Nuclear magnetic resonance (NMR)-based untargeted metabolomics in the serum of Giant Cell Arteritis and Polymyalgia Rheumatica patients: a preliminary study

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INTRODUCTION: Giant Cell Arteritis (GCA) is an inflammatory disease following a chronic, relapsing course. Despite the intense inflammatory process during the active phase and the consequent rapid response to steroids, metabolic pathways and metabolites have not been studied so far. The aim of this study is to investigate the serum metabolome in active and inactive disease state.

METHODS: 110 serum samples from 50 consecutive patients (33-GCA and 17-PMR) at 3 time points; 0, 1 and 6 months of treatment with steroids (remission) were evaluated in the study. A Nuclear magnetic resonance (NMR)-based untargeted metabolomics was exploited for the metabolic characterization of patients. Analysis of LED spectra and the SMolesY-select platform were utilized for the determination of lipid signals and small molecules, respectively. CRP and ESR parameters were correlated with the findings. All univariate analyses were adjusted for multiple hypothesis testing at Bonferroni 5%.

RESULTS: Distinct metabolic profiles were observed between patients in diagnosis and the two remission periods. N-acetylglycoproteins (directly) and cholines of phospholipids (reversely), emerged as predictive markers of disease activity. Altered levels of 3 out of the 21 small molecules were also observed, including increased levels of phenylalanine and decreased levels of glutamine and alanine in active disease, highlighting the role amino acid metabolism. Moreover, metabolic fingerprinting was able to discriminate GCA from PMR patients in remission, but not in diagnosis. GCA and PMR patients were shown to exhibit different degree of ketosis as a response and/or adverse effect of treatment with corticosteroids. Correlation analysis showed that the identified biomarkers, except from glutamine, were further associated with CRP and ESR inflammation markers.

CONCLUSION: The study of the serum metabolome of GCA patients could identify new disease associated pathways and propose disease biomarkers with higher sensitivity than CRP. Thus, larger studies of GCA patients should be carried out.