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AUTOINFLAMMATORY DISORDERS ARE COMMON IN PATIENTS WITH MYELODYSPLASTIC SYNDROME AND LINKED TO KARYOTYPE ABNORMALITY AND SOMATIC MUTATIONS STATUS AND A WORSE PROGNOSIS

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Background: Many autoinflammatory diseases are associated with mutations in myeloid lineage cells including neutrophils and macrophages. Myelodysplastic syndrome (MDS) is clinically linked to autoinflammatory diseases e.g. Sweets syndrome and NLRP3 inflammasome activation, is an intrinsic feature of some MDS cases.

Objectives: We tested the hypothesis that autoinflammatory disease is common in MDS cohorts and we further theorised that MDS with somatic mutations and karyotypic abnormalities were associated with autoinflammation.

Methods: 140 MDS patients referred to St. James's University Hospital in Leeds during the period 2012-2018 were systematically and retrospectively recruited with karyotypes and somatic mutations status being performed. Patients with autoinflammation were classified as well-defined autoinflammatory disease or poorly defined "autoinflammatory state" (non-infection related elevated CRP over 10.0 mg/L in 5 consecutive times, taken at separate occasions) based on their final diagnosis and compared in terms of demographic, clinical, laboratory, cytogenetics charts, and outcomes.

Results: The average age was 77.08±11 years (median 79 years), with (n=91, 65.0%) male. 72 (51%) patients had an autoinflammatory state and were younger (75.15±11.23 versus 79.15±11.92, p<0.05), and had more frequent arthritis (n=25, 34.7%, versus n=12, 17.6%, p=0.0225), arthralgia (n=32, 44.4%, versus n=18, 26.5%, p=0.0271), skin rash (n=22, 30.6%, versus n=10, 14.7%, p=0.0261), pleuritis (16, 22.2%, versus n=3, 4.4%, p=0.0022). 26.3% of MDS patients with autoinflammatory state had a well-defined autoinflammatory disorder (neutrophilic dermatosis, and polymyalgia rheumatic being the commonest). Mutations affecting the transcription factors pathway (NPM1, RUNX1, BCOR, WT1, TP53, MYD88) (OR 3.15 [95%CI 1.04-9.56], p=0.0426) and deletion of chromosome 5 (OR 3.37 [95%CI 1.01-11.22], p=0.0479) were associated with autoinflammation. Stratifying autoinflammatory state, deletion of chromosome 7 and chromosome 5 were found independent predictors for well-defined autoinflammatory disorder and poorly-defined autoinflammatory state, respectively. Furthermore, acute leukaemia transformation was more frequently in MDS patients with autoinflammatory status (n=25, 34.7%, versus n=8, 11.8%, p=0.0002).

Conclusion: Both well-defined and poorly defined autoinflammatory diseases are common in MDS. Transcription factors pathway somatic mutations and abnormal karyotype are associated with the risk of autoinflammation. Autoinflammation is linked to a worse prognosis which may be linked to the higher risk of malignant transformation.

Abstract Figure 1. Autoinflammatory state stratified to well-defined and poorly-defined autoinflammatory disorder in MDS patients

Abstract Table 1. Predictors of overall, well-defined or poorly-defined autoinflammatory conditions.

Predictor	OR [95%CI]	p-value
Overall autoinflammation		
Genes mutated	2.28 [95%CI 1.08 to 4.78]	0.0296
Abnormal karyotype	2.67 [95%CI 1.27 to 5.64]	0.0097
Transcription factors pathway	3.15 [95%CI 1.04 to 9.56]	0.0426
Deletion chromosome 5	3.37 [95%CI 1.01 to 11.22]	0.0479
Well-defined autoinflammatory disease		
Genes mutated	3.09 [95%CI 1.01 to 9.46]	0.0486
Abnormal karyotype	3.13 [95%CI 1.03 to 9.48]	0.0439
Transcription factors pathway	4.50 [95%CI 1.04 to 19.47]	0.0441
Deletion chromosome 7	6.13 [95%CI 1.16 to 32.33]	0.0325
Number of mutations	3.39 [95%CI 1.08 to 10.66]	0.0441
Poorly-defined autoinflammatory state		
Abnormal karyotype	2.64 [95%CI 1.82 to 5.88]	0.0179
Deletion chromosome 5	3.57 [95%CI 1.02 to 12.48]	0.0465

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RELATIONSHIP BETWEEN SERUM ADENOSINE DEAMINASE LEVELS AND DISEASE ACTIVITY IN AUTOIMMUNE HEPATITIS

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Background: Autoimmune hepatitis(AIH)^[1] is a chronic liver inflammation mediated by autoimmune response, characterized by serum autoantibodies, high immunoglobulin G(IgG), and interface hepatitis histology, which can develop into cirrhosis and liver failure. Adenosine deaminase(ADA) is an enzyme involved in purine metabolism, which can catalyze the irreversible conversion from deoxyadenosine to deoxyinosine. As adenosine is an important immunoregulatory factor in the physiological microenvironment, ADA plays an important role in regulating the balance of the human immune system. Previous studies have reported the associations between ADA and disease activity in a variety of autoimmune diseases, such as systemic lupus erythematosus^[2], rheumatoid arthritis^[3] and juvenile idiopathic arthritis^[4].

Objectives: To investigate the relationship between serum adenosine deaminase levels and disease activity in patients with autoimmune hepatitis.

Methods: Thirty patients with autoimmune hepatitis and 30 healthy individuals were included in the study. We enrolled 30 patients who met the simplified criteria suggested by the International Autoimmune Hepatitis Group. All of the cases had been diagnosed with AIH between 2013-2018 at Northern Jiangsu People's Hospital, Department of Gastroenterology or Rheumatology, and the diagnosis was confirmed by liver biopsy. Serum adenosine deaminase levels were measured by enzyme-coupled assay, and >25U/L were determined to be high level 25U/L.

Results: The mean serum ADA levels were prominently higher in AIH patients than those in healthy controls (29.13 ± 8.70 U/L vs 14.50 ± 4.63 U/L, P < 0.001). Serum ADA levels were > 25 U/L in 70% AIH patients and in 0% healthy controls(P < 0.001). Mean serum ADA levels were significantly increased in each stage of disease activity: 26.32 ± 8.78 U/L for mild patients, 31.33 ± 4.23 U/L for moderate patients and