CLINICAL ADVANCES OF ANTI-TIF1Γ AUTOANTIBODY IN A HUNGARIAN MYOSITIS COHORT

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IDIOPATHIC INFLAMMATORY MYOPATHIES

- Polymyositis (PM)
- Dermatomyositis (DM)
- Juvene PM/DM
- Inclusion body myositis (IBM)
- Overlap myositis (OM)

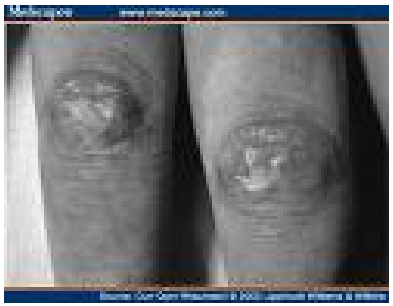
- Necrotizing autoimmun myopathy (NAM):
  - Cancer associated myositis (CAM)
  - Statin induced myopathy
  - Infection induced myopathy

IDIOPATHIC INFLAMMATORY MYOPATHIES – SKIN SYMPTOMS







Gottron's sign and papule

IDIOPATHIC INFLAMMATORY MYOPATHIES – SKIN SYMPTOMS



Heliotrop rash

Linear extensor erythema


Periungual teleangiectasia


IDIOPATHIC INFLAMMATORY MYOPATHIES – SKIN SYMPTOMS

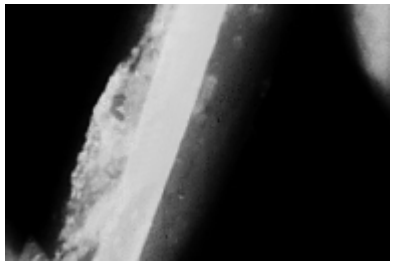
V-sign

Facial erythema

Shawl sign

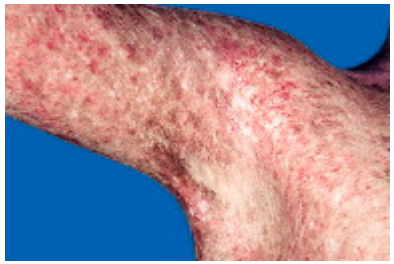
Periorbital oedema

IDIOPATHIC INFLAMMATORY MYOPATHIES – SKIN SYMPTOMS



Calcinosis cutis

Alopecia



Poikiloderma athrophicans vasculare

Livedo reticularis

CAM (CANCER ASSOCIATED MYOSITIS)

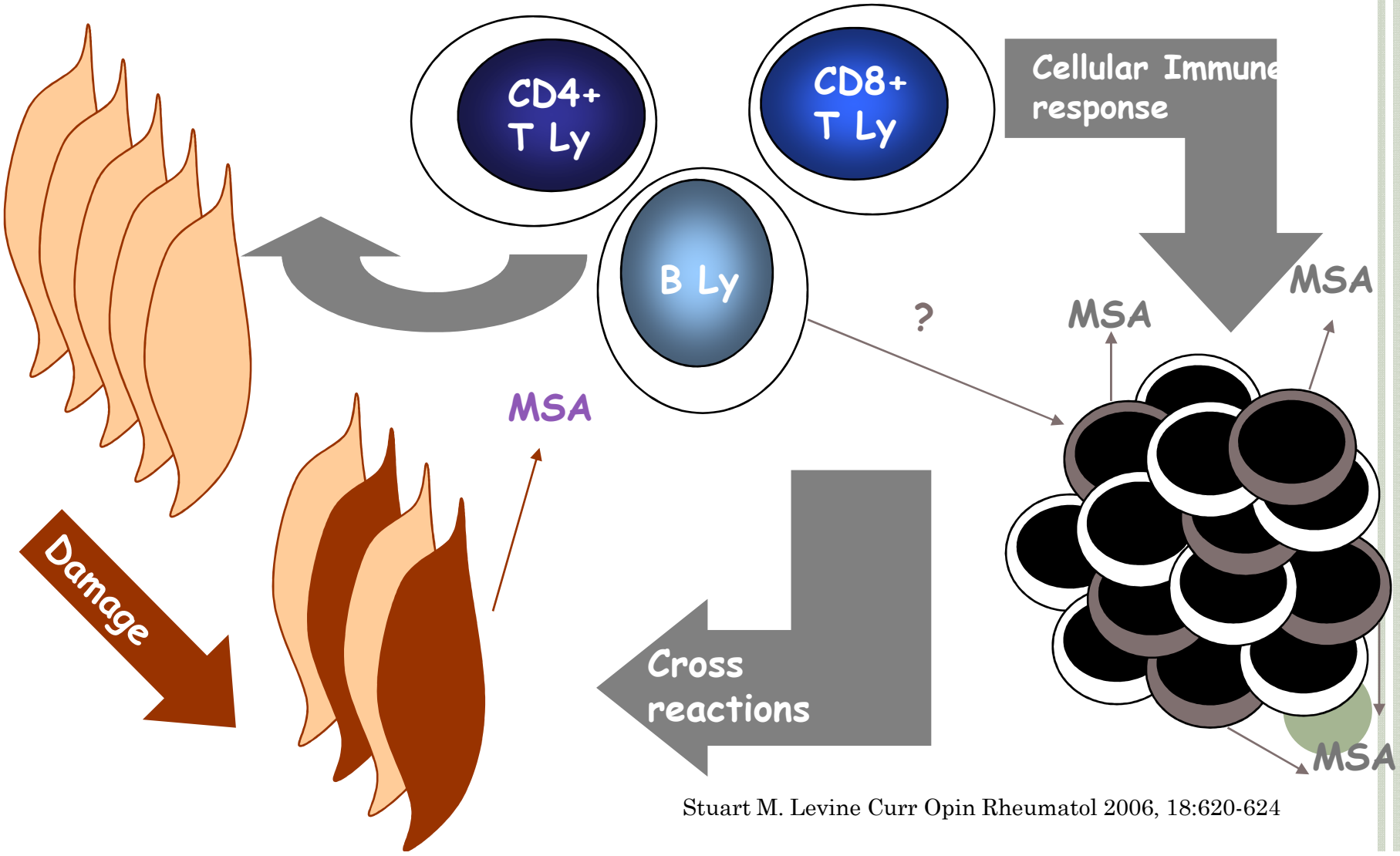
- Frequency 7-66%
- Relative risk for malignancy
  - 3x in DM
  - 1,3x in PM-ben
- Tumor types: ovarium, breast, lung, colon, endometrium, nasopharyngeal, lymphoma, prostata)
- In time:
  - Before myositis symptoms (> 1 years)
  - **Real paraneoplasia (- 1 – +5 years)**
  - After myositis diagnosis (> 5 years) – role of immunosuppressive therapy?

R. Aggarwal, C.V. Oddis Paraneoplastic myalgias and myositis Rheum Dis Clin N Am 2011

CAM - Etiology

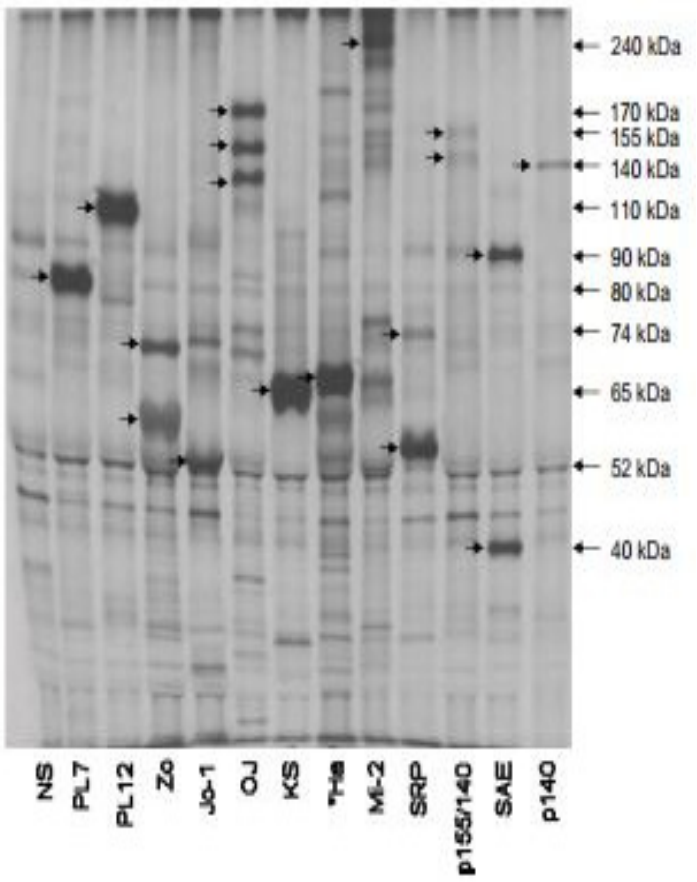
- Paraneoplasia
- Cytotoxic/immunesuppressive treatment (Methotrexat, cyclophosphamid)
- Common trigger (EBV?)

CROSSOVER IMMUNITY IN CAM



Stuart M. Levine Curr Opin Rheumatol 2006, 18:620-624

Anti-TIF1γ



- antigen: transcription intermedier factor 1 gamma
  - 155/140kDa protein
- 13–21% in adult and 23–29% in juvenile DM cases
- severe skin symptoms,
- high tumor risk in adults

OUR STUDY

- Autoantibody analysis from IIM patients' serum (n=202) with ELISA and/or IPP
- Frequency of anti-TIF1γ positivity
- Frequency of TIF1γ negative CAM
- Clinical and lab findings associated with anti-TIF1γ positivity

PARAMETERS

- Clinical symptoms
  - Proximal muscle weakness
  - Distal muscle weakness
  - Skin rash
  - Dysphagia
  - Raynaud phenomen
  - Arthralgia
  - ILD
  - Fever
- Lab results:
  - CK and LDH levels
  - CRP
  - ESR
  - ANF positivity
  - Tumor markers

TIF1Γ POSITIVE PATIENTS (N=12)

- CAM n=3
  - Real paraneoplasia in DM (n=1)
  - After myositis diagnosis in DM (n=1) and in PM (n=1)
- Subsets:
  - DM n=7
  - JDM n=4
  - PM n=1
- Gender:
  - Female 75% (n= 9)
  - Male 25 % (n=3)

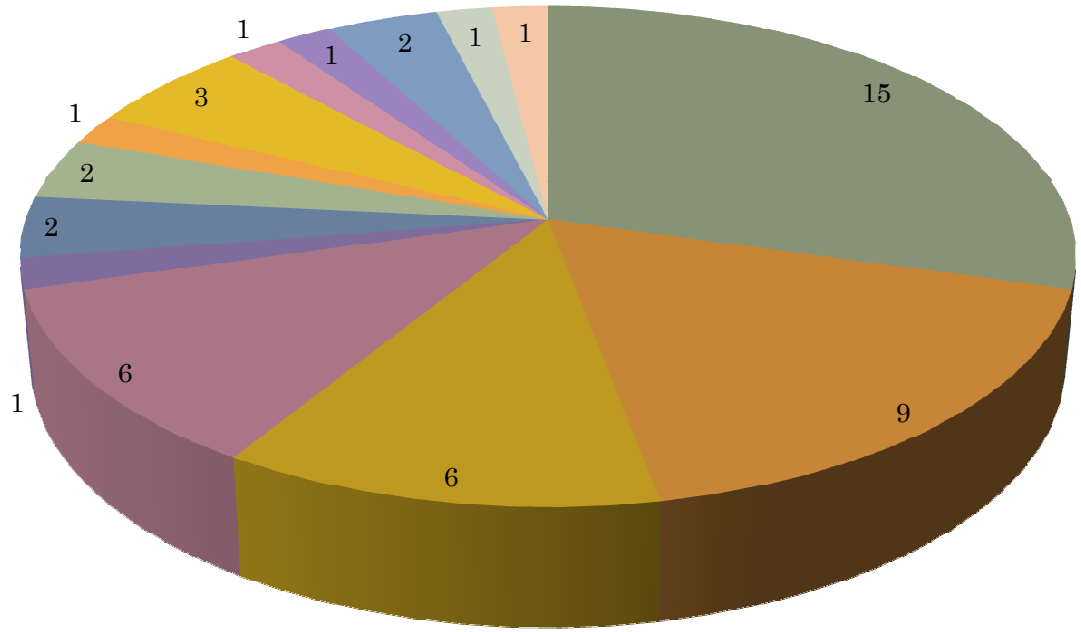
TIF1Γ POSITIVE CAM PATIENT – REAL PARANEOPLASIA

- 34 years old, women
- First symptoms in April 2007:
  - Skin rash
  - Muscle weakness
  - Dysphagia
  - Arthralgia
- In July 2007 – ovarium tumor
- Histology: adenocarcinoma with peritoneal metastasis
- Operation and chemotherapy
- She died in November 2007 due to heart failure

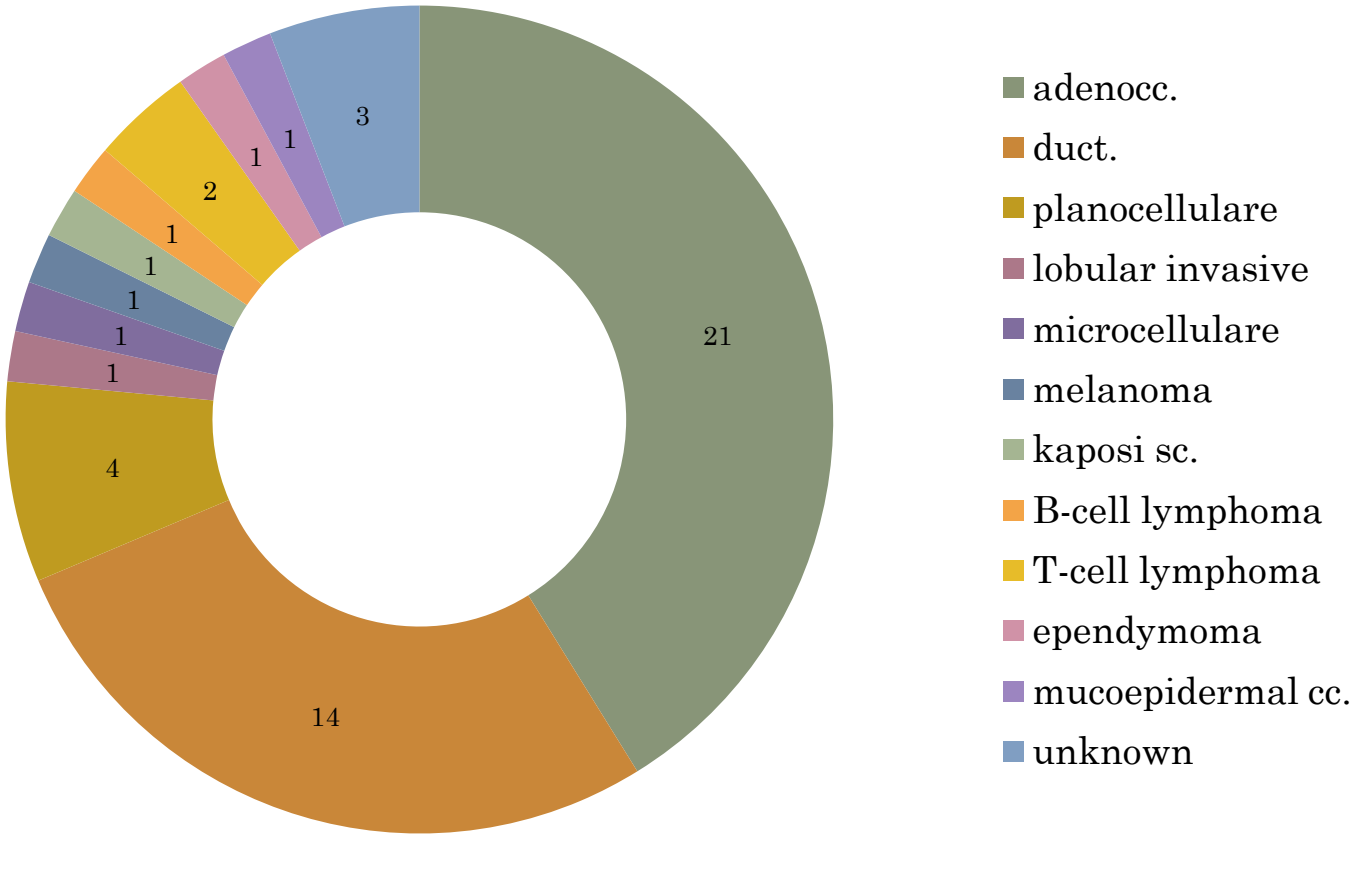
TIF1Γ NEGATIVE CAM PATIENTS (N=51)

- Subsets:
  - DM(n=33)
  - PM (n=18)
- Gender:
  - Female 68% (n= 35)
  - Male 32 % (n=16)
- In time:
  - real paraneoplasia (n=37) - 5 months
  - before myositis (n=2) - 73,5 months
  - After diagnosis (n=12) – 181 months

TIF1Γ NEGATIVE CAM (N=51)



HISTOLOGY


21
14
4
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1
1
1
2
1
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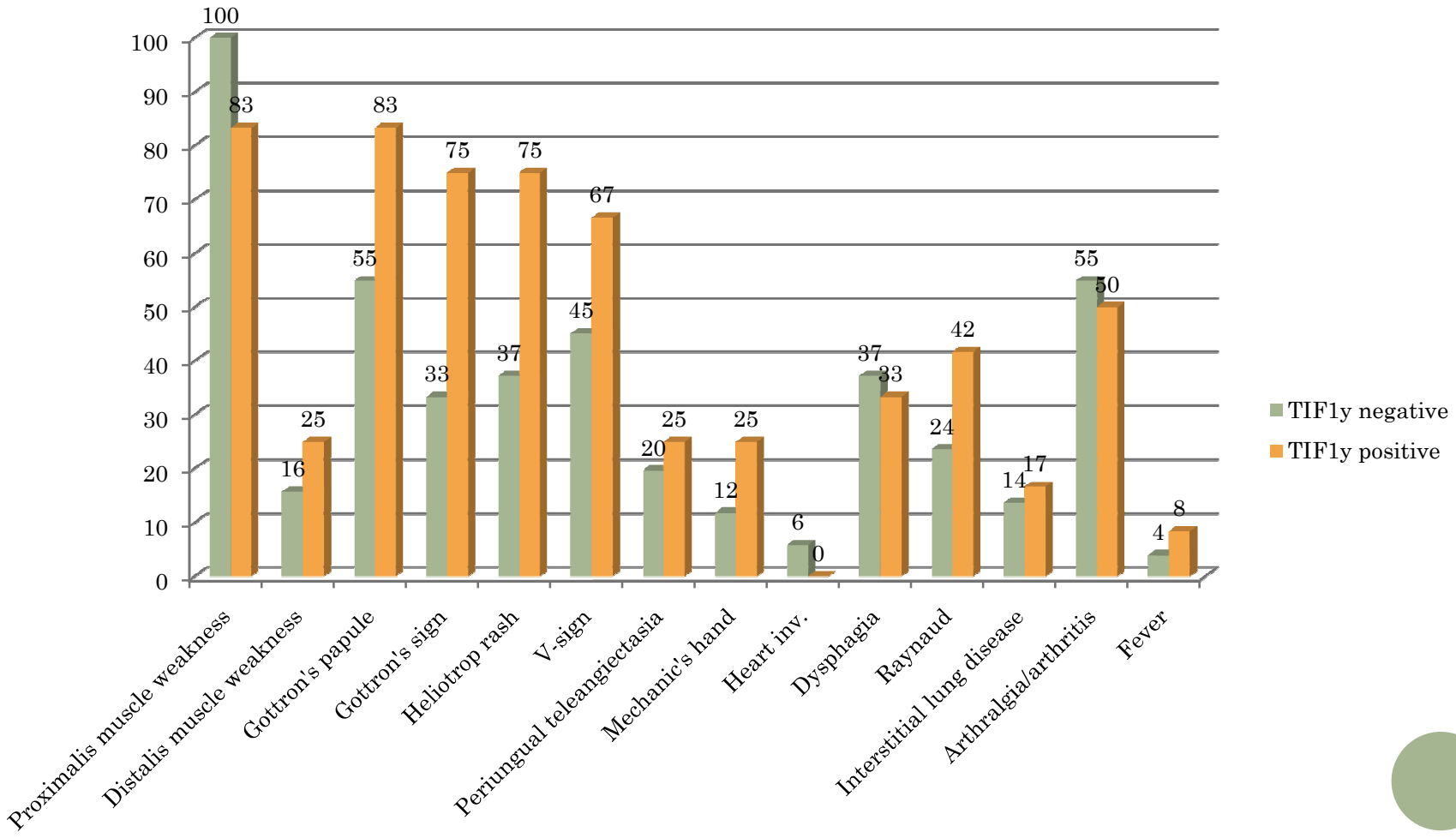
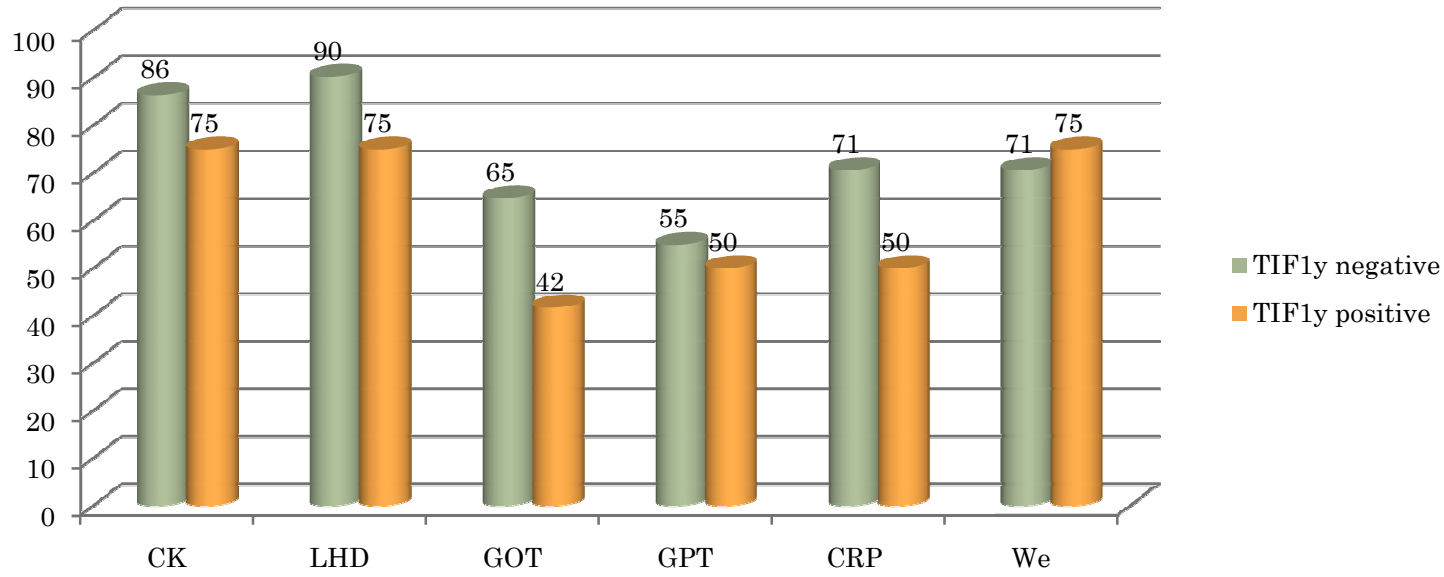
3
adenocc.
duct.
planocellulare
lobular invasive
microcellulare
melanoma
kaposi sc.
B-cell lymphoma
T-cell lymphoma
ependymoma
mucoepidermal cc.
unknown

DIFFERENCES IN CLINICAL SYMPTOMS (%)



LAB FINDINGS (%)



- No differences in tumor markers
- No differences in other antibodies (ANF, APA)

CONCLUSION

- TIF1γ positivity is associated with several and severe skin rashes
- Tumor specificity did not confirmed
- Autoantibody tests help us in the diagnosis
- But tumor searching is necessary, specially in DM

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