FRI0501

CARDIOVASCULAR DISEASE RISK ASSESSMENT IN PATIENTS WITH FAMILIAL MEDITERRANEAN FEVER RELATED AMYLOIDOSIS

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Background: FMF is an autosomal recessive disorder. Systemic inflammation in autoinflammatory disorders cause secondary systemic AA amyloidosis, which has been suggested as an important contributing factor to the excess cardiovascular disease (CVD) risk in patients with FMF.

Objectives: Our aim was to investigate the CVD-related clinical outcomes in patients with FMF-related amyloidosis and to define risk factors for CVD events (CVDEs).

Methods: A cross-sectional evaluation with prospective follow-up of consecutive patients with FMF-related amyloidosis or other non-diabetic primary glomerulonephropathy (PGN) was performed. Patients were followed for CVDEs. Flow-mediated dilatation (FMD), FGF-23 levels, serum lipid levels, hsCRP, BMI and homeostasis model assessment (HOMA) were assessed. A Cox regression analysis was performed to evaluate the probability of CVDEs associated with each risk factor.

Results: There were 107 patients in FMF-related amyloidosis group and 126 patients with PGN group. Forty-seven CVDEs were registered during the 4.2-years follow up; all 28 patients in the FMF-related amyloidosis versus 14/19 patients with PGN group who developed CVDEs before 40 years of age ($P=0.002$) (Figure 1). CVD mortality was 2.8 times higher (95% CI 1.02-7.76, $p=0.03$) in patients with FMF-related amyloidosis ($n=12$) than PGN ($n=5$). Mortality due to CVD was higher in patients less than 40 years old with amyloidosis than PGN (12/107 and 3/126 respectively, $RR=4.71$, 95% CI 1.36-16.25, $p=0.006$). Patients with CVDEs had higher levels of proteinuria, hsCRP and FGF23, and lower FMD compared to patients without CVDEs. Across both groups, FGF23 and FMD levels were independently associated with the risk of CVDEs (Table 1).

Conclusion: Patients with FMF-related amyloidosis are at increased risk of CVDEs with early mortality age. These patients should be closely monitored and

Figure 1. Comparison of cardiovascular disease survival between patients with FMF-related amyloidosis or primary glomerulopathy.

Table 1. Multivariate analysis of factors associated with the risk of suffering a cardiovascular event

		B	HR	95.0% CI for Exp(B)		p
Variables				Lower	Upper	
All Groups	FGF23	.033	1.034	1.017	1.051	<.001
	FMD	-.946	.388	.262	.575	<.001
Primary glomerulopathy	FGF23	.050	1.051	1.019	1.084	.002
	FMD	-.651	.522	.300	.908	.021
Amyloidosis	FGF23	.034	1.035	1.012	1.058	.003
	FMD	-1.531	.216	.109	.430	<.001
	hsCRP	-.040	.961	.915	1.009	.108

FMD, Flow-mediated dilatation; hsCRP, high sensitivity C reactive protein; CI, Confidence interval

if inflammation is poorly controlled with colchicine, biological agents must be added to treatment even if they develop amyloidosis. We also found that hsCRP, FGF 23 and FMD levels were the strongest predictors of CVD risk in patients with FMF. These biomarkers can stratify risk of early CVD in patients with FMF-related amyloidosis.

References:

- [1] Yilmaz, M.I., et al., *Endothelial function in patients with familial Mediterranean fever-related amyloidosis and association with cardiovascular events*. Rheumatology (Oxford), 2014, **53**(11): p. 2002-8.

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FRI0502

SEASONAL CLUSTERING OF ACUTE SARCOIDOSIS IN GERMANY AND ASSOCIATIONS WITH AIR POLLUTION

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Background: Sarcoidosis is a multisystemic granulomatous disorder of unknown origin. The central role of macrophages and granuloma formation, the predominant involvement of lung and skin, and certain risk populations (e.g. firefighters^{1,2}) might be explained by causative airborne antigen(s)³. Whether air pollution is involved in pathogenesis and seasonal clustering of sarcoidosis is uncertain.

Objectives: This study has been set to analyze seasonal clustering of acute sarcoidosis and associations to air pollution.

Methods: Patients with acute sarcoidosis, defined by bilateral lymphadenopathy, ankle swelling, and/or erythema nodosum plus physician's diagnosis, were included in this retrospective study. Disease onset (seasonal clustering) and associations to air pollution (particulate matter (PM₁₀) and nitrogen dioxide (NO₂)) were analyzed. Google Trends queries were conducted to address seasonal clustering on a global scale.

Results: A total of 185 patients with acute sarcoidosis were included; 48.7 % of the enrolled patients were female and Löfgren triad was complete in 73.5 % of patients. Acute sarcoidosis clustered from December to June in West Germany ($p<0.005$, Kendall $\tau=-0.68$), peaking in January (17.8 % of cases) and in the first third of the year (54.5 %). Mean PM₁₀ values clustered from December to April with values between 15 and 40 $\mu\text{g}/\text{m}^3$. NO₂ levels were measured highest from November to March (45 $\mu\text{g}/\text{m}^3$) and lowest between April and August (25 $\mu\text{g}/\text{m}^3$). Elevated air pollution markers (PM₁₀ and NO₂) were associated with higher monthly incidence rates of acute sarcoidosis (Cross correlation coefficient ranging between 0.7 -0.8). Google Trends analysis yielded seasonal clustering ($p<0.005$, Kendall $\tau = -0.64$) in winter and spring months on the northern hemisphere.

Conclusion: In Central Europe acute sarcoidosis peaks in winter and spring months (December until March) shortly after PM₁₀ and NO₂ maxima are reached. Whether components of particulate matter might be involved in the pathogenesis of sarcoidosis has to be elucidated by further studies.

References:

- [1] Prezant DJ, Dhala A, Goldstein A, Janus D, Ortiz F, Aldrich TK, et al. The incidence, prevalence, and severity of sarcoidosis in New York City firefighters. Chest. 1999;
- [2] Webber MP, Yip J, Zeig-Owens R, Moir W, Ungprasert P, Crowson CS, et al. Post-9/11 sarcoidosis in WTC-exposed firefighters and emergency medical service workers. Respir Med [Internet]. 2017;132:232-7.
- [3] Newman LS, Rose CS, Bresnitz EA, Rossman MD, Barnard J, Frederick M, et al. A case control etiologic study of sarcoidosis: Environmental and occupational risk factors. Am J Respir Crit Care Med. 2004;170(12): 1324-30.

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FRI0503

VALIDATION OF THE 2019 ACR/EULAR CLASSIFICATION CRITERIA FOR IGG4-RELATED DISEASE IN A JAPANESE KIDNEY DISEASE COHORT: A MULTI-CENTER RETROSPECTIVE STUDY BY THE IGG4-RELATED KIDNEY DISEASE (IGG4-RKD) WORKING GROUP OF THE JAPANESE SOCIETY OF NEPHROLOGY

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Background: The 2019 ACR/EULAR classification criteria for IgG4-RD have recently been published¹. In the criteria, patients with an inclusion criteria score of >20 without exclusion criteria are classified as having IgG4-RD.

Objectives: To validate the 2019 ACR/EULAR classification criteria for IgG4-RD in a Japanese kidney disease cohort.

Methods: The study involved Japanese patients diagnosed as having kidney disease between April 2012 and May 2019, for whom sufficient clinical information and data on serum IgG4 values and/or immunohistological staining for IgG4 in renal biopsy samples were known. These patients were classified as having IgG4-RKD or non-IgG4-RKD (mimickers) based on the 2019 ACR/EULAR classification criteria for IgG4-RD, and the results were evaluated by expert opinion.

Results: Among 105 included patients, the expert panel diagnosed 55 as having true IgG4-RKD and 50 as mimickers. The final diagnoses among the mimickers were vasculitis (n=11), idiopathic tubulointerstitial nephritis (TIN) (n=5), drug-induced TIN (n=5), Sjögren's syndrome (n=4) and others. Among the 55 true IgG4-RKD patients, 4 had exclusion criteria, and 50 of the remaining 51 had an inclusion criteria score of ≥20 points (sensitivity 90.9%). On the other hand, 49 of the 50 mimickers were classified as having non-IgG4-RKD (specificity 98.0%) (Table 1).

Table 1. General characteristics and prevalence of individual items of true IgG4-RKD and non-IgG4-RKD (mimicker)

	IgG4-RKD (true IgG4-RKD) (n=55)	Non-IgG4-RKD (mimicker) (n=50)	P
Age at diagnosis, mean ±SD (years)	69.9 ± 9.4	56.7 ± 17.4	<0.001
Male (%)	76.4	44	0.001
Elevated serum IgG4	54/55 (98.2%)	18/50 (36.0%)	<0.001
Serum IgG4 (mg/dl), mean±SD	1028 ± 796	226 ± 261	<0.001
Dense IgG4+Plasma cells (>10/hpf) in the kidney biopsy	48/51 (94.1%)	13/40 (32.5%)	<0.001
Storiform fibrosis in the kidney biopsy	28/51 (54.9%)	3/50 (6%)	<0.001
Hypocomplementemia	39/55 (70.1%)	7/42 (16.7%)	<0.001
Renal pelvis thickening/ soft tissue	5/55 (9%)	1/50 (2%)	0.20
Bilateral renal cortex low-density areas	29/55 (52.7%)	7/50 (14.0%)	<0.001
Exclusion criteria present	4/55 (7.3%)	22/50 (44%)	<0.001
Total inclusion criteria points >20 without exclusion criteria	50/55 (90.9%)	1/50 (2%)	<0.001

Conclusion: The 2019 ACR/EULAR classification criteria for IgG4-RD showed good agreement with expert classification in this Japanese kidney disease cohort.

References:

- [1] Wallace ZS, et al. The 2019 American College of Rheumatology/European League Against Rheumatism classification criteria for IgG4-related disease. *Ann Rheum Dis*. 79:77-87, 2020

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FRI0504

TOCILIZUMAB IN GRAVES' ORBITOPATHY. MULTICENTER STUDY OF 48 PATIENTS.

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Background: Tocilizumab (TCZ) has shown promising results in the treatment of inflammatory ocular disease, especially in uveitis (1-3). Graves orbitopathy (GO) is the most common complication of Graves' disease (GD). Conventional immunosuppressive drugs are not always effective or well tolerated. TCZ may be useful in the treatment of GO.

Objectives: To assess the efficacy of TCZ in corticoid-resistant GO.

Methods: Multicenter open study of corticoid-resistant GO. We measured clinical activity using the clinical activity score (CAS). CAS evaluates 10 different ocular items, ranging from 0 (no symptoms) to 10. We defined remission as the presence of CAS ≤ 3.

Results: We studied 48 (95 eyes) patients (TABLE). Besides oral corticosteroids, they had received iv Methylprednisolone (n=43), methimazole (n=20), selenium (n=11) or radioactive iodine (n=5). According to the classification of severity (EUGOGO group), before of TCZ onset our patients had severe (n=19) or moderate (n=29) disease. TCZ was used in monotherapy (n=45) or combined with methotrexate (n=2) or azathioprine (n=1) at a dose of 8 mg/kg/iv/4 weeks (n=43) or 162 mg/sc/week (n=5). TCZ yielded rapid and maintained improvement and most patients achieved remission (FIGURE).

After a mean follow-up of 16.1±2.1 months, most patients experienced ocular improvement, with TCZ withdrawal in 29 cases due to remission (n=25) or inefficacy (n=4). Only 5 relevant adverse events were observed (neutropenia, external otitis, otitis media, costal osteitis and gingival hyperplasia). None of these events resulted in discontinuation of the treatment.

Conclusion: TCZ appears to be an effective and safe treatment in corticoid-resistant GO.

TABLE:

Number of patients/eyes affected, n/n	48/96
Age, mean (SD), years	50.96 (11.78)
Sex, men/women, n/n (%)	10/38 (20.8 / 79.2)
Regimen of TCZ therapy	
Monotherapy/combined treatment, n (%)	45/3 (93.8/6.2)
• AZA	1 (2.1)
• MTX	2 (4.2)
TCZ dosage, n (%)	
• 8 mg/kg/iv/4 weeks	43 (89.6)
• 162 mg/sc/week	5 (10.4)
Follow-up on TCZ therapy, mean (SD), months	16.05±2.06
• Remission, n (%)	72 (75.8)
• Discontinuation treatment, n (%)	29 (60.4)
• Remission	25 (86.2)
• Inefficacy	4 (13.8)
• Side effects	0

FIGURE.

References:

- [1] Santos-Gómez M, et al. *Clin Exp Rheumatol* 2016; 34 Suppl 102(6):34-40
- [2] Calvo-Río V, et al. *Clin Exp Rheumatol*. 2014; 32 (4 Suppl 84): S54-7
- [3] Vegas-Revena N et al. *Am J Ophthalmol*. 2019 Apr; 200:85-94.