CHARACTERIZING THE ROLE OF NET-DERIVED IL-33 IN SLE PATHOGENESIS

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Background: Interleukin (IL)-33 is a cell necrosis-derived alarmin with immunosuppressive properties which depend on the context of immune cells and the inflammatory milieu (1). In Systemic Lupus Erythematosus (SLE), extracellular DNA (as in extracellular chromatin traps [NETs] or immune complexes [ICs]) combined with alarmins stimulate innate immunity receptors (such as Toll-like receptors [TLRs]) and the production of IFNa by plasmacytoid dendritic cells (pDCs) (2, 3, 4).

Methods: Peripheral blood polymorphonuclear cells (PMNs) were isolated from spontaneous-released NETs from peripheral blood PMNs of active SLE nephritis patients. PMNs with ICs led to the release of NETs with extended IL-33 decoration and cytokine load. NETs structure may be biomarker of disease activity.

Results: IL-33 is a network of cytokines produced by immune cells against extracellular DNA. NETs are decorated with IL-33 to larger extent as compared to healthy PMN. Extracellular DNA-derived IL-33 might enhance the interferogenic capacity of pDCs.

Conclusion: NET-derived IL-33 is a novel mediator of the nucleic acid-driven aberrant type I IFN response which exacerbates SLE disease. NET structure may be crucial in regulating the bioactivity of IL-33.

REFERENCES


Disclosure of Interests: None declared


REDUCED FCGR IIB AND ENHANCED FCGR III EXPRESSION ON MONOCYTES IN PATIENTS WITH BEHÇET DISEASE

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Background: Behçet’s disease (BD) is a systemic inflammatory disease without clear pathogenesis. Previous studies have shown the association between FcγR gene polymorphisms and BD1,2. FcγRs, the receptor of IgG, has both activatory and inhibitory subtypes, and the imbalance of them on monocytes has been illustrated to have significant pathogenic roles in many autoimmune diseases3,4.

Objectives: This study was aimed to investigate the potential abnormal expression of FcγRs in BD patients

Methods: We recruited 27 newly-onset treatment-naive BD patients (according to 2014 International Criteria for BD) and 23 gender-and age-matched healthy controls (HC). Flow cytometry was used for detecting the expression of the inhibitory receptor (FcγRIIB) and activating receptors (FcγRI and FcγRIII) on the neutrophils, monocytes, B cells, natural killer cells, dendritic cells, and T cell from the whole blood of BD and HC. The correlation between the expression of FcγR and disease activity index of BD was evaluated.

Results: BD patients had increased numbers of monocytes (60.1±3.38 vs. 47.56±4.92, p=0.0365) compared with HC. FcγRIIB expression on monocytes, rather than other subtypes (p>0.1), was significantly lower in BD patients (4.87±0.61% vs. 7.67±1.10%, p=0.0199). FcγRIIB expression on monocytes was negatively correlated to ESR (r=-0.576, p=0.031) and CRP (r=-0.539, p=0.047), positively correlated to serum IgG (r=0.785, p=0.001) and uncorrelated to serum IgM, IgA and PLT (p>0.05). FcγRIII expression on monocytes was higher in BD patients (19.61±0.46% vs 9.34±0.17%, p=0.0091). FcγRIII expression on monocytes was positively correlated to ESR (r=0.2551, p=0.0274) and CRP (r=0.2354, p=0.0352), and uncorrelated to serum IgG, IgM, IgA and PLT (p>0.05).

Furthermore, FcγRIIB expressions of monocyte were comparable between BD patients in active disease or remission, while FcγRIII expression was significantly decreased (p=0.0158) after 3-month of treatment.

Conclusion: Our research demonstrated, for the first time, that the decreased expression of inhibitory receptor FcγRIIB and increased expression of activatory receptor FcγRIII on monocytes in BD. Furthermore, the abnormal expression was correlated with disease activity. These findings suggested that FcγRs ratio imbalance might play a role in the pathogenic role of BD.

REFERENCES


Disclosure of Interests: None declared


CHANGES OF INNATE LYMPHOCYTES CELLS IN PERIPHERAL BLOOD OF PATIENTS WITH PRIMARY SJÖGREN’S SYNDROME AND ITS CORRELATIONS WITH CLINICAL MARKERS

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Background: Innate Lymphoid Cells (ILCs) are a novel group of innate immune cells, according to the cytokine profile, they were divided into three major subsets:
INFLAMMASOME DRIVES RELEASE OF MITOCHONDRIAL DNA ENCLOSED IN EXTRACELLULAR MEMBRANE VESICLES AND PROPAGATION OF INFLAMMATION IN BEHÇET’S DISEASE

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Background: It has been reported that mitochondrial DNA (mtDNA) is released into the cytosol by mitochondrial stress and induces pro-inflammatory cytokine production via inflammasome and intracellular DNA sensors. Also, mtDNA in the extracellular space is known to result in sterile inflammation. However, the molecular mechanism of mtDNA release and its pathological significance in autoimmune diseases (ADs) has not been elucidated.

Objectives: To clarify the molecular mechanism of mtDNA release and its pathological significance in ADs.

Methods: We collected the serum from various AD patients and analyzed the levels of mtDNA in serum. We digested mtDNA in serum by DNase treatment. We collected the serum from various AD patients and analyzed the levels of mtDNA in serum. We digested mtDNA in serum by DNase treatment.

Results: We first measured the levels of mtDNA in serum of the various ADs. We found that mtDNA levels were significantly increased in primary SS (P<0.0001). We also found that mtDNA levels were significantly increased in systemic lupus erythematosus (SLE) (P<0.0001) and psoriasis (Psoriasis) (P<0.0001). In comparison, the mtDNA levels were not significantly increased in rheumatoid arthritis (RA) and systemic sclerosis (SSc) (P>0.05).

Conclusion: The levels of mtDNA in serum were significantly increased in primary SS and psoriasis, but not in RA and SSc. These results suggest that mtDNA release may play a role in the pathogenesis of primary SS and psoriasis.

Disclosure of Interests: None declared


AB0049C

Cytokines and inflammatory mediators

AB0050 DETECTION OF SERUM AND SYNOVIAL FLUID LEVELS OF VISFATIN DURING FLARE-UPS AND REMISSION OF PRIMARY OSTEOARTHRITIS OF THE KNEES

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Background: OA is the most common form of joint disease and a major contributor of disability in older people. OA is a chronic joint disease characterized by cartilage breakdown, bone remodeling, osteophyte development and synovial inflammation [1]. Adipose tissue expresses and secretes a large number of proteins that often share functional and structural properties of cytokines and are therefore classified as adipokines [2]. These include leptin, adiponectin, resistin, visfatin, and others. These factors are associated with inflammation and immune response. Visfatin is an adipokine identified in 2004 and was identified first as Pre B cell Colony Enhancing Factor [3]. Visfatin is a potent inducer of PGE2 release in both human and immature mouse chondrocytes, as a result of increased messenger prostaglandin E synthase and decreased 15 15prostaglandin dehydrogenase synthases [4].

Objectives: The aim of the study was to measure the level of visfatin in serum and synovial fluid of patients with knee osteoarthritis in flare-up and after they enter in remission. Methods: to achieve the target of our study 20 patients with OA of the knee in flare-up were selected from out-patients clinic. The patients were followed up every two weeks after the first setting until they entered into remission. Twenty normal controls age, sex and body mass index (BMI) matched were recruited. In the first setting sera and synovial fluid measured for Visfatin, in the second setting sera and synovial fluid (if any) was drawn for visfatin measurement. Measurement of Visfatin by (ELISA) for quantitative determination of human visfatin in biological fluids.

Results:

1: serum visfatin of patients and control groups:

<table>
<thead>
<tr>
<th>P value</th>
<th>I</th>
<th>Control ng/ml</th>
<th>Patients ng/ml</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.0001</td>
<td>42.09</td>
<td>216.60±30.25</td>
<td>847.90±59.86</td>
</tr>
<tr>
<td>0.01</td>
<td>23.6</td>
<td>216.60±30.25</td>
<td>542.45±59.60</td>
</tr>
</tbody>
</table>

Patients recorded higher VIS-S readings than the controls with high significant difference in both situations.

2: serum and SF visfatin of patients during flare up and remission:

<table>
<thead>
<tr>
<th>Flare up ng/ml</th>
<th>Remission ng/ml</th>
<th>T</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>847.90±59.86</td>
<td>542.45±59.60</td>
<td>19.65</td>
<td>0.0001</td>
</tr>
<tr>
<td>694.60±77.35</td>
<td>384.00±30.61</td>
<td>7.85</td>
<td>0.001</td>
</tr>
</tbody>
</table>

There was a significant increase in Visfatin in serum and synovial fluid during flare-ups.

Conclusion: Visfatin was elevated both systemically and locally in the patients with knee OA, it was elevated during flare-ups and decrease during remission, was higher in serum than in synovial fluid of patients and There was no difference in the level of visfatin in relation to aging or gender difference.

REFERENCES