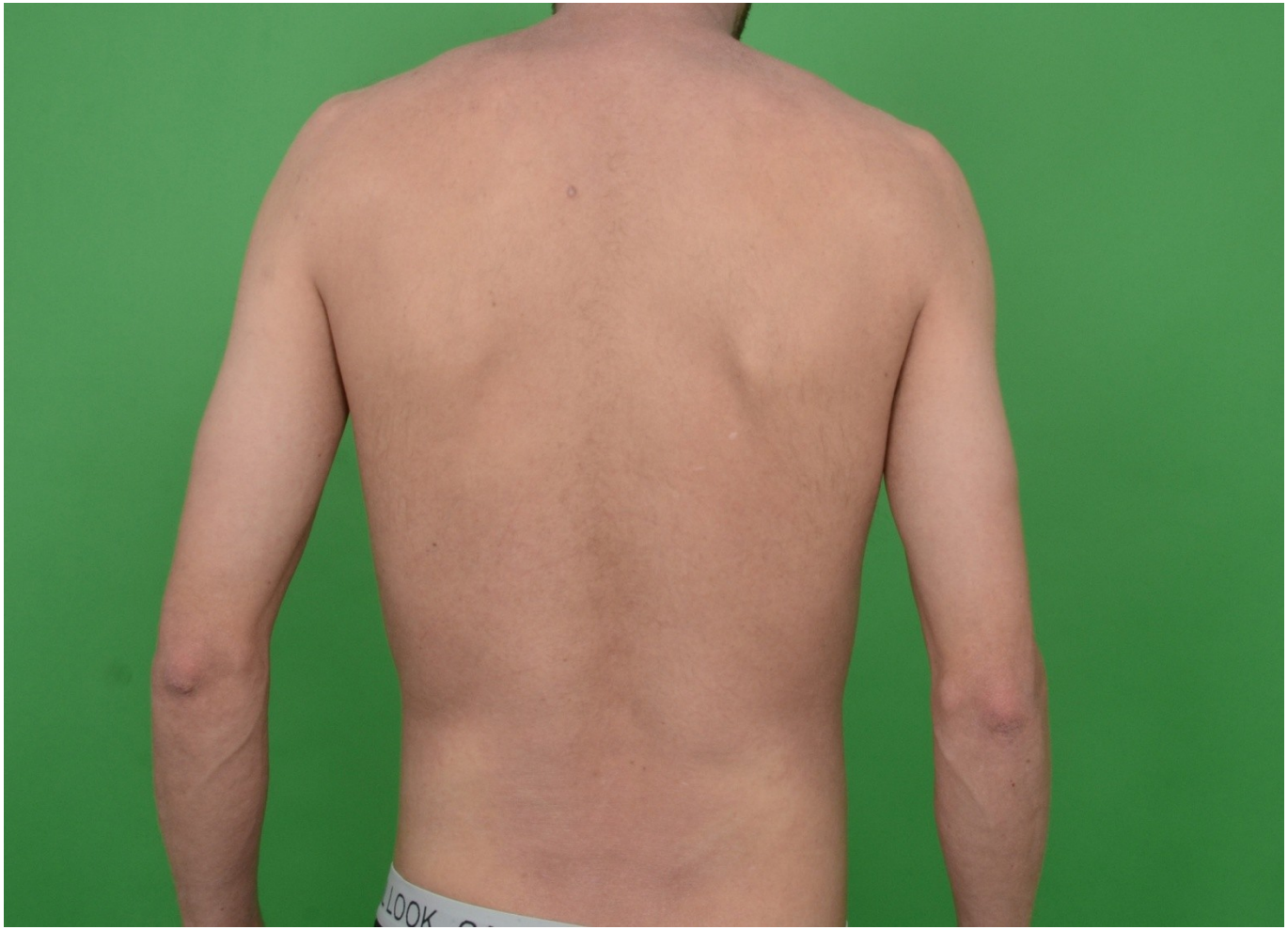
Sept/2016



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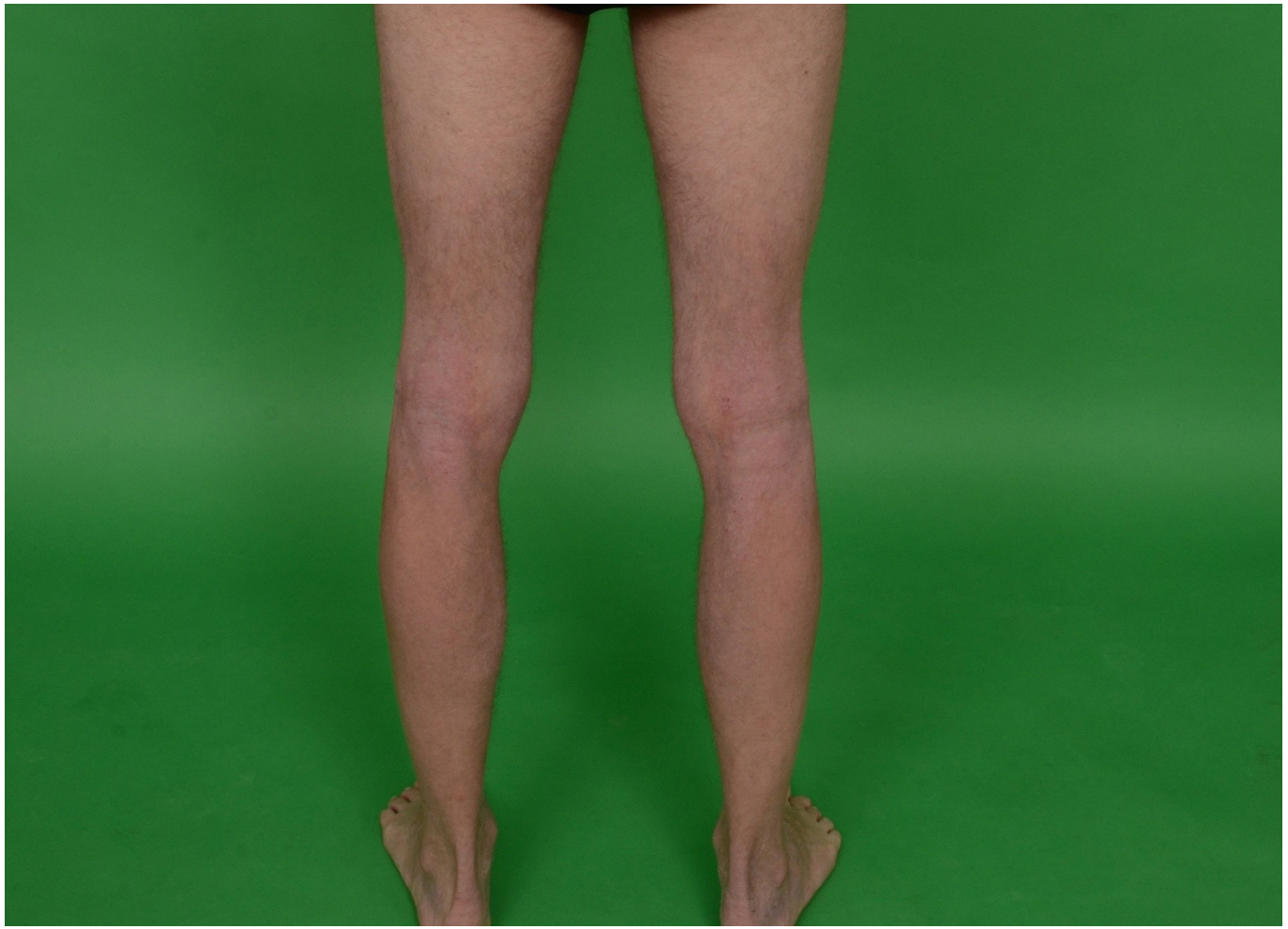

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Classification of CTCL

Primary cutaneous T-cell and NK-cell lymphomas

Mycosis fungoides

Variants of mycosis fungoides: Folliculotropic mycosis fungoides
Pagetoid reticulosis
Granulomatous slack skin

Sezary syndrome

Leukemia/adult T-cell lymphoma

CD30+ T-cell lymphoproliferative hyperplasias: CD30+ anaplastic large T-cell lymphoma
Lymphomatoid papulosis

Subcutaneous panniculitis-like T-cell lymphoma

Extranodal NK/T-cell lymphoma, nasal type

Primary cutaneous peripheral T-cell lymphomas, unclassified

Primary cutaneous aggressive epidermotropic CD8+ T-cell lymphoma

Cutaneous γ/δ T-cell lymphoma

Primary cutaneous small/medium CD4+ T-cell lymphoma

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Discussion

AD associated CTCL – quite rare:

CD30+ lymphomas (8 cases)

Sezary syndrome (2 cases)

Mycosis fungoides (3 cases)

Probably underdiagnosed (or unpublished)

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Discussion

- **Mechanisms leading to the development of malignant T cell population:**

- Chronic antigenic stimulation (of cutaneous
- lymphocytes) or chronic inflammation itself
- Immunosupressive nature of the disease,
- Treatment (cyclosporine, TIMs)
- Phototherapy??

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Conclusion

In a long lasting severe AD dermatologist must be aware of **posssible transformation of the condition to a CTCL** especially if the diseases does not react properly to usual treatment of AD

Repeated histology, immunophenotyping, flow cytometry, TCR gene rearrangement (clonality)

Staging (X-ray, CT, PET/CT, US of LN or biopsy, bone marrow biopsy or trepanobiopsy)

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Markers to differentiate AD/CTCL

sIL-2R, serum LDH, IgE - elevated in both

Low specific IgE, high CD4/8 ratio - usualy in CTCL

CCL 17 (TARC) – CCL 8 or CCR 4	elevated in both
CCR 11 and CCR 26 – CCR 3	elevated in both
CCL 27 (CTAC) – CCR 10	**elevated in CTCL**

FoxP3+ regulatory T cells (T regs) elevated in AD not CTCL

Hanafusa T, Matsui S, Murota H, Tani M, Igawa K, and Katayama I. Increased frequency of skin-infiltrating FOXP3+ regulatory T cells as a diagnostic indicator of severe atopic dermatitis from cutaneous T cell lymphoma. Clin Exp Immunol. 2013 Jun, 172(3): 507-512

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Thank you for your attention

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