Quantitative measurement of 18F-FDG PET/CT uptake reflects the expansion of circulating plasmablasts in IgG4-Related Disease.

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Objective:

18F-fluorodeoxyglucose positron emission tomography/computed tomography (18F-FDG PET/CT) scan is increasingly used to assess organ involvement and response to treatment in IgG4 Related Disease (IgG4-RD), but clear correlations between 18F-FDG uptake, disease activity, and the immunological perturbations occurring in this condition have not been established yet. In the present work we aim to correlate the intensity and distribution of 18F-FDG uptake with clinical, serological, and immunological biomarkers of IgG4-RD activity.

Methods:

Twenty patients with active untreated IgG4-RD were prospectively studied. All patients underwent a baseline 18F-FDG PET/CT scan. Ten patients underwent a control 18F-FDG PET/CT after immunosuppressive treatment. 18F-FDG uptake of the most metabolically active IgG4-RD lesion was measured using the mean Standardized Uptake Value corrected for the Partial Volume Effect (PVC-SUV). The metabolic disease burden was measured using the Total Lesion Glycolysis with (TLG_{tot+ln}) and without (TLG_{tot-ln}) lymph nodes. Disease activity was assessed through clinical (IgG4-RD Responder Index (RI)), serological (erythrocyte sedimentation rate (ESR) and C reactive protein (CRP)), and immunological (serum IgG4 and circulating plasmablasts) biomarkers. The Enhanced Liver Fibrosis (ELF) score was measured as a biomarker of systemic collagen deposition and fibroblast activation.

Results:

Thirteen patients (65%) had multiorgan IgG4-RD. The median levels of IgG4-RD RI, ESR, CRP, serum IgG4, ELF score, and plasmablasts at baseline were 9 (range 6-15), 19 mm/h (range 4-121 mm/h), 4.3 mg/L (range 0.0-48.0 mg/L), 308 mg/dL (range 80-2100 mg/dL), and 2270 cells/mL (range 130-40840 cells/mL), respectively. Circulating plasmablasts positively correlated with PVC-SUV ($r=0.49$, $p=0.027$), inversely correlated with TLG_{tot-ln} ($r=0.50$, $p=0.023$), and did not correlate with TLG_{tot+ln} ($p>0.05$). No statistically significant correlation was found between PVC- SUV or TLG and IgG4-RD RI, ESR, CRP, serum IgG4 levels, or ELF score ($p>0.05$). Clinical response induced by immunosuppressive treatment was associated with a consensual reduction of circulating plasmablasts, PVC-SUV, TLG_{tot-ln} and TLG_{tot+ln}.

Conclusions:

18F-FDG uptake of IgG4-RD lesions seems to reflect the immunological perturbations of the B cell compartment rather than processes related to fibroblasts activation and extracellular matrix deposition. IgG4-RD RI, ESR, CRP, and serum IgG4 levels do not appear to correlate with the metabolic activity of IgG4-RD lesions, as assessed by quantitative 18F-FDG PET/CT.