AB1101

ANA SUBSETS ANTIBODY PROFILE OF EARLY UNDIFFERENTIATED ARTHRITIS (UA) IN PAKISTAN

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Background: Undifferentiated Arthritis (UA) is a group of inflammatory disorders where early synovitis (duration less than 12 months) is present, however patients do not meet criteria for established rheumatologic disorders such as Rheumatoid arthritis, Lupus or Spondyloarthritis (1). On long term follow up, a subpopulation of UA patients converge into definitive Rheumatologic disorders. Up to 50% of early arthritis in European cohorts has been reported to be UA (1, 2).

Objectives: Identify Anti-nuclear antibody (ANA) Subset antibodies in patients presenting with early UA.

Methods: Over a 1-year period (2017-18) patients with early UA were prospectively evaluated. This included clinical exam, routine laboratory investigations including ESR and CRP, RF and anti-CCP as well as Musculoskeletal ultrasound (MSKUS) (3). These patients underwent further testing for ANA Subset antibodies. ANA subsets (17 antibodies) were performed using standard immunoblot assays (EUROIMMUN) at our clinical laboratory (4).

Results: 110 UA patients were found to have positive ANA subsets. The most frequent antibodies were Ku (77.3%) and Mi2 (73.6%) followed by dsDNA (30%) and Nucleosome antibody (29%) (Figure 1). Low frequency antibodies included Sm (n=1), Ribosomal-P and PCNA (n=2 each), Jo-1 (n=3), PM-Scl100 (n=4) and SSB (n=5), whereas Scl70 antibodies were absent. SSA (n=9) and Ro-52 (n=14) together constituted 21% frequency. These antibodies had high signal intensities (mean $\pm$ SD SSA = 52 $\pm$ 35 and Ro-52 = 46 $\pm$ 25). Ku (17 $\pm$ 11) and Mi2 (22 $\pm$ 15) had modest signal intensities (Figure 2). Clinically 42 patients were classified as RA (RF+ = 33%; anti-CCP+ = 14%) and 41 patients met ACR criteria for SLE while 2 patients met criteria for both and were classified as Rhupus. ANA subset antibody frequencies did not statistically differ between the RA and SLE groups signifying that the clinically classified RA patients in fact had early Rhupus which did not meet ACR criteria for SLE.

Conclusion: Early UA is difficult to categorize clinically, sometimes even after long term follow up, though a substantial portion converge into RA. This study shows that there is a significant portion of early Rhupus in the RA group whose steroid discontinuation leads to a disease flare. ANA Subset antibody profile in such patients may help in their more accurate diagnoses and treatment.

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Abstract AB1101 Figure 1. ANA Subsets Antibody Frequency

Abstract AB1101 Figure 2. ANA Subsets Antibody Intensity

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AB1102

SCHNITZLER SYNDROME IN THE CLINICAL PRACTICE OF A RHEUMATOLOGIST

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Background: Schnitzler syndrome (SchS) is a rare autoinflammatory multifactorial disease, manifested by urticaria, monoclonal immunoglobulin (usually IgM) secretion, bone pain, and clinical and laboratory signs of systemic inflammation (fever, leukocytosis, and CRP increase) [1]. SchS is included in the differential diagnosis of the adult Still's disease, autoinflammatory diseases, and Waldenstrom macroglobulinemia. Interleukin 1 (IL-1) inhibitors (anakinra and canakinumab) have been shown to the efficient pathogenetic therapy of SchS [2,3].

Objectives: To provide clinical and laboratory characteristics and the results of IL-1 inhibitors therapy in the SchS patients from 2015 to 2018 observed in the V.A. Nasonova Research Institute of Rheumatology (Moscow, Russia).

Methods: The study included 4 patients (1 female, 3 males) aged from 32 to 56 years. Patients with suspected SchS were studied with electrophoresis of serum and urine proteins, histological and cytological examination of the bone marrow (in 3 of 4 patients), and testing of mutations in *NLRP3* and *TNFRSF1A* genes (in 3 of 4 patients).

Results: SchS was diagnosed 3 to 22 years (median 3.5 years) after the onset of clinical manifestations. Three patients had a fever. All patients showed chronic urticaria and musculoskeletal manifestations (arthralgia and leg bone pain). Two patients showed fluid collections in serous cavities. Pericarditis was observed in one patient, and pleurisy in another patient. To our knowledge, serositis was not described in SchS previously. Three patients had leukocytosis from 16.0 to 23.6 $\times 10^9/L$. In all patients, ESR (from 31 to 140 mm/h) and CRP level (from 29 to 192 g/L) increased. In all patients, secretion of monoclonal IgM was detected, not exceeding 7.8 g/L. In three cases, IgM included kappa chain, and in one patient biconal secretion was found (IgM kappa and IgM lambda). Mutations in *NLRP3* and *TNFRSF1A* genes were not identified. None of the patients showed lymphoplasmacytic infiltration of bone marrow. All patients before the diagnosis were prescribed with glucocorticosteroids with a temporary positive response and relapse of the disease after the dose reduction or withdrawal. Two patients received canakinumab 150 mg subcutaneously once every 8 weeks for 1.5-3.5 years, with a complete response. In one, the interval between injections was increased during the last year to 5 months, with the preservation of clinical and laboratory remission of SchS. Against the background of canakinumab therapy, one patient became a father of a healthy baby. One patient received anakinra 100 mg subcutaneously of daily, with the complete clinical and laboratory response after 2 weeks of therapy. During the use of the IL-1 inhibitors, we have observed none clinically significant side effects.

Conclusion: To diagnose SchS in adult patients with chronic urticaria, fever, and acute phase signs of inflammation, one should perform serum proteins electrophoresis. SchS can manifest with serositis. IL-1 inhibitors in SchS patients are the efficient by and safe therapy.

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AB1103 NEUROLOGICAL IMPAIRMENT DURING SARCOIDOSIS

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Background:

Objectives: To describe neurological impairment characteristics in sarcoidosis.

Methods: This was a descriptive and retrospective study including 65 patients with sarcoidosis, followed in the departments of internal medicine and neurology at the Military Hospital of Tunis over a period of 20 years from 1997 to 2017.

Results: A total of 65 patient files have been selected, of which 38 have neurological involvement.

Thirty-eight patients met the inclusion criteria for Neurosarcoidosis. According to Zajicek's criteria, the diagnosis of neurosarcoidosis was certain in 2 cases, probable in 18 cases and possible in 18 cases.

Neurological disorders were symptomatic in 58.5% of the studied population. Neurological signs were inaugural in 9 patients (14% of cases). A central neurological involvement was demonstrated in 33 patients (86.8%), the peripheral nervous system was affected in 5 patients (13.1%), and cranial nerve involvement was found in 10 patients (26.3%). Ten patients have had both central and peripheral impairment.

Neurological involvement was significantly associated with cardiac, renal extra-thoracic, ophthalmologic, articular and cutaneous involvement (p <0.05)

Genotyping of the conversion enzyme and HLA typing did not show any particular pattern of neurosarcoidosis in comparison with patients without neurological signs.

Conclusion: Neurological impairment was frequently observed in our series. It was also significantly associated with multivisceral involvement without particular genetic pattern.

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AB1104 GENETIC ASPECTS OF SARCOIDOSIS IN A TUNISIAN POPULATION

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Background:

Objectives: To determine the frequencies of the HLA alleles and genotypes of the ACE gene.

Methods: This is a cross sectional study of 65 patients with sarcoidosis, followed in the departments of internal medicine and neurology at the Military Hospital of Tunis. The genetic study involved only 50 patients. DNA extraction was performed to determine the frequencies of the HLA alleles and genotypes of the ACE gene.

Results: 1. HLA typing

The analysis of HLA typing allowed us to estimate the different frequencies of alleles in patients. The calculation of the allelic frequency found that the most frequent alleles are HLA-DRB1 * 1501 alleles with a frequency of 38% and HLA-DRB1 * 0301 of 28%. Other alleles are at lower frequencies (Table1).

HLA	N	%
N=50		
HLA-DRB1*1501	19	38%
HLA-DRB1*0301	14	28%
HLA-DRB1*1106	9	18%
HLA-DRB1*0401	8	16%

2. Genotyping of the ECA gene

Genotyping of the polymorphism of the angiotensin converting enzyme (ACE) involved 50 patients. Genotypic frequencies (II, ID and DD) and allele frequencies (I and D) were estimated in order to evaluate the frequencies of each genotype and the 2 alleles for this pathology. The genotypic and allelic frequency results were summarized in Table 2.

Genotypes	N	%
II	11	22%
ID	24	48%
DD	15	30%
Alleles		
I	46	46%
D	54	54%

Conclusion: The most frequent alleles in Tunisian patients with sarcoidosis are HLA-DRB1 * 1501 alleles with a frequency of 38% and HLA-DRB1 * 0301 of 28%. The genotypic and allelic results showed that genotype ID was the most frequent with 48% with a predominance of the D allele in 54%.

References:

DISCLOSURE OF INTERESTS

None declared

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AB1105 A NOVEL AUTOINFLAMMATORY AND LYMPHOPROLIFERATIVE SYNDROME ASSOCIATED WITH PIM1 MUTATIONS

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Background: Whole exome sequencing can allow genetic diagnosis in subjects with long lasting clinical stories not supporting any well-defined disorder.

A 35-year-old man was referred to ophthalmologist's evaluation for blurry vision in his left eye. The fundus examination showed choroidal lesions in both eyes. His past medical history was relevant for celiac disease, recurrent episodes of fever and skin rashes with leukocytoclastic vasculitis, inflammatory lesions of the osteoarticular and muscular system, one episode of aseptic meningitis, an intracranial granuloma and two episodes of anterior uveitis. He had also splenomegaly with non-caseating granulomas. Brain TC founded multiple lytic and sclerotic skull lesions. He was diagnosed with atypical sarcoidosis and treated with oral steroid and methotrexate.

Laboratory data always showed elevated erythrocyte sedimentation rate, strong positive C-reactive protein and polyclonal gammopathy.

Objectives: To describe functional and genetic data supporting the role of a PIM1 mutation in the multisystemic inflammation and lymphoproliferation of the patient.

Methods: Whole exome sequencing (WES) analysis. Flow-cytometry to evaluate Pim1 expression, Bad phosphorylation (target of Pim1 kinase) and the effect of PIM inhibitor on peripheral blood mononuclear cell (PBMC) viability. RNAseq was on primary fibroblasts from the patient and