Background: The underlying cause of autoimmune diseases is not known, infections, especially viral infections, is thought to be a possible reason. However, the immune response status of different types of infections in the context of autoimmune diseases is poorly understood.

Objectives: To evaluate the differences of lymphocyte subsets in connective tissue disease (CTD) with different types of pathogen bloodstream infections.

Methods: We analyzed 40 CDT patients with bloodstream infections, including 11 with virus infections, 7 with fungal infections, 13 with Gram negative bacteria infections (G- infection), 9 with Gram positive bacteria infections (G+ infection), and 10 newly diagnosed CTD patients without co-infection were included as controls. The percentage and absolute numbers of lymphocyte phenotypes and subsets in peripheral blood were examined by flow cytometry.

Results: Th1 cells are increased in virus infections and fungal infections but decreased in G- infection. Th2 cells are decreased in G- infection and increased in G+ infection. Treg cells had no significant difference between different groups. Whereas for the G+ infection group, while the G- infection was increased than G+ infection, and the virus infection was increased than fungal infection. The percentage of Th1, Th17 and Treg had no significant difference between different groups. Whereas for the absolute value comparison, the absolute value of Treg cells in the virus infection was lower than G- infection, and Th17 response was higher than G- infection, and Th2 response was lower than G- infection. The T, B, NK, CD4+ T, CD8+ T cell counts in different infection groups and in non-infection group. Among comparison of the CD4+ T subsets, the percentage of Th2 in the fungal infection was decreased than G- infection group and no-infection group, while the G- infection was increased than G+ infection, and the virus infection was increased than fungal infection. The proportion of Th1, Th17 and Treg had no significant difference between different groups. Whereas for the absolute value comparison, the absolute value of Treg cells in the virus infection was lower than G- infection, and G+ infection, and G- infection, and the G+ infection was higher than G- infection, and G+ infection. The Th2 response was lower than virus infection and fungal infection. The G+ infection was increased than G- infection, and the virus infection was increased than fungal infection. The Th17 response was lower than virus infection and fungal infection. The G+ infection was increased than G- infection, and the virus infection was increased than fungal infection.

Conclusion: Different types of pathogen blood may lead to development of specific immunological dysbalance, especially in the case of autoimmune disease hosts. CDT patients with fungal infection had lower Th2 response, higher Th17 cells and a characteristic of CDT combined with virus infection compare with other types of infection.

REFERENCES:

Keywords: Adaptive immunity, Systemic lupus erythematosus, Rheumatology, Taipan, China

References:

Disclosure of Interests: None declared

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AB0662 PERIPHERAL PLATELET-GENERATING MEGAKARYOCYTE REDUCED IN PRIMARY SJÖGREN'S SYNDROME.

Keywords: Sjögren syndrome

References:
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Background: Primary Sjögren’s Syndrome (pSS) is a complex and heterogeneous systemic autoimmune disease characterized by dysfunction of the sero-mucous glands following chronic inflammation of lymphocytic infiltration. 1 Megakaryocytes (MKs), the precursor cells responsible for platelet production, act across the immune continuum. However, the underlying pathogenesis of pSS involving MKs is still to be elucidated.

Objectives: This study aimed to determine the changes in megakaryocyte subsets in pSS patients and to explore the role of different subsets in the pathogenesis of pSS.

Methods: The scRNA-seq dataset of five patients with pSS and five HCs were obtained from the GEO database to identify megakaryocytes (MKs) among PBMCs and further define the subpopulations. Then, cellular identity was determined by identifying the DEGs for each cluster using the Wilcoxon rank-sum test with the FindAllMarkers function and comparing the markers to known cell-type-specific genes from previous datasets. Finally, to investigate the hierarchy and developmental relationship between MK subpopulations, the monocle3 analysis was used to reconstruct pseudotime trajectories.

Results: First, four putative subpopulations (MK1-MK4) of MKs were identified by sub-clustering (Figure 1A). MK3 referred to as platelet-generating MKs, expressed key genes involved in hemostasis, cell-extracellular matrix interactions and so on. (Figure 1B) MK2 shared the same marker as MK3, but exhibited lower expression, which means MK2 may be an early stage of MK3, known as proplatelet-generating MKs. Then, compared with other MKs, MK2 and MK3 had the highest platelet activation-related and platelet aggregation-related pathways scores generated by ssGSEA (Figure 1F). Remarkably, the inflammatory response subpopulation (MK4), consisting of MKs expressing LSP11 and CD53 at high levels, was enriched in Immune system development and T-cell activation (Figure 1D). And, the proportion of the MK1, MK2, and MK4 subpopulations increased and that of the MK3 subpopulation was decreased in patients with pSS vs. HCs (Figure 1C), indicating the impaired maturation of platelet-generating MKs in pSS patients. Finally, with the trajectory analysis, we inferred that MK4 could exist independently of other MK subpopulations, and MK1 may characterize the point of initiation of a developmental trajectory (Figure 1E).

Conclusion: In summary, we have presented evidence for the reduction of peripheral platelet-generating MKs in patients with pSS, and identified changes in platelet-generating MKs via scRNA-seq analyses. The findings provide clues to the impaired maturation of platelet-generating MKs in the pathogenesis of pSS.

REFERENCES:
Results: 238 SLE patients were included in the cohort; 117 patients (49%) had follow-up at an average of three months (interval 60-120 days), 59 patients (25%) had follow-up at a low intensity (interval >120), and 62 (26%) at a high intensity (interval <60 days). Characteristics of these groups are shown in Table 1. The patients with high intensity follow-up were younger, more often non-white and had more severe disease at diagnosis. Upon evaluation, these patients had a more severe disease course as demonstrated by more treatment intensifications, hospitalizations, ER visits, a higher SLICC damage index and more frequent renal involvement. Conversely, the patients that were monitored at a low intensity were older had longer disease duration and showed a more quiescent disease with less negative health outcomes. Figure 1 shows the linear relationship between the frequency of tests and the number of abnormal results in Hb.

Conclusion: This study shows that the frequency of follow-up varies substantially between SLE patients. A majority of patients had follow-up at a frequency of 3 months, patients that differed from this norm had distinct features. At this moment frequency of follow-up depends on clinical judgment of the physician. Potentially, this process might be captured in prognostic modelling. Patients at high risk should be identified and have a high frequency of follow-up, while in other patients resources could be spared.

REFERENCES:

Table 1. Characteristics per follow-up group

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Low intensity (n = 59)</th>
<th>Average intensity (n = 117)</th>
<th>High intensity (n = 62)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mn (SD)</td>
<td>54 (16.3)</td>
<td>52 (14.6)</td>
<td>46 (14.7)</td>
</tr>
<tr>
<td>% abnormal values – Hb, mn (IQR)</td>
<td>0 (0 - 25)</td>
<td>27 (3 - 63)</td>
<td>47 (15 - 76)</td>
</tr>
<tr>
<td>Kidney biopsy, n (%)</td>
<td>2 (0 - 11)</td>
<td>8 (1 - 22)</td>
<td>22 (10 - 50)</td>
</tr>
<tr>
<td>Intensification of therapy per yr, m (%)</td>
<td>3 (5)</td>
<td>21 (18)</td>
<td>24 (39)</td>
</tr>
<tr>
<td>Hospitalizations per yr, m (%)</td>
<td>1 (2)</td>
<td>10 (9)</td>
<td>13 (21)</td>
</tr>
<tr>
<td>SLICC DI, n (%)</td>
<td>11 (19)</td>
<td>41 (35)</td>
<td>22 (35)</td>
</tr>
</tbody>
</table>

Figure 1. Relationship between frequency and number of abnormal blood tests.