PERSISTENT LOW-GRADE VASCULAR INFLAMMATION IN LARGE VESSEL VASCULITIS: A LONGITUDINAL STUDY USING FULLY INTEGRATED 18F-FDG PET/MR

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Background: Persistent low-grade vascular inflammation in large vessel vasculitis (LVV) treated patients could represent the expression of persistent subclinical disease activity or post-inflammatory vascular remodeling. Whether these findings have any impact on future vascular outcomes is still an unmet need.

Objectives: To evaluate the frequency and evolution of the low-grade vascular inflammation using a fully integrated 18F-FDG PET/MR in a longitudinally followed cohort of LVV patients.

Methods: All consecutive patients with LVV who underwent at least 2 PET/MR scans (median time 9[6] months) between January 2015 and January 2019 were included. For each scan vessel's metabolic activity was assessed using the Meller’s grading and the standard uptake value (SUV).

Low-grade inflammation was defined as Meller 1 and 2 (inferior or equal to 0.8 mg/kg/day might be optimal initial dose of GC for treatment of elderly-onset patients with AV.

REFERENCES:

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THU0312 ADVENTITIAL FIBROBLAST, AN IMPORTANT PLAYER IN GIANT CELL ARTERITIS

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Background: Giant cell arteritis (GCA) is a systemic vasculitis affecting large vessels. The diagnosis is based on the temporal artery biopsy (TAB) which shows a segmental and focal arterial infiltration composed of CD4 T cells and macrophages. It is accompanied by a destruction of the internal elastic layer of the media and a hyperplasia of the intima by proliferation of myofibroblasts (Weyand). The origin of these myofibroblasts is controversial (Ly). Evidences suggest the activation of adventitial fibroblasts into myofibroblasts and their migration into the intima (Stennar).

Objectives: The objective of this study was to determine whether adventitial fibroblasts migrate to the intima and thereby contribute to intimal hyperplasia during GCA.

Methods: Arterial sections from TAB of patients with GCA (n=24) and control subjects (n=24) were analyzed. Immunohistochemical analysis was
performed using antibodies directed against fibroblasts (CD90, vimentin), myofibroblasts (alpha smooth muscle actin (ASMA)) and vascular smooth muscle cells (desmin). Staining of prolly-4-hydroxylase (P4H) and myosin were also performed. Stainings were quantified using the ODPviewer® software (Kamax Innovative System, France) by two double-blind observers. Moreover, co-expression of CD90 with different stainings (ASMA, myosin and P4H) was also performed. Cells in culture were identified by immunocytochemistry using anti-CD90 and markers of activity such as myosin and P4H. Functional assays were performed using culture cells obtained from GCA patients’ BATs (n=4) and controls (n=4). The BATs were dissected to separate the adventitia from the other two layers. Each dissected fragment was seeded separately. The proliferation was studied using a bromodeoxyuridine incorporation test under different conditions: DMEM, fetal calf serum (FCS), PDGF and supernatants of cells in culture. The study of migration was performed using a scratch test under the same conditions.

Results: CD90 was significantly higher in GCA than controls in adventitia and intima. Vimentin and ASMA were significantly higher in the 3 tunics of patients with GCA. Expression of desmin was only present in the media for both groups with no significant difference. P4H was present in adventitia significantly different between both groups. The adventitial and intimal CD90+ cells co-expressed P4H, ASMA and myosin more importantly during GCA. Cultured cells from BATs’ adventices expressed CD90 and did not express desmin. These cells had a greater myosin staining during GCA and had an increased proliferation ability during GCA in the presence of FCS, PDGF and fibroblast supernatants of control or GCA patients. The migration rates of these cells were also significantly increased during GCA in the presence of FCS or PDGF.

Conclusion: Vascular remodeling during GCA would start in the adventitial layer with a key role of fibroblasts. Adventitial fibroblasts could be activated into myofibroblasts and acquire proliferative and migratory abilities. They would participate in the intimal hyperplasia, responsible for ischemic complications. Their inhibition could be a therapeutic way to limit these complications. The activating signal of adventitial fibroblasts into myofibroblasts is not yet known during GCA and requires further studies.

REFERENCES:

Disclosure of Interests: None declared

COMPARATIVE STUDY OF CLINICAL, ANALYTICAL AND VASCULAR 18F-FDG UPTAKE EVOLUTION IN PATIENTS WITH GIANT CELL ARTERITIS TREATED WITH METHOTREXATE VS TOCILIZUMAB


Background: Glucocorticoids remain to be the cornerstone therapy in giant cell arteritis (GCA). However, relapses are common when the prednisone dose is tapered. Thus, additional therapies are required in relapsing GCA. The most widely used conventional immunosuppressive drug is methotrexate (MTX) which efficacy is modest. Consequently, in some cases biological therapy in needed. Among them, the most frequently used is the recombinant humanized anti-IL6 receptor antibody tocilizumab (TCZ).

Objectives: To compare clinical evolution, normalization of acute phase reactants and normalization of vascular 18F-FDG uptake assessed by PET/CT in patients with GCA treated with MTX vs TCZ.

Methods: Comparative multicentric study of 23 patients with GCA treated with MTX vs 36 patients with GCA treated with TCZ who had a baseline and follow-up PET/CT scan. We assessed clinical improvement (no improvement/ partial/comlete), normalization of acute phase reactants (CRP ≤ 0.5mg/dl and/or ESR ≤ 20 mm/1 st hour) and reduction of 18F-FDG uptake in PET/CT (no reduction/ partial/complete normalization). Images were evaluated qualitatively by experienced nuclear medicine physicians. Prednisone tapering was also assessed. Statistical analysis was performed with SPSS. Student’s t test or Mann-Whitney U test was used to compare continuous variables, and Chi-squared test or Fisher’s exact test for categorical variables as appropriate.

Results: We included 23 patients with GCA treated with MTX (20 women/3 men); mean age 65.6 ± 7.9 years; and 36 patients treated with TCZ (27 women/9 men); mean age 67.5 ± 8.3 years. Clinical, analytical and vascular 18F-FDG uptake evolution is shown in the TABLE. After one year of treatment, the percentage of patients who experienced complete clinical improvement was higher in those who received TCZ (88.9% vs 44.4%; p=0.003). Normalization of acute phase reactants was also more frequent in patients who received TCZ (92.6% vs 47.6%; p<0.001). In regard with reduction of vascular 18F-FDG uptake, complete normalization was only achieved in 25% of patients who received TCZ and 14.3% of those who received MTX.

Conclusion: Patients with GCA who received TCZ experienced a more rapid and effective clinical and analytical improvement than patients who received MTX. Besides, prednisone tapering was quicker in patients with TCZ. However, no significant differences were found in complete normalization of 18F-FDG vascular uptake between both treatments.

Abstract THU0313 – Table 1

<table>
<thead>
<tr>
<th>TABLE</th>
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<tbody>
<tr>
<td>METOTREXATE VS TOCILIZUMAB</td>
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<tr>
<td>Age, mean ± SD</td>
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<tr>
<td>Age (between 60-80) (%)</td>
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<tr>
<td>Complete clinical improvement, n (%)</td>
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<td>Normalization of EB and/or CRP, n (%)</td>
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<td>Normalization of 18F-FDG PET/CT, n (%)</td>
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Dose of Prednisone [mg/day], median (IQR) |
| 6 months | 7.5 (5.0-15.0) | 5.0 (0-3.5) | < 0.01 |
| 12 months | 5.0 (0-15.0) | 0.0 (0-0.5) | < 0.01 |
| 18 months | 5.0 (0-15.0) | 0.0 (0-0.5) | 0.01 |
| 24 months | 2.5 (0-3.5) | 0.0 (0-0.5) | 0.07 |

REFERENCE: