Clinical and Autoantibody Associations in Myositis Patients with anti-p155/140kDa Autoantibodies
A Multicenter European Study

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Disclosures
Supported by:
- grant #0021620812 from the Czech Ministry of Education, Youth and Sports
- European Science Foundation – EUMYONET project
- AutoCure

References

• Targoff IN et al. A novel autoantibody to a 155-kd protein is associated with dermatomyositis. Arthritis Rheum. 2006;54:3682-9

Risk of malignancy in patients with DM and PM data from epidemiological studies

Anti p155/140 antibodies

• First described in 2006 1
• Detected by immunoprecipitation 2,2
• Myositis specific (DM and JDM)
• Associated with malignancy
  – in adult DM patients, not in JDM 1,3
• No cases of lung involvement in initial reports

Anti p155/140 antibodies


Image courtesy of Zoe Betteridge
Anti p155/140 antibodies

- Directed against transcriptional intermediary factors
  - p155 against TIF-1γ aka TRIM33
  - p140 against TIF-1α aka TRIM24

- Both antigens play role in carcinogenesis
  - TIF-1γ is a regulator of the TGF-β tumor suppressor pathway
  - TIF-1α prevents retinoic acid induced liver cancer in mice
  - Overexpression of the TIF-1α gene in breast cancer is associated with poor prognosis


Anti p155/140 antibodies in myositis

<table>
<thead>
<tr>
<th>Author</th>
<th>All myositis</th>
<th>JDM</th>
<th>DM</th>
<th>PM</th>
<th>CAM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Targoff</td>
<td>21%</td>
<td>29%</td>
<td>21%</td>
<td>0</td>
<td>75%</td>
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<tr>
<td>Kaji</td>
<td>13%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gunawarden</td>
<td>23%</td>
<td>30%</td>
<td></td>
<td>0</td>
<td>100%</td>
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<tr>
<td>Chinoy</td>
<td>18.4%</td>
<td></td>
<td></td>
<td></td>
<td>50%</td>
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<tr>
<td>Trallero-Araguás</td>
<td>19%</td>
<td>23%</td>
<td>n=1</td>
<td></td>
<td>62%</td>
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<tr>
<td>Vencovský</td>
<td>10.5%</td>
<td></td>
<td>19%</td>
<td>n=1</td>
<td>41%</td>
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<tr>
<td>Fujimoto</td>
<td>36%</td>
<td>11% (17%)</td>
<td>0</td>
<td>n/a</td>
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</table>

Patients and methods

- Multi-center cross sectional study (CZ, UK, Sweden)
- Sera from 808 myositis patients with (probable/definite myositis based on Bohan&Peter criteria)
- Antibody detection by IP using K562 cells in single lab (Bath, UK)
  - Line immunoassay (LIA) (CZ, Sweden)
- CAM defined as cancer diagnosis within 3 years of myositis onset
- Control group: 26 CAM patients without p155/140 Ab (CZ, Sweden)

Results

- 57 patients were p155/140 positive
  - 83% female
  - 2PM, 1CTD associated myositis, rest had DM
  - 22 patients (41%) had CAM (all DM)
  - In p155/140+ non-CAM group:
    1 patient had colon cancer 10 years prior to myositis onset
    1 patient had breast cancer 8 years after myositis onset

Arthritis and ILD

<table>
<thead>
<tr>
<th>p155/140+ All</th>
<th>p155/140+ CAM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arthritis</td>
<td>7%</td>
</tr>
<tr>
<td>ILD</td>
<td>9%</td>
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</table>
### Onset of cancer

There was **no difference** between CAM patients with and without p155/140 antibodies

- in age at cancer diagnosis
  
  60.0 years ± 10.4 vs 56.6 years ± 12.4, p=0.31

- in time between myositis onset and cancer diagnosis
  
  +9 month ±10.3 vs +11.4 month ±11.5, p=0.45

### Types of malignancy

### Other antibodies in p155/140+

### Conclusions

- Presence of the p155/140 autoantibody is not restricted to DM patients, but the increased risk of cancer seems to be confined to the DM population

- Prevalence of arthritis and ILD is lower in p155/140 positive patients compared to myositis in general and DM

- p155/140 positive CAM patients were older at myositis onset compared to p155/140 positive patients without cancer

- There was no difference between CAM patients with and without p155/140 Ab
  
  – in age at myositis onset
  
  – in age at cancer diagnosis

- Certain common cancer types were not present in our p155/140 positive CAM pts

- 22% of patients had another autoantibody (including myositis specific) in addition to p155/140

- 83% of CAM patients had a defined autoantibody
Acknowledgements

Lenka Pleštilová, Jiří Vencovský
Institute of Rheumatology, Prague, Czech republic

Hector Chinoy
University of Manchester, Manchester, UK

Robert G. Cooper
Hope Hospital, Salford, UK

Lara Dani, Ingrid E. Lundberg
Karolinska Institutet, Stockholm, Sweden

Zoe Betteridge, Neil J. McHugh
National Hospital for Rheumatic Diseases, Bath, UK

SIR of cancer by year after diagnosis of myositis

<table>
<thead>
<tr>
<th>Type of cancer</th>
<th>0-1 year follow-up</th>
<th>2-5 years follow-up</th>
<th>&gt;5 years follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dematoplasia</td>
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<tr>
<td>Polymyalgia</td>
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Hill CL et al. Lancet 2001; 357: 96–100