Introduction

Proteinase 3 (PR3) is a phosphatidylserine-binding protein that can bind microparticles: Relevance in the context of granulomatosis with polyangiitis (GPA)

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Objective

To explore the role of PR3 in the pathogenesis of GPA, we investigated whether PR3 can bind to microparticles derived from different cell types.

Methods and results

Surface plasmon resonance experiments and phospholipid-coated membranes provided evidence that PR3 was a PS-binding protein. PR3 binding was found to be dependent on its hydrophobic regions.

Conclusion

We conclude that PR3 can bind to microparticles derived from different cell types, and that this interaction is mediated by its hydrophobic regions. Further studies are needed to understand the biological relevance of this interaction.

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A5

Orthotopic heart transplantation in eosinophilic granulomatosis with polyangiitis


Introduction

Heart involvement is the leading cause of death in eosinophilic granulomatosis with polyangiitis (EGPA). We present the largest case series of patients who have undergone orthotopic heart transplantation (OHT) for EGPA-related cardiomyopathy.

Patients

We conducted a retrospective study of patients who underwent OHT for EGPA between 2000 and 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. Four patients died of sudden death after OHT, with survival ranging from 3 to 60 months. EGPA relapse after OHT occurred in six patients, within a period of 2 to 48 months.

Conclusion

This is the largest case series of patients who have undergone OHT for EGPA-related cardiomyopathy. Further studies are needed to understand the biological relevance of this interaction.
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 OHT, 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**


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


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**Introduction.**— Results from descriptive studies of eosinophilic granulomatosis with polyangiitis (EGPA) suggest distinct clinical subclasses that may be determined by anti-neutrophil cytoplasmic antibody (ANA) status. We used hierarchical cluster analysis to explore whether EGPA could be subclassified.

**Methods.**— We used standardized retrospective data for a cohort with clinical diagnoses of EGPA followed in four tertiary referral centers. Hierarchical cluster analysis involved the Ward method with 12 input variables assessed at diagnosis: constitutional symptoms; mucocutaneous, ophthalmologic, ear, nose and throat, cardiovascular, gastrointestinal, renal, and central nervous system involvement; peripheral neuropathy; non-fixed lung infiltrates; and ANCA positivity. The resulting clusters were described by their most prominent summary characteristics. The distribution of clinical variables was analyzed by ANCA status with chi-square test.

**Results.**— The dataset included 262 EGPA cases diagnosed between 1984 and 2012. ANCs were detected in 30.9% of cases. Cluster analysis revealed three clusters of 39 (cluster 1), 92 (cluster 2) and 131 subjects (cluster 3). Cluster 1 was characterized by renal involvement (84.6%) and high ANCA positivity (92.3%), cluster 2 by virtually absent renal involvement (3.3%) and ANCA positivity (4.3%) and cluster 3 by an intermediate phenotype with renal involvement (13%), ANCA positivity (31.3%) and frequent cardiovascular involvement (59.5% vs. 17.9% and 35.9% for clusters 1 and 2, respectively) and gastrointestinal involvement (42% vs. 15.4% and 12%, respectively). ANCA positivity was associated with renal disease (P < 0.0001), peripheral neuropathy (P = 0.005) and constitutional symptoms (P = 0.02).

**Conclusion.**— Cluster analysis of EGPA, although reinforcing the link between ANCA positivity and renal involvement in the disease, does not suggest that it is composed of clearly separated and mutually exclusive subclasses.

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

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**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 (α3) at day 0 develop autoantibodies to α3 and CGN by day 18, and have lung haemorrhage (LH) at day 36. In study 1, animals (n = 8/group) 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 by ELISpot assay.

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 α3-specific B cells in FOS treated rats (P < 0.01), as demonstrated by ELISpot assay.