AB1110

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

Abdulla Watad¹, Mark Kacar², Nicola Luigi Bragazzi³, Qiao Zhou², Catherine Cargo², Jan Taylor², Eve Roman⁴, Alexandra Smith⁴, Richard A. Jones², Howard Amital¹, Sinisa Savic², Dennis McGonagle². ¹Tel Aviv University, Tel Aviv-Yafo, Israel; ²University of Leeds, Leeds, United Kingdom; ³University of Genoa, Genoa, Italy; ⁴University of York, Heslington, United Kingdom

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

Disclosure of Interests: Abdulla Watad: None declared, Mark Kacar: None declared, Nicola Luigi Bragazzi: None declared, Qiao Zhou: None declared, Catherine Cargo: None declared, Jan Taylor: None declared, Eve Roman: None declared, Alexandra Smith: None declared, Richard A. Jones: None declared, Howard Amital Grant/research support from: Pfizer, AbbVie, Janssen, Grant/research support from: Pfizer, AbbVie, Janssen, Consultant for: Pfizer, Merck Sharp & Dohme, Consultant for: Pfizer, Merck Sharp & Dohme, Speakers bureau: Pfizer, Merck Sharp & Dohme, Janssen, Sanofi, Bristol-Myers Squibb, Abbvie, Neopharm, Speakers bureau: Pfizer, Merck Sharp & Dohme, Janssen, Sanofi, Bristol-Myers Squibb, Abbvie, Neopharm, Sinisa Savic Grant/research support from: Novartis and Sobi, Dennis McGonagle Consultant for: Lilly, Novartis UCB, Speakers bureau: Lilly, Novartis UCB

DOI: 10.1136/annrheumdis-2019-eular.2082

AB1111

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

Jing Xie¹, Hua Wei², Xiaoxing Xiang². ¹Dalian Medical University, Dalian, China; ²Northern Jiangsu People's Hospital, Yangzhou, China

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

37.20 $\pm$ 7.36 U/L for severe patients ($P = 0.03$). Correlation analysis showed that there was a positive association between serum ADA levels and disease activity ($r = 0.43$, $P = 0.02$). Receiver operating characteristic analysis showed that 38.5 U/L was the optimum cut-off point of ADA level for severe disease activity (sensitivity 60%, specificity 92%, area under the curve: 0.81).

Conclusion: The evaluation of serum adenosine deaminase level in patients with autoimmune hepatitis should be considered a useful biomarker in the monitoring of their disease activity.

REFERENCES

- [1] Hennes, E.M., et al., *Simplified criteria for the diagnosis of autoimmune hepatitis*. Hepatology, 2008. 48(1): p. 169-76.
- [2] Gao, Z.W., et al., *Serum adenosine deaminase activity is increased in systemic lupus erythematosus patients and correlated with disease activity*. Immunol Res, 2018. 66(2): p. 299-304.
- [3] Zamani, B., R. Jamali, and A. Jamali, *Serum adenosine deaminase may predict disease activity in rheumatoid arthritis*. Rheumatol Int, 2012. 32(7): p. 1967-75.
- [4] Doudkani-Fard, M., et al., *Sensitivity and specificity of adenosine deaminase in diagnosis of juvenile idiopathic arthritis*. Med J Islam Repub Iran, 2014. 28: p. 113.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2019-eular.3679

AB1112

DIAGNOSTIC DELAY AND DAMAGE OF POLISH ADULT PATIENTS AFFECTED BY HEREDITARY AUTOINFLAMMATORY SYNDROMES

Ewa Wiesik-Szewczyk¹, Dariusz Soldacki¹, Beata Woska-Kuśnierz², Marcin Milchert³, Aleksandra Matyja-Bednarczyk⁴, Violetta Opoka-Winiarska⁵, Stanisław Niemczyk⁶, Karina Jahnz-Różyk¹. ¹Central Clinical Hospital of the Ministry of National Defense, Military Institute of Medicine, Department of Internal Medicine, Pneumology, Allergology and Clinical Immunology, Warsaw, Poland; ²The Children's Memorial Health Institute, Department of Immunology, Warsaw, Poland; ³Pomeranian Medical University, Department of Rheumatology, Internal Medicine, Geriatrics, Szczecin, Poland; ⁴The University Hospital, Department of Allergy and Immunology, Cracow, Poland; ⁵Medical University of Lublin, Department of Pediatric Pulmonology and Rheumatology, Lublin, Poland; ⁶Central Clinical Hospital of the Ministry of National Defense, Military Institute of Medicine, Department of Internal Medicine and Nephrology, Warsaw, Poland

Background: Autoinflammatory diseases (AIDs) cover a spectrum of diseases, which lead to chronic or recurrent inflammation caused by activation of the innate immune system, typically in the absence of high titre autoantibodies.¹ The most common monogenic AIDs are cryopyrin-associated periodic syndromes (CAPS), familial Mediterranean fever (FMF) and tumour necrosis factor receptor-associated periodic fever syndrome (TRAPS). In hereditary AIDs, chronic and recurrent inflammation can lead to both acute disease and irreversible damage.²

Objectives: To describe irreversible damage and diagnostic delay of AID in Polish adult patients (age ≥ 18).

Methods: We reviewed the records of 11 Caucasian (2 women, 9 men) and one female patient with Middle Eastern ancestry followed in our center from Aug 2012 to Jan 2019. We analysed demographic features, diagnostic delay, previous diagnosis and organ damage.³

Results: Eleven patients had documented variant mutation and AID diagnosis (6-TRAPS, 4-CAPS, 1-FMF). One patient with AA amyloidosis had negative genetic results. The mean age of the patients at the time of disease onset was 9.1 years (0.1- 37) and 33 years (16-62) at diagnosis. In all Caucasian patients diagnosis was established after the age of 18. Previous diagnosis was: JIA (2), AOSD (2), UCTD (4), vasculitis (1), seronegative RA (1), FMF (3 finally confirmed TRAPS) and allergy (3). Prior treatment included GCS (12/12), cDMARDs (7), antimalarials (6), colchicine (4), bDMARDs: tocilizumab-1, etanercept-2, adalimumab-1, CYC (2). After diagnosis 11 patients received IL-1 inhibitor, anakinra. Only one, 62 year old woman with TRAPS, did not need biological treatment. Only 3 TRAPS patients were free from damage accrual. We documented following damage categories: renal/amyloidosis (5 male cases), developmental (3 growth retardation), ear (severe hearing loss -3 CAPS cases). CINCA male patient at age 29 had multiple organ damage: neurological (epilepsy), severe hearing loss, severe ocular involvement (including optic nerve atrophy), joint restriction and deformity leading to complete physical disability. One FMF woman was advised elective abortion, one MWS had miscarriage. Two of 3 women had history of malignancy (one: breast cancer and ovarian cancer, and another thyroid cancer). No any mental

retardation occurred. During follow up 2 male patients with extensive amyloidosis died despite anakinra treatment.

Conclusion: AID are misdiagnosed and have high risk of damage. We advocate the need for efforts in order to increase awareness of AID to reduce the diagnostic delay. The frequency of malignancy in AID should be addressed in future international collaborative studies.

REFERENCES

- [1] Masters SL, et al. *Horror autoinflammaticus: the molecular pathophysiology of autoinflammatory disease*. Annu Rev Immunol 2009;27:621-68.
- [2] Federici S, et al. *Evidence-based provisional clinical classification criteria for autoinflammatory periodic fevers*. Ann Rheumatic Dis 2015;74:799-805.
- [3] ter Haar NM, et al. *Development of the autoinflammatory disease damage index*. Ann Rheum Dis 2017;76:821-830

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2019-eular.4948

Diagnostics and imaging procedures

AB1113

RELATION BETWEEN RESTRICTIVE PULMONARY FUNCTION TESTS AND ULTRASONOGRAPHIC CHANGES OF ASYMPTOMATIC ANTERIOR CHEST WALL JOINTS IN RHEUMATOID ARTHRITIS PATIENTS

Fatma Ibrahim Abdelrahman¹, Mohammed A. Mortada², Amal Abdul-Sattar². ¹Zagazig University, Rheumatology and Rehabilitation, zagazig, Egypt; ²Zagazig University, Rheumatology and Rehabilitation, zagazig, Egypt

Background: Ultrasonography can detect different changes in anterior chest wall (ACW) joints in patients with Rheumatoid Arthritis (RA) even before being clinically manifested.⁽¹⁾ Pulmonary functions may be affected during the course of RA due to interstitial lung problem or chest wall problem.⁽²⁾

All studies usually demonstrate the interstitial pulmonary affection in RA but the chest wall joints is usually underestimated by the rheumatology community. Up to the best of our knowledge, there are no previous studies about the relationship between ultrasound detected subclinical changes in ACW and the pulmonary functions in RA patients.

Objectives: To detect the relation between ultrasonographic changes of asymptomatic ACW joints and pulmonary function tests (PFTs) in patients with RA.

Methods: The study included 44 subjects (22 RA and 22 control) in whom 88 sternoclavicular joints (SCJ) and 44 manubriosternal joints (MSJ) were studied. None of the participants had a history of respiratory complaints such as dyspnea, chronic cough, or chest pain. High resolution Computed Tomography (HRCT) was done on the chest to exclude interstitial lung problem that may affect chest expansion and PFTs. Ultrasound (US) assessments were performed to detect synovitis, erosions, ankylosis, osteophytes, or Doppler signals. Chest expansion was measured. PFTs was done and included measurement of the forced expiratory volume in 1 s (FEV1), forced vital capacity (FVC), and the ratio of forced expiratory volume in 1 s to the forced vital capacity (FEV1/FVC). In RA group, DAS28 and Health Assessment Questionnaire Disability Index (HAQDI) were recorded.

Results: US detected subclinical changes of ACW joints in (74.2%) of RA patient with significant difference between total US changes in RA (74.2%) and control (21.2%) ($p < 0.001$). MSJ ankylosing and erosions were highly associated with limited chest expansion in RA group ($P < 0.001$). PFTs were found to be restrictive in 13 RA patient (59.1%) with mean of FVC (65.5 $\pm$ 5.5)%, FEV1 (70.4 $\pm$ 9.1)%, FEV1/FVC (80.1 $\pm$ 2.6) with significant difference to control with mean of FVC (93.6 $\pm$ 7.2)%, FEV1 (94.3 $\pm$ 4.5)%, FEV1/FVC (95.1 $\pm$ 2.4). These restrictive PFTs were associated with SCJ synovitis ($p = 0.04$), SCJ PD activity ($p = 0.04$), SCJ erosions (0.02) and highly associated with MSJ ankylosing and erosions ($p < 0.001$). All RA patients (100%) with MS ankylosing and erosions and SCJ PD activity by US had limited chest expansion and restrictive PFTs. Restrictive PFTs were associated also with limited chest expansion with mean of (2.3 $\pm$ 0.5) with significant difference ($p < 0.001$) to non-restrictive PFTs in RA with mean of (5.2 $\pm$ 1.4).

In RA group, ultrasonographic changes and restrictive PFTs were found to be higher with smoking, longer disease duration and high DAS28.

Conclusion: Our study demonstrated that ultrasonographic subclinical changes in ACW joints is associated with restrictive pattern of PFTs and limited chest expansion in RA patients.