POS1351

CAUSES OF HOSPITALIZATION IN BEHÇET SYNDROME

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Background: The causes of hospitalization may provide important information on the course of diseases and treatment-related adverse effects.

Objectives: We aimed to determine the causes and outcome of hospitalizations among patients with Behçet Syndrome (BS) in a dedicated center.

Methods: We surveyed hospitalization records in our clinic between January 2002 and December 2019 and identified those with a diagnosis of BS. The records of these patients were reviewed for demographic and clinical features, causes of hospitalization and outcome. We divided hospitalization causes into 2 as being BS related (organ involvement or deterioration) and non-BS related (treatment complication or others).

Results: Three-hundred and thirty BS patients (75% men, mean age 37.7 ±11.4 SD years) were hospitalized for a total of 456 times during 18 years. The mean disease duration was 10.8± 8.8 SD years. Two-hundred and ninety-one (64%) patients were using immunosuppressives (IS) with or without corticosteroids (CSs) and 72 (16%) of them were under biologic treatment at the time of hospitalization. The mean duration of hospitalization was 12.7±10.7 SD days. The reasons for hospitalization were directly related to BS in 259 patients (57%) and non-related to BS in 191 (42%). Six patients were hospitalized for both BS and non-BS related reasons at the same time. The most common reasons were vascular involvement (n=169, 64%) for BS related reasons and infections (n=64, 32%) for non-BS related reasons (Table 1). Patients hospitalized for BS related causes were younger (35.2±10.6 vs 41.1±11.7, p<0.001), had short mean disease duration (8.5±7.5 vs. 13.6±9.4 years, p<0.001), stayed shorter in the hospital (11.6±8.6 vs 14.0±12.9 days p=0.03) and had less frequent IS+CSs use (59% vs 70%, p=0.02) compared to those with non-BS related hospitalizations. There were no differences between the groups regarding gender distribution (203 M/62 F vs. 143 M/54 F) and use of biologic agents (15% vs 17%). Three patients died during hospitalization. The reasons were malignancy, infection and right heart failure due to pulmonary artery thrombosis and pulmonary hypertension, respectively.

Conclusion: Vascular involvement is the leading cause of hospitalization among BS patients, followed by infections. The predominance of men among

Table 1. Distributions of BS related and non-BS related reasons of hospitalizations

	BS patients hospitalized with BS related reasons (n of pts=195, n of hospitalizations=265)*	BS patients hospitalized with non-BS related reasons (n of pts=170, n of hospitalizations=197)*
Causes of hospitalizations (per hospitalization)		
	Vascular inv. (n=169, 64 %)	Infection (n=64, 32%)
	Pulmonary artery inv. (n=64, 24 %)	Pneumonia (n=17, 8%)
	Deep vein thrombosis (n=39, 15 %)	Tuberculosis (n=8, 4%)
	Budd-Chiari synd. (n=24, 9%)	Urinary tract inf (n=7, 4%)
	Vena cava inf. thrombosis (n=19, 7 %)	Gastroenteritis (n=4, 2%)
	Peripheral artery inv. (n=15, 6 %)	Osteomyelitis (n=3, 2%)
	Vena cava sup. thrombosis (n=14, 5 %)	Septic arthritis (n=3, 2%)
	Aorta inv. (n=14, 5%)	Aspergillosis (n=2, 1%)
	Coronary artery inv. (n=4, 2 %)	Nocardia (n=1, 1%)
	Neurologic inv. (n=50, 19 %)	Salmonella (n=1, 1%)
	Parenchymal inv. (n=37, 14%)	Others (n=18, 9%)
	Dural sinus thrombosis (n=13, 5%)	
		Drug side effects other than infections (n=29, 15 %)
		Interferon (n=10, 5%)
		Azathioprine (n=7, 4%)
		Cyclosporine (n=5, 3%)
		Steroid (n=3, 2%)
		TNF antagonists (n=3, 2%)
		IVIg (n=1, 1%)
	GI inv. (n=18, 7%)	Additional rheumatologic diseases (n=17, 9%)
		Renal disease (n=16, 8 %)
	Joint inv. (n=12, 5%)	Cardiovascular dis. (n=12, 6%)
	Mucocutaneous inv. (n=10, 4%)	Avascular necrosis (n=4, 2%)
	Eye inv. (n=8, 3%)	Malignancy (n=11, 6%)
	Others (n=8, 3%)	Others (n=40, 20%)

*Some patients were hospitalized more than one times and for both BS related and non-BS related reasons at different time and had more than one type of BS related and/or non-BS related reasons.

hospitalized patients underlines the relatively severe course of BS in men. The retrospective design and inclusion of patients who were hospitalized only in the rheumatology unit are limitations of this study.

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POS1352

ANTIINFLAMMATORY, ANTIOXIDANT AND ANTI-ATHEROSCLEROTIC EFFECTS OF A COMBINATION OF NATURAL SUPPLEMENTS ON PATIENTS WITH FMF RELATED AA AMYLOIDOSIS: A NON-RANDOMIZED 24 WEEKS OPEN LABEL INTERVENTIONAL STUDY

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Background: Few studies have focused on Familial Mediterranean Fever (FMF)-related AA amyloidosis and cardiovascular disease event risk. Systemic inflammation stimulates the development and progression of atherosclerosis which is accelerated by vascular endothelial inflammation and enhanced oxidative stress. Excessive reactive oxygen species (ROS) generation has been reported in FMF, which correlated with attack severity. ROS may also be involved in amyloid formation, and in the pathogenesis of progressive renal injury.

Objectives: In this non-randomized, 24 weeks open label interventional study, we aimed to evaluate the effect of a combination of natural products on parameters related to inflammation, endothelial dysfunction and oxidative stress in a cohort of FMF patients with AA amyloidosis.

Methods: Morinda citrifolia (anti-atherosclerotic liquid- AAL), omega-3 (anti-inflammatory capsules- AIC) and extract with Alaskan blueberry (anti-oxidant liquid- AOL) were given to patients with FMF related AA amyloidosis. We included patients with biopsy proven AA amyloidosis, older than 18 years who have normal estimated glomerular filtration rate (eGFR) and proteinuria (>3500mg/day). Flow-mediated dilatation (FMD), asymmetric dimethylarginine (ADMA), hs-CRP, serum PTX3, Carotid intima media thickness (CIMT), malondialdehyde (MDA), Cu/Zn-superoxide dismutase (Cu/Zn-SOD), glutathione peroxidase (GSH-Px) levels were studied in baseline and after 24 weeks.

Results: 67 FMF-related amyloidosis [52 male (77.6%); median recruitment age 36 years (range 21-66)] were enrolled. M694V mutation was the most common mutation found (74%), with 50.7% of the patients in homozygosity. All patients were treated with colchicine, and most of them (83.6%) has been on colchicine treatment at the time of enrollment. Serum ADMA, MDA, PTX3, hsCRP, cholesterol, and proteinuria were significantly decreased compared to baseline, while CuZn-SOD, GSH-Px and FMD levels were significantly increased following AAL, AIC and AOL therapies (Table 1). The change of the inflammatory markers PTX3, and hsCRP were negatively correlated with the change in FMD and positively correlated with the change of proteinuria, ADMA, MDA, cholesterol and CIMT.

Conclusion: 24 weeks of AAL, AIC and AOL combined supplementation was significantly associated with reduction in serum inflammatory markers (PTX3 and hsCRP), improved endothelial functions (FMD, ADMA), and oxidative state (MDA). Our findings highlight the link among the three pathogenetic mechanisms including inflammation, endothelial function and oxidative status in progression of atherosclerosis and renal injury in patients with FMF related AA amyloidosis. Efficient control of these three mechanisms can have long term benefits from the cardiovascular and renal perspective of the patients with AA amyloidosis.

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Table 1. Comparison of clinical and laboratory characteristics at the baseline and after 24 weeks of AAL, AIC and AOL supplementation

	Baseline	24th week	Delta	
	Mean (SD)	Mean (SD)	Mean (SD)	p
Total Cholesterol (mg/dl)	221.2 (60.3)	155.8 (35.4**)	-65.3 (55.5)	<0.001
eGFR (ml/min/1.73 m2)	110.2 (12.8)	104.1 (11.2**)	-6.1 (11.9)	<0.001
Malondialdehyde (MDA) (nmol/ml)	4.2 (1.8)	1.8 (0.5**)	-2.2 (1.8)	<0.001
CuZn-SOD (U/ml)	431.5 (154.7)	538.1 (146.4**)	159.7 (211.8)	<0.001
GSH-Px (U/ml)	47.8 (13.2)	74.1 (20.3**)	26.3 (21.1)	<0.001
ADMA (μmol/l)	4.5 (2.6)	1.3 (0.6**)	-3.2 (2.5)	<0.001
FMD (%)	5.0 (0.7)	6.4 (0.8**)	1.3 (0.9)	<0.001
CIMT (mm)	0.9 (0.2)	0.7 (0.1)	-0.2 (0.2)	<0.001
Proteinuria (mg/24h)	6855.3 (3116.9)	4079.9 (2359.6)	-2775.3 (2874.5)	<0.001
hs-CRP (mg/l)	25.5 (4.4-48.0)	3.0 (1.0-9.1)*	-20.8 (11.2)	<0.001
PTX3 (ng/ml)	13.4 (2.3-67.0)	2.3 (0.4-14.5)*	-17.5 (17.5)	<0.001

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POS1353

SERUM PROTEOMICS REVEALS INSULIN-LIKE GROWTH FACTOR BINDING PROTEINS-1 AS BIOMARKERS FOR IDIOPATHIC MULTICENTRIC CASTLEMAN'S DISEASE

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Background: Castleman's disease (CD) is a lymphoproliferative disorder¹ and presents as two distinct clinical entities: the localized form, unicentric CD (UCD) and the multicentric form, multicentric CD (MCD)². MCD without human herpesvirus-8 (HHV-8) infection is defined idiopathic MCD (iMCD)³ and most MCDs in Japan are iMCDs. TAFRO syndrome is a group of disease that present with T: thrombocytopenia, A: anasarca, F: fever, R: reticulon fibrosis/renal dysfunction, O: organomegaly⁴. iMCD-TAFRO is present in the TAFRO syndrome and it is thought that pathology of lymph node biopsy shows an MCD-like appearance, and some clinical features overlap with MCD⁵. That do not belong to any of the above categories is classified as iMCD-not otherwise specified (iMCD-NOS). No biomarkers stratifying iMCD-NOS and iMCD-TAFRO have been identified, and no biomarkers defining treatment response have been identified for iMCD.

Objectives: We will identify biomarkers that discriminate iMCD-NOS and iMCD-TAFRO or predict the treatment responsiveness.

Methods: We performed a comprehensive analysis of serum proteins using the L-Series Human Antibody Array L-507 on the 4 iMCD-NOS and 2 iMCD-TAFRO patients from which pre- and post-tocilizumab treatment samples were obtained. An analysis by L-507 identified insulin-like growth factor binding proteins-1 (IGFBP-1) as a protein with a high rate of reduction post treatment. Sera from 28 healthy controls, 8 patients with iMCD-NOS, and 6 patients with iMCD-TAFRO were used to validate IGFBP-1 by ELISA. The mean ages of healthy controls, iMCD-NOS, and iMCD-TAFRO used in the validation ELISA were 50, 56, and 47 years, respectively, with no significant differences among the groups. The ratio of male to female was almost 1:1.

Results: The 4 patients who responded well to treatment with tocilizumab all had a high rate of IGFBP-1 reduction by L-507 serum protein arrays. In ELISA, serum IGFBP-1 was significantly higher ($p=0.0016$) before the introduction of treatment in iMCD patients than healthy controls. In addition, serum IGFBP-1 level of iMCD-TAFRO was significantly higher than iMCD-NOS ($p=0.024$). Furthermore, post-treatment serum IGFBP-1 was decreased in many cases.

Conclusion: Serum IGFBP-1 may play a particularly important role in the pathogenesis of iMCD-TAFRO and may be useful in discriminating between iMCD-NOS and iMCD-TAFRO. In the future, we will accumulate more cases, compare it with other inflammatory diseases, and examine the difference in response to treatment.

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POS1354

GENDER DIFFERENCES IN CLINICAL FEATURES AND BURDEN IN PATIENTS WITH FAMILIAL MEDITERRANEAN FEVER: PRELIMINARY REPORT

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Background: Familial Mediterranean fever (FMF) is the most common hereditary auto-inflammatory disease, which is more common in groups in the Mediterranean basin, characterized by recurrent attacks of febrile peritonitis, pleuritis and arthritis.

Objectives: The aim of this study is to investigate the gender differences in clinical and demographic features in patients with familial Mediterranean fever (FMF). **Methods:** Patients with FMF diagnosed according to Tel-Hashomer criteria were included in this multi-center study. Data about age, sex, disease duration, symptom duration, age at diagnosis, comorbid diseases and medications were noted. All patients were screened with Hospital Anxiety and Depression Scale (HADS), Health Assessment Questionnaires (HAQ), Short Form 36 (SF-36). The severity of FMF was assessed by the PRASS scoring system.

Results: Of the 286 patients, 199 (69.6%) were female with the mean age 36,2(SD:12.32) years and 87 (30.4%) were male with the mean age 32,9(SD:12.6) years ($p=0,017$). Age of diagnosis in male patients was lower than in females ($p=0,008$). The most common genetic mutation in both genders was M694V gene mutation. Homozygous M694V positivity was higher in males (31,79% vs 17,4%). More than 90% of patients were receiving colchicine, 10 (3,5%) patients were receiving anakinra and 5 (1,75%) patients were receiving canakinumab. Among the patients regularly taking colchicine, 86.2% were females and 86% were males ($p=0,981$). There were no differences between male and females in terms of clinical findings, frequency and duration of attacks, presence of colchicine resistance, and the presence of amyloidosis ($p>0,05$). ESR was detected higher in female group ($p=0,011$). Headache ($p=0,001$), migraine ($p=0,031$), and concomitant diseases ($p=0,017$) were also more common in females than males. Anxiety and depression scores were higher in females ($p<0,05$). The PRASS activity scores were similar between genders ($p>0,05$). All parameters of SF-36 were higher in male patients, while HAQ score was higher in females ($p<0,05$).

Conclusion: Although clinical findings, disease severity and treatment compliance are similar in both genders, males are diagnosed with FMF earlier than females, but findings such as anxiety, depression, migraine, and headache are more common in female patients.

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Table 1. Demographic and clinical features between female and male FMF patients.

	Female (n:199)	Male (n:87)	P
Demographic features, mean (SD)			
Age	36,2 (12.32)	32,9 (12,6)	0,017
BMI	26,87(5,73)	25,79(5,28)	0,177
Educational level, years	8,77(4,36)	12,08(3,23)	0,000
Age at diagnosis	28 (13,31)	23,7 (13,42)	0,008
Age at onset of disease	19,2 (12,6)	17 (10,6)	0,265
Clinical features, n (%)			
Fever	166 (83,4)	77 (88,5)	0,268
Abdominal pain	180 (90,5)	78 (89,7)	0,835
Chest pain	62 (31,2)	20 (23)	0,160
Erysipelas like erythema	12 (6)	4 (4)	0,628
Arthritis	46 (23,1)	24 (24)	0,419
Arthralgia	102 (51,3)	42 (48,3)	0,643
Myalgia	101 (50,8)	47 (54)	0,611
MEFV mutations, n (%)			
M694V/M694V	24 (12,3)	19 (22)	0,047
M694V heterozygous	38 (19,5)	14 (16,3)	0,523
M694V/any	25 (12,8)	15 (17,4)	0,307
PRASS disease severity, n (%)			
Mild	99(49,7)	46(52,9)	0,813
Moderate	88(44,2)	35(40,2)	
Severe	12(6)	6(6,9)	
ESR, mm/hour, mean (SD)	23,77(16,27)	18,25(18,41)	0,011
HAQ, mean (SD)	0,49 (0,63)	0,16 (0,43)	0,000
HAD, mean (SD)			
Anxiety	8,4 (4,4)	6,7 (3,44)	0,003
Depression	7,1 (4,27)	5,7 (3,81)	0,006
SF-36, mean (SD)			
Physical functioning	63,56 (23,81)	79,93 (19,32)	0,000
Physical role limitation	45,78 (40,95)	61,41 (39,14)	0,003
Emotional role limitation	47,36 (42,04)	66,20 (40,69)	0,020
Energy/fatigue	42,50 (20,64)	53,64 (19,82)	0,000
Emotional well-being	51,61 (18,47)	58,74 (18,30)	0,003
Social functioning	57,06 (23,09)	70,52 (23,82)	0,000
Pain	51,66 (24,05)	65,72 (24,51)	0,000
General health	39,53 (20,01)	52,46 (23,83)	0,000