Mitophagy Balance in Various Cell Subsets in Patients with ANCA-Associated Vasculitis and Correlation with the Presence of Anti-Neutrophil Cytoplasmic Antibodies

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ABSTRACT

ANCA-associated vasculitides (AAVs) are characterised by heterogeneous molecular and pathophysiological traits, causing ambiguous differential diagnosis and taxonomy. Response to therapy has proven far from successful, contributing to high mortality. Transcriptome analysis of different vasculitis subtypes adds new leads in elucidating mechanisms of disease and the role of specific cell subsets to them. Recent findings have shown that mitophagy is a procedure whose imbalance could lead to immune dysregulation with certain involvement to autoimmunity. Inflammatory response related mitophagy is yet to be described in AAVs. We here describe a research protocol to investigate mitophagy in monocytes, neutrophils, and T cells in AAV patients, and the relationship of disturbed mitophagy with ANCA seropositivity.

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INTRODUCTION

ANCA (anti-neutrophil cytoplasmic antibodies) associated vasculitides (AAV) include granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA), and eosinophilic granulomatosis with polyangiitis (EGPA) subtypes, being the most aggressive as to morbidity and mortality rates compared to other systematic vasculitides. Worldwide incidence of AAVs is approximately 26/106 individuals, with higher impact at ages of 65 to 74 years. At the same time, epidemiological studies in Greece are sparse, while in Crete, the respective incidence is 19.5/106 individuals, with younger patients presenting GPA, and older ones with MPA. Despite the intensive therapeutic approaches including corticosteroids and immunosuppressant drugs (cyclophosphamide, azathioprine, methotrexate, mycophenolate mofetil) or their combination, patients suffer from subsequent relapses and high mortality, estimated at approximately 25% in 5 years. Recently, rituximab has been approved as therapeutic solution for induction of remission and maintenance of GPA and MPA, resulting to encouraging outcomes. Independent prognostic
Mitophagy plays a significant role in inflammation and autoimmunity. The results of this study will elucidate the involvement of mitophagy in AAV and add mechanistic insights in the pathophysiology of the disease. Moreover, assessment of mitophagy in different cell subsets will shed light on their role as effectors in the phenotype of the disease, linking transcriptome to function.

**ANTICIPATED BENEFITS**

Mitophagy plays a significant role in inflammation and autoimmunity. The results of this study will elucidate the involvement of mitophagy in AAV and add mechanistic insights in the pathophysiology of the disease. Moreover, assessment of mitophagy in different cell subsets will shed light on their role as effectors in the phenotype of the disease, linking transcriptome to function.

**CONFLICT OF INTEREST**

The authors declare no conflict of interest.
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REFERENCES