Results.— Serum IgG in the HC sera pool recognized 85 protein spots and serum IgG from patients with AAV recognized 134 ± 65 different protein spots. We focused on protein recognized by at least 3/4 pools of patients with GPA and 2/3 pools of patients with MPA and CSS and not by HC and identified 20, seven and eight proteins, respectively. In addition, among the 330 spots recognized by at least one pool of patients with AAV, ten different spots were recognized by at least 6/10 pools. Among identified proteins, IgG reactivity was detected against alpha-glucosidase, lamin A/C and protein disulfide-isomerase A3. Interestingly, Ingenuity Pathway Analysis revealed that most of these antigens interact with TGF-β and signalling pathways such as Jun and MAPK.

Conclusion.— ACCA detected in patients with AAV recognize cellular targets playing key roles in cell biology. Target antigens interact with protein and complexes known to play a crucial role in AAV pathophysiology.

http://dx.doi.org/10.1016/j.lpm.2013.02.005

A5
Orthotopic heart transplantation in eosinophilic granulomatosis with polyangiitis

M. Groh1, G. Masciocchi2, E. Kirchner3, A. Kristen4, G. Bortman5, S. Vannous6, M. Rosenberg7, A. Darmini8, C. Pellegrini9, A. Brucato9, G. Gregorini10, M. Frigerio11, J.J. Scalì12, L. Calabrese3, L. Guellevin1

1. Department of Internal Medicine, Paris, France
2. Department of cardiology and heart Transplantation, Milan, Italy
3. Department of Rheumatologic and Immunologic Disease, Cleveland, USA
4. Department of Cardiology, Angiology, and Respiratory Medicine, Heidelberg, Germany
5. Department of cardiovascular surgery, Buenos Aires, Argentina
6. Department of cardiovascular and thoracic surgery, Paris, France
7. Department of Internal Medicine III (Cardiology and Angiology), Kiel, Germany
8. Department of cardiothoracic surgery, Pavia, Italy
9. Department of Rheumatology, Internal Medicine and Emergency Medicine, Milan, Italy
10. Division of Nephrology, Brescia, Italy
11. Department of cardiology and heart Transplantation, Brescia, Italy
12. Department of Rheumatology, Autoimmune and Metabolic Bone Diseases, Buenos Aires, Argentina

Introduction.— Heart involvement is the leading cause of death in eosinophilic granulomatosis with polyangiitis (EGPA) [1]. Transplant outcome after orthotopic heart transplantation (OHT) due to EGPA-related cardiomyopathy has been reported in a single patient [2].

Patients.— We conducted an international retrospective study of patients who went through OHT for EGPA-related cardiomyopathy between October 2000 and December 2009. A complete PubMed review was also performed.

Results.— Nine patients were identified. All had negative ANCA serology and acute congestive heart failure due to severe eosinophilic myocarditis (mean troponin level 14.6 ± 20.5 μg/L and LVEF value 24 ± 6%). EGPA and EGPA-related cardiomyopathy diagnoses were synchronous in five patients and in the other four patients were separated by 12 to 21 months.

Six patients’ explanted hearts (67%) showed histologic evidence of EGPA. Four patients (44%) died of sudden death after OHT, with survival time ranging from three to 60 months. Follow-up for the five surviving patients (56%) is 55 to 102 months.

Conclusion.— This is the largest case series of patients who have gone through OHT for EGPA-related cardiomyopathy. It is essential to identify cardiac involvement early during the course of EGPA, for prompt treatment with corticosteroids and cyclophosphamide may allow recovery of the cardiac function [3,4]. In refractory patients, OHT can be performed with respect to the International Society of Heart and Lung Transplantation (ISHLT) guidelines [5], but it is of poor-prognosis. After OHT, recent data suggests that tacrolimus (TAC) and mycophenolate
mofetil (MMF) are superior to micro-emulsion cyclosporine A and azathioprine respectively [6,7]. However, data regarding the use of TAC and MMF in EGPA is scarce.

Conclusion.– EGPA should not be a limitation to OHF, which can be performed with respect to the ISHLT guidelines. There is no optimal immunosuppressive strategy. Arrhythmia is a burden. Further data is needed.

References


A6 Cluster analysis to explore subclassification of eosinophilic granulomatosis with polyangiitis (Churg-Strauss)


A7 Spleen tyrosine kinase (SYK) inhibition in experimental autoimmune glomerulonephritis (EAG)

S.P. Mcadoo1, J. Reynolds1, J. Smith1, G. Bhangal1, E. Masuda2, T.H. Cook1, C.D. Pusey1, F. Tam3

Introduction.– SYK has a critical role in immunoreceptor signalling. SYK inhibition with Fostamatinib (FOS) prevents immune-mediated injury in several animal models. The effect of SYK inhibition on autoantibody production, however, is not well defined. We aimed to address this question in EAG, an autoantibody dependent model of crescentic glomerulonephritis (CGN).

Methods.– In EAG, rats immunized with rat GBM antigen (c3) at day 0 develop autoantibodies to c3 and CGN by day 18, and have lung haemorrhage (LH) at day 36. In study 1, animals \( n = 8 \) received either FOS 40 mg/kg or vehicle (VEH) by twice daily gavage from day 0–18, in order to examine the effects of SYK inhibition on induction of autoimmunity. In study 2, animals received FOS 40 mg/kg or VEH from day 18–36, to study the effects of treatment on established disease. In both studies, animals were monitored until Day 36. Cytokine production by nephritic glomeruli was examined ex vivo. SYK expression in rat and human tissue was assessed by immunohistochemistry (IHC).

Results.– Results of studies 1 and 2 are summarised in figure 1. There was a 58% reduction in the number of c3-specific B cells in FOS treated rats \( P < 0.01 \), as demonstrated by ELISpot assay.