VIRUS-NEGATIVE LYMPHOCYTIC MYOCARDITIS: A SYNDROME OF RECURRENT IDIOPATHIC HYDROPS

ABSTRACTS

VIRUS-NEGATIVE LYMPHOCYTIC MYOCARDITIS: CLINICAL AND DIAGNOSTIC FEATURES FROM A MONOCENTRIC ITALIAN COHORT

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Background: Virus-negative lymphocytic myocarditis (VNLM) is defined by endomyocardial biopsy (EMB) established histological, immunological and immune-histochemical criteria; it may occur as a distinct disease or in the context of systemic autoimmune or inflammatory disorders.

Objectives: To describe the demographic, clinical, histological and immune-histochemical features of VNLM from a monocentric Italian cohort.

Methods: 42 patients (mean age 45.5±14.9 years; male to female ratio 1:1) were diagnosed with EMB-proven VNLM at our Centre from January 2015 to December 2017. In all patients, comprehensive demographic, clinical and histological data were collected.

Results: The most common initial clinical feature was chest pain (40.5%), followed by palpitations (26.2%) and syncope (23.8%). Aborted sudden cardiac death (SCD) was the first manifestation in 3 cases, while arrhythmias were overall present in 47.6% of patients, being life-threatening in 10 of them. Interestingly, 4 patients had only few constitutional symptoms and 2 patients were completely asymptomatic. The distribution of traditional cardiovascular risk factor reflected that of the general population, apart for a more common familiarity for SCD (31.7%) and for autoimunity (31.7%). Serum levels of troponin T and NT-proBNP were increased in 40.5% and 30.9%, respectively. Both echocardiography and standard ECG were unremarkable in half of the patients, while nearly all patients (92.5%) had at least one Lake-Louis criterion at cardiac magnetic resonance (CMR) evaluation. The most common CMR finding was delayed enhancement (45.2%), while ventricular dysfunction was evident in 38.1% of EMBs.

Conclusions: Almost third of NIHF are idiopathic (iNIHF), not caused by red cell alloimmunization. The pathogenesis of tissue hypoxia and fetal loss may result from thrombophilia and Hydrops fetalis (HF). HF is described as fetal pathological fluid accumulation in serious cavities and soft tissues. It is accompanied with placental thickening and hydramnios. Most of the cases refer to non-immune (NIHF), not caused by red cell alloimmunization. Almost third of NIHF are idiopathic (NIHF). The pathogenesis of tissue hypoxia with capillary leakage remains unclear. With advanced in-utero therapy mortality is still high (50%-95%).

Objectives: To describe the entity of recurrent idiopathic NIHF, resulting in habitual miscarriages. To document the use of APS prophylactic regimen for fetal loss, and its effect on NIHF occurrence.

Methods: Data from medical files of women with previous NIHF, who were treated in the rheumatology clinic, Hadassah Mount Scopus Hospital in Jerusalem, between years 2002–2017 were summarised (table 1).

Results: The present series illustrates the impact of the prophylactic regimen of APS in preventing obstetrical morbidities, including miscarriages and fetal death due to Hydrops fetalis (table 1). Thrombophilia and APLs profiles were normal. Five women who had multiple early abortions and 8 pregnancies with NIHF, following treatment had a total of 12 successful pregnancies with uneventful delivery to healthy babies. ANA anti-nuclear antibodies, IUF/D:intra uterine fetal death, IVF:in vitro fertilisation, CLX:Clexan,Exonaparin (SC 40 mg/d), HCG:Hydroxy-Chloroquine (200 mgx 2/d), PRD:Prednisone (10-20 mg/d)

On EMB, myocarditis was classified as active in 23 cases (54.8%) and as chronic in 18 (42.3%), while 7 patients (16.7%) had evidence of both features. CD3 T-lymphocytes>7/mm² were detectable in 27 patients (64.3%), necrosis in 20 patients (47.6%), oedema in 28 patients (66.7%), while only 4 patients showed signs of vasculitis or thrombotic microangiopathy. At time of diagnosis, myocardial fibrosis was evident in 73.8% of EMBs and dilated cardiomyopathy in 6 patients (14.3%). All patients were treated with steroids and azathioprine as first line therapy, and 17 patients (40.5%) were initially referred for device implantation.

Conclusions: VNLM is an overlooked disease characterised by a broad spectrum of clinical features and peculiar immune-mediated hallmarks. The early recognition of myocarditis, allowing a prompt therapeutic intervention, should be a major goal for rheumatologists.

Disclosure of Interest: None declared.

Conclusions: Idiopathic NIHF is a very serious condition with high fetal mortality and limited effective therapy, so prevention is very crucial. APS prophylaxis regimen, based on MBL-platelets and anti-coagulant therapy during pregnancy, may have promising effects.

Disclosure of Interest: None declared


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**FAMILIAL MEDITERRANEAN FEVER AS AN OUTCOME OF UNDIFFERENTIATED ARTHRITIS**

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Background: The term «undifferentiated arthritis» (UA) was proposed to empha-
sise the heterogeneity of unclassifiable arthritides and their potential into a defin-
able form of arthritis. A patient with UA have an early stage of defined arthritis that will meet criteria in time, a forme fruste or partial form of a classifiable disease, an overlap of more than one disease entity, or an arthritis of unknown or in that may (or may not) become differentiated in the future. The heterogeneity associated with the term «UA» emphasise the need for continued follow-up and reassess-
ment of the diagnosis and management of these patients.

Objectives: The aim of this study was revelation of MEFV gene mutations in patients with UA.

Methods: We have examined 80 patients (34 male, 46 female, mean age 36.4 ±3.4 years) with UA. The patients were observed every 6 months in follow-up per-
iod of 5 years. The anamnestic and treatment data were obtained. Joint dis-
ease activity scores and presence of extra-articular manifestations were deter-
mined. The CBC, urinalysis, serum concentrations of creatinine, bilirubin, transaminases, glucose, CRP were determined every 6 months, X-ray examina-
tion and ultrasonography of joints were performed once a year. Molecular-genetic analysis of 12 MEFV-mutations, common for Armenians, were carried out in Medi-
cal Genetic Centre of Armenia.

Results: From 80 investigated patients with UA 10 had repeated episodes of mono- and oligoarthritis of ankle and/or knee joints with local skin hyperemia and hyperthermia, without subsequent joint deformities, 45 – sacroiliitis (26 bilateral, 19 unilateral), accompanied by enthesopathy, 2 – joint syndrome, resembling rheumatoid arthritis. In 23 patients joint syndrome was accompanied by erythema rash, livedo reticularis, photosensitivity and alopecia. The latter group of patients was diagnosed as SLE-like syndrome. All patients didn’t fulfil accepted classifica-
tion criteria of any autoimmune or autoinflammatory disease. The 80% of investi-
gated patients had no classic febrile attacks of abdominalgia and/or thoracalgia, specific for FMF. In remaining 20% of patients febrile attacks hadn’t preceded joint
syndrome, but appeared during 5 year follow-up period.

All investigated patients had MEFV gene mutations, which’s compositions (homo-
zygous or compound heterozygous) were enough to confirm Familial Mediterrane-
nean Fever (FMF). The most common mutations were: M694V–41.2%, V726A– 18.8%, M680I –10.7%. The most common compositions were M694V/M694V, M694V/V726A, M680I/M680I.

Conclusions: As FMF is widely distributed in Mediterranean region, and it had changed its phenotype in last decades, as well as taking into account the increas-
ing rate of migration worldwide, every single case of UA, which doesn’t fulfil classi-
fication criteria of any disease, should be tested for presence of MEFV-mutations. The diagnosis of FMF changes the approach to follow-up, management, outcome and prognosis of UA.

Disclosure of Interest: None declared


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**DIAGNOSTIC UTILITY OF LYMPH NODE BIOPSY IN DIFFERENTIAL DIAGNOSIS OF IGG4-RELATED DISEASE, IDIOPATHIC MULTICENTRIC CASTLEMAN’S DISEASE AND PRIMARY DISSEMINATED MALT-LYMPHOMA**

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Background: Lymphadenopathy (LA) is a frequent and challenging syndrome in rheumatic patients. It requires comprehensive clinical and expert pathological evaluation. IgG4-related disease (IgG4-RD) groups a combination of fibroinflamma-
tory conditions characterised by formation of tumor-like lesions with unique mor-
phological features and hyper-IgG4 secretion in different organs and tissues. LA is frequent in IgG4-RD and doesn’t have a unique morphology. Idiopathic multi-
centric Castleman’s disease (IMCD) is a rare lymphoproliferative disorder of a hyper-IL-6 spectrum with oblige lymph nodes (LN) affection and less frequent extranodal lesions. Pathologic features of the LN in IMCD overlap with IgG4-LA and there can be IgG4 hypersecretion in IMCD patients as well. Primary dissemi-
nated MALT-lymphomas (DMALT) are also in the spectrum of differential diagno-
sis because of the involvement of salivary and lacrimal glands.

Objectives: To evaluate the diagnostic utility of LN biopsy in differential diagnos-
sis of IgG4-RD, IMCD and DMALT.

Methods: Retrospective study. We reviewed medical records from 2009 to 2017 and identified 13 pts. who were examined in our clinic due to some rheumatologi-
diagnosis suspicion and whose leading symptom at the onset of the disease was LA. All patients had prior multiple LN biopsy (25 LN biopsies in total) which was reviewed by an expert pathologist during our examination. 11 pts. had extra-
nodal lesions and underwent extranodal biopsy.

Results: Eight pts. were men, 5 women with average age at the onset 34.7 years (15–71 years). The directional diagnoses established on the LN pathology were as following (in some cases a few diagnosis): IMCD (4 pts), non-Hodgkin lym-
phoma (3 pts), reactive LN (12 pts). 11 pts. had some extranodal lesions (3.9 per
patient, from 1 to 8); orbit – 8, major salivary glands – 8, hepatosplenomegaly – 5, lungs – 5, thyroid – 5, kidneys – 3, sinusitis – 3, skin, cholangitis – 2 each, retropo-
teritoneum, mediastinum, pancreas and soft tissues – 1 each. Due to orbital and major salivary glands involvement some patients had directional diagnosis of Sipigen’s syndrome or IgG4-RD. In all 13 pts. the directional diagnosis was changed to some other based on the extranodal biopsy pathology results (in 11 pts) and/or clinical presentation (in 2 pts with isolated LA). LN pathology was not conclusive in all cases. In all cases LN pathology fell into I-V type of LN morpho-
logical picture as reported by J. Ferry et al.1 Clinical presentation in 13 pts see in table 1. The final diagnosis were: IgG4-RD in 7 pts, IMCD in 2 pts and DMALT in 4 pts.

Abstract AB1162 – Table 1. Clinical-laboratory features of patients

Table 1. The final diagnosis were: IgG4-RD in 7 pts, IMCD in 2 pts and DMALT in 4 pts

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Abstract AB1163

Conclusions: It seems to be very challenging to set a reliable diagnostic diago-
nsis based on the LN pathology thus extranodal biopsy is preferable. Orbital and major salivary glands involvement is a feature of IgG4-RD or DMALT, but not iMCD. Prominent constitutional symptoms with high laboratory inflammatory markers (CRP, IL-6) are characteristic of IMCD.

REFERENCE:
[1] Ferry, J. IgG4-related lymphadenopathy and IgG4-related lymphomas: mov-
ing targets/Diagnostic Histopathology. — 2013.— Vol. 19.— Nr. 4.— P. 128–139

Disclosure of Interest: None declared


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**MY BEHÇET’S DISEASE AND MY MENSTRUATION CYCLE: OBSERVATION FROM AN IRISH COHORT**

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Background: The menstrual cycle is regulated by the rise and fall of sex hor-
mones in the body. Literature has demonstrated anti-inflammatory properties in both progesterone and oestrogen hormones.1 There has been recent interest to determine the association between Behçet’s Disease (BD), a poorly understood autoimmune disorder and menstruation.

Disclosure of Interest: None declared

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