Microscopic Polyangiitis

P120
Long-term outcome of 123 microscopic polyangiitis patients in a monocentric German cohort
S. Schinke¹, E. Reinhold-Keller¹, M. Both², B. Nolle², M. Laudien³, W. Gross⁵, J. Holle¹

1. Campus Lübeck and Klinikum Bad Bramstedt, University Hospital-Schleswig-Holstein, Department of Rheumatology, Lübeck, Germany
2. Campus Kiel, University Hospital Schleswig-Holstein, Department of Radiology, Kiel, Germany
3. Campus Kiel, University Hospital Schleswig-Holstein, Department of Ophthalmology, Kiel, Germany
4. Campus Kiel, University Hospital Schleswig-Holstein, Department of Otolaryngology, Kiel, Germany
5. Campus Lübeck, University Hospital-Schleswig-Holstein, Department of Rheumatology, Lübeck, Germany

Introduction.-- The aim of the study was to determine the course and outcome of Microscopic Polyangiitis (MPA) in a German vasculitis center over 20 years.

Table 1

<table>
<thead>
<tr>
<th>Involved arteries</th>
<th>Any lesion* (percentage)</th>
<th>Stenosis</th>
<th>Occlusion</th>
<th>Wall thickening</th>
<th>Aneurysm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brachiocephalics.</td>
<td>3 (10)</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Right subclavian a.</td>
<td>11 (36)</td>
<td>5</td>
<td>6</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Left subclavian a.</td>
<td>17 (56)</td>
<td>13</td>
<td>4</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Left carotid a.</td>
<td>8 (26)</td>
<td>3</td>
<td>2</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Right carotid a.</td>
<td>4 (13)</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Left vertebral a.</td>
<td>1 (3)</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Right vertebral a.</td>
<td>2 (6)</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Left axillary a.</td>
<td>5 (16)</td>
<td>4</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Right axillary a.</td>
<td>3 (10)</td>
<td>2</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Right brachial a.</td>
<td>2 (6)</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Left brachial a.</td>
<td>2 (6)</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Thoracic aorta</td>
<td>2 (6)</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Abdominal aorta</td>
<td>6 (20)</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Celiac</td>
<td>1 (3)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Sup mesenteric a.</td>
<td>3 (10)</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Iliac a.</td>
<td>1 (3)</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Right renal a.</td>
<td>2 (6)</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Left renal a.</td>
<td>5 (15)</td>
<td>5</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Common hepatic a.</td>
<td>1 (3)</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

*The percentage does not correspond to the sum of each single lesion percentages because an artery can be affected by more than one lesion.

Conclusion.-- Our study concluded to the high proportion of type I1A and the predominance of stenosis lesions.

http://dx.doi.org/10.1016/j.lpm.2013.02.190

Methods.-- All MPA patients attending the center from 1990 to 2012 were included in the study. Patients were split into two cohorts (with diagnosis from 1990 to 2002 and with diagnosis from 2003 to 2012) and analysed with respect to disease manifestations, treatment regimens and side effects and mortality.

Results.-- One hundred and twenty-three patients fulfilled ACR and/or EMA criteria and were included in the study. The median follow-up period was 22 (range 0–180 months, 46 [0–180] for the old cohort and 13.5 (0–92) for the new cohort, P < 0.0001). 102 patients (83%) had generalized and 14 (11%) severe disease on admission. Most patients received cyclophosphamide (cyc) and glucocorticoids for remission induction (n = 101, 82%). Complete remission/response was induced in 99 patients (80%), 17 (14%) were refractory (no follow-up in 2 pts.). Relapse was common (41% of patients). Forty-two percent retained a GFR of < 50 ml/min and 30% had persistent peripheral neuropathy. The duration of induction and cumulative cyc were significantly curtailed without any differences in remission rates (old vs. new cohort, median months and range: 6 [3–14] vs. 5 [3–11], P < 0.0001; median cyc dose: 16 [3–56] vs. 8 [3–35], P = 0.0095, complete remission: 47% vs. 44%, P = 0.750, partial remission: 40% vs. 31%, P = 0.345). The time to diagnosis, organ involvements, damage rates and relapse rates did not differ significantly between the old and new cohort; there was 1 death in the old vs. 0 in the new cohort.

Discussion.-- Time to diagnosis is still long. Patients present most frequently with organ-threatening generalized disease on admission. Cyc can be spared and reduced to a median of 8 g without reducing remission rates. Refractory disease, dam age and relapse rates could not be reduced over time.

Conclusion.-- MPA is still a life- and organ-threatening disease requiring intense immunosuppression and being associated with high rates of damage.

http://dx.doi.org/10.1016/j.lpm.2013.02.191

P121
The role of MPO-positive cells and MPO deposition in glomerular capillary injury in patients with various glomerulonephritis
S. Kawashima, Y. Arimura, Y. Komagata, S. Kaname, A. Yamada
Kyorin University School of Medicine, Tokyo, Japan

Introduction.-- Myeloperoxidase anti-neutrophil cytoplasmic antibody MPO-ANCA-associated glomerulonephritis (GN) is characterized by pauci-immune necrotizing glomerulonephritis (NCGN). We have recently reported that in human MPO-ANCA-associated GN MPO exists along the glomerular capillary walls near infiltrated MPO-positive cells, suggesting that MPO released from neutrophils may directly cause capillary injury (Clin Nephrol, inpres). Here we investigated a possible role of MPO in the pathogenesis of glomerular capillary injury in various types of GN including MPO-ANCA-associated GN.

Methods.-- We analyzed 1102 kidney specimens obtained from two patients with anti-GBM GN, 11 patients with lupus nephritis, two patients with post-streptococcal acute GN (PSAGN) 12 patients with Henoch-Schönlein purpura nephritis (HSPN) and 13 patients with IgA nephropathy (IgA N) as well as 20 patients with MPO-ANCA-associated GN. Glomerular infiltration of MPO-positive cells, deposition of extracellular MPO and endothelial cell injury were analyzed for samples of GN. Glomerular infiltration of MPO-positive cells, deposition of extracellular MPO on glomerular capillary walls were observed in any...
types of GN, especially in an active injury phase. Of note is that MPO deposition, especially diffusely distributed MPO deposits along the glomerular capillary wall, was significantly related to glomerular capillary injury and necrotic changes not only in MPO-ANCA-associated GN but also in anti-GBM GN, lupus N, HSPN and IgA N. In contrast, the distribution of MPO was limited at only a small part of the glomerular capillary wall in PSAGN, although the MPO deposition and MPO-positive cells were widely seen in almost glomeruli.

Conclusion.– These results indicate that MPO deposition caused by infiltrated MPO-positive cells may play important roles in the pathogenesis of glomerular capillary injury.

http://dx.doi.org/10.1016/j.lpm.2013.02.192

P122
Comparison of phenotype and outcome in microscopic polyangiitis between Europe and Japan

1. Addenbrooke’s Hospital, Cambridge, United Kingdom
2. Tokyo Metropolitan Geriatric Hospital, Tokyo, Japan
3. University of Miyazaki, Miyazaki, Japan
4. St. Marianna University School of Medicine, Kawasaki, Japan
5. Okayama University, Graduate School of Medicine Dentistry and Pharmaceutical Science, Okayama, Japan
6. Nagoya University, Graduate School of Medicine, Nagoya, Japan
7. Kitano Hospital, Osaka, Japan
8. Jichi Medical University, Tochigi, Japan
9. Chiba University Hospital, Chiba, Japan
10. Asahi General Hospital, Asahi, Japan
11. Skane University Hospital, Malmo, Sweden

Introduction.– Both genetic and environmental factors contribute to the onset of microscopic polyangiitis (MPA). Europe and Japan have different ethnicities and different environments. Indeed, there are differences in the incidence and ANCA serotype of MPA patients between Europe and Japan. However, differences in phenotype or outcome have not been explored. We aimed to identify differences in phenotype and outcome of MPA between Europe and Japan.

Methods.– Sequential cohorts of MPA patients were collected from European and Japanese centres (n = 147 and n = 312 respectively). Trial databases from the European Vasculitis Society and the Japanese patients with MPO-ANCA-associated vasculitis (JMAAV) trial were studied (n = 254 and n = 48 respectively). We evaluated baseline characteristics including ANCA status and organ involvement, treatment, survival and renal survival. Differences in survival and renal survival were studied by multivariate analysis.

Results.– MPA patients in Japan had a higher age at onset, more frequent MPO-ANCA positivity, lower serum creatinine and more frequent interstitial pneumonitis than those in Europe (all P < 0.01). Comparisons between the trial databases demonstrated similar results. Cumulative patient survival and renal survival rates were not different between Europe and Japan (P = 0.71 and 0.38 respectively). Multivariate analysis identified age at onset, serum creatinine, respiratory involvement and azathioprine use as predictive factors for patient survival, and serum creatinine, use of any immunosuppressant and plasma exchange as factors for renal survival.

Conclusion.– Phenotypes in MPA patients were different between Europe and Japan. However, the outcomes of patient survival and renal survival were similar.

http://dx.doi.org/10.1016/j.lpm.2013.02.193

P123
Prediction of outcome of treatment by gene expression profiling of peripheral blood in patients with microscopic polyangiitis

1. Hokkaido University, Sapporo, Japan
2. Genetic Lab Co., Ltd., Sapporo, Japan
3. Okayama University, Okayama, Japan
4. St. Marianna University, Kawasaki, Japan

Introduction.– The open-labeled prospective clinical trial, JMAAV study, proposed the severity-based treatment protocols for patients with microscopic polyangiitis (MPA) [1]. The results of JMAAV study suggest the proposed protocols are useful (remission rate: 89.4%) but are also indicative of relapse or patient demise regardless of the treatment (recurrence rate: 19.0%; mortality rate: 10.6%). The aim of this study is to discover the prognostic factors that can predict outcome of the treatment in patients with MPA.

Methods.– Transcriptome analysis was performed using peripheral blood from patients enrolled in JMAAV study before and 1-week after the beginning of treatment.

Results.– The gene expression profile before treatment was not directly related to the outcome of the treatment. However, when the samples from nine patients with good outcome (persistent remission) were examined, the expression of 88 genes was significantly altered by the treatment. Thirty statistically reliable genes were selected, and then the alteration of expression by the treatment was examined among 22 patients, including 17 with good outcome (persistent remission) and five with poor outcome (relapse after remission or no remission). Multiple regression analysis between the alteration of expression of the 30 genes by the treatment and the outcome identified a combination of 16 genes as the most valuable gene set for prediction of outcome of the treatment.

Discussion.– Prediction of the outcome of treatment at an early point during the therapy brings useful information for conducting the appropriate follow-up of the patients.

Conclusion.– This preliminary study identified IRF7, IFI1, IFIT5, OAS1, CLC, GBP-1, PSMB9, HRC5, CCR1, CD36, MS4A4A, BIRC4BP, PLSCR1, DEFA1/DEFA3, DEFA4, and COL9A2 as the prognostic factors that can predict outcome of the treatment in patients with MPA at an early point during the therapy.

Reference

http://dx.doi.org/10.1016/j.lpm.2013.02.194