THU0590

COMPARISON OF FMF PATIENTS WITH AGE OF ONSET BEFORE 20 VERSUS 40 YEARS AND OVER

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Background: Familial Mediterranean fever (FMF) is a disease with an onset before 20 years of age in 90% of the patients. However late onset FMF defined as age of onset over 40 years is being recognised more frequently.

Objectives: To better define patients with FMF who had their first attack before age 40 and compare them with early onset patient group in Turkish population

Methods: The files of 2180 FMF patients followed in a single center between 2008-2017 who have fulfilled Tel-Hashomer criteria, were reviewed with regard to age of onset 40 years and over (index patients, Group 1). For control purposes files before and after the index patients were browsed and first patients with an onset before age 20 years (Group 2) were included. The demographic, clinical and genetic characteristics are compared between these 2 subgroups.

Results: Patients with an onset after 40 years consisted 2.7% of our FMF population. 50 of the 59 patients with an onset 40 years or over were re-evaluated and compared with early onset group consisting of 100 patients (Table 1). The delay in diagnosis, and disease duration were significantly longer and number of patients with M694V homozygosity and M694V allele frequency were significantly more frequent among group 2. In general, phenotypes of both onset groups were similar, the only significant differences being the frequency of fever and myositis which were less common among group 1. Also response to colchicine was more pronounced in group 1. One other interesting observation was the low incidence of amyloidosis in a group with such a significant delay in diagnosis and thus treatment.

Table 1. Demographic, clinical and genetic features of the study groups

	≥40 years n=50	≤20 years n= 100	p
Sex (F:M); present age (mean±SD) (yr)	32:18; 57.2±7.9	62:38; 31.8±9.1	NS;
Mean age at onset,(mean±sd) (yr)	45.6±5.2	8.7±4.8	<0.001
Mean age at diagnosis (mean ±sd) (yr)	50.4±7.3	19.1±11.2	<0.001
Delay in diagnosis (mean ±sd) (yr)	4.8±5.5	10.4±11.8	<0.001
Mean disease duration (mean ±sd) (yr)	11.5±6.4	23.1±10.8	<0.001
Abdominal pain, n (%)	44(88)	89(89.0)	NS
Chest pain, n (%)	7(14.0)	27 (27.0)	NS
Fever, n (%)	30(60.0)	81(81.0)	0.005
Arthritis, n (%)	12(24.0)	33(33.0)	0.25
Myalgia, n (%)	1(2.0)	12(12.0)	0.04
Amyloidosis, n (%)	1(2.0)	3(3.0)	NS
Positive family history, n (%)	33(66.7)	62 (65.2)	NS
Response to colchicine, n (%)	37(82.2)	93 (94.8)	0.014
M694VHomozygous, n (%)	2(4.5)	23(25.8)	0.003
N of M694V alleles	24(48)	82 (82)	0.014
No mutation, n (%)	3(6.8)	2(2.2)	NS

Conclusion: FMF should be included among the differential diagnosis of patients over 40 years of age with recurrent autoinflammatory manifestations. Less than 3% of FMF patients experience their first attacks after 40 years of age. The frequency of M694V is significantly less in the late onset group, pointing out a milder disease.

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THU0591

SALIVARY GLAND INVOLVEMENT DISPARITIES IN CLINICAL AND LABORATORY CHARACTERISTICS OF IGG4-RELATED DISEASE: A RETROSPECTIVE STUDY OF 428 PATIENTS

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Background: IgG4 related disease (IgG4-RD) is recently recognized as a fibro-inflammatory condition featured by tumefactive lesions in multiple organs, among which salivary gland is one of the most commonly involved sites. Some previous studies have suggested that salivary gland involved IgG4-RD (IgG4-RD SG+) patients may present different features compared to IgG4-RD patients without salivary gland lesions (IgG4-RD SG-), however, only dozens of patients were examined and the comparison has not been studied in detail.

Objectives: We undertook this study to compare detailed demographic, clinical and laboratory characteristics of IgG4-RD patients with salivary gland lesion (IgG4-RD SG+) and salivary gland free IgG4-RD (IgG4-RD SG-) in a large cohort.

Methods: We carried out a retrospective review of the medical records of 428 cases of IgG4-RD diagnosed at Peking University People's hospital between March 2006 and May 2018.

Results: Among 428 patients, 249 had salivary gland affected. IgG4-RD SG+ patients showed younger age at disease onset and diagnosis, and a longer interval between symptom onset and diagnosis. IgG4-RD SG+ group involved more female patients, and allergic diseases were more common in this group. In terms of organ involvement, IgG4-RD SG+ group were more frequently presented with lacrimal gland involvement, while lymph node, retroperitoneal fibrosis, pancreas, biliary system, kidney, and aorta were more prominent in IgG4-RD SG- group. In addition, the serum IgG4 levels, IgG4/IgG ratio and IgE level were significantly higher in IgG4-RD SG+ patients. Patients with eosinophilia were more common in IgG4-RD SG+ group, while elevated ESR, CRP, and positive ANA were more common in IgG4-RD SG- group.

Conclusion: We have revealed demographic, clinical and laboratory differences between IgG4-RD SG+ and SG- patients, which indicated potential differences in pathogenesis and important implications for the diagnosis and management of these two phenotypes.

REFERENCES:

- [1] Kamisawa T, Zen Y, Pillai S, Stone JH. IgG4-related disease. *Lancet*. 2015;385(9976):1460-71.
- [2] Moriyama M, Ohta M, Furukawa S, Mikami Y, Tanaka A, Maehara T, et al. The diagnostic utility of labial salivary gland biopsy in IgG4-related disease. *Mod Rheumatol*. 2016;26(5):725-9.
- [3] Higgs BW, Liu Y, Guo J, Sebastian Y, Morehouse C, Zhu W, et al. High-throughput RNA sequencing reveals distinct gene signatures in active IgG4-related disease. *Sci Rep*. 2017;7(1):17567.
- [4] Inoue D, Yoshida K, Yoneda N, Ozaki K, Matsubara T, Nagai K, et al. IgG4-related disease: dataset of 235 consecutive patients. *Medicine (Baltimore)*. 2015;94(15):e680.

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THU0592

PREDICTORS OF RELAPSE OF IGG4-RELATED DISEASE AFTER INDUCTION THERAPY: A RETROSPECTIVE STUDY

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Background: IgG4-related disease (IgG4-RD) is a systemic fibroinflammatory condition characterized by tumefactive lesions and, often but not always, elevated serum IgG4 levels [1]. Glucocorticoids (GC) are usually used as induction therapy for IgG4-RD. However, relapse often occurs following GC tapering, and predictors of relapse remain unclear.

Objectives: To identify predictors of relapse of IgG4-RD after induction therapy.

Methods: We retrospectively reviewed 57 patients diagnosed with IgG4-RD and treated with GC in our hospital between January 2004 and November 2018. Clinical features at baseline, including organ involvement and blood markers (total hemolytic complement [CH50], its fractions [C3 and C4], IgG4, IgG, IgE, anti-nuclear antibody, rheumatoid factor, C-reactive protein, soluble interleukin-2 receptor, eosinophils), were collected. We divided patients into 2 groups on the basis of clinical features and examined whether they relapsed. In this study, hypocomplementemia was defined as decreased serum C3, C4, or CH50 less than the lower limit of normal. A relapse was defined as any new or worsened state of disease activity that required an escalation in treatment (immunosuppressants and/or GC). The follow-up period was defined as 182 days.

Results: Forty-three men and 14 women (mean age 68.1 ± 10.9 years) were included. Both serum IgG4 and IgG were measured at baseline in all patients (mean IgG4 798.8 ± 873.1 mg/dL and mean IgG 2874.0 ± 1934.1 mg/dL, respectively). All of the serum C3, C4, and CH50 were measured at baseline in 34/57 patients (mean C3 75.7 ± 33.3 mg/dL; mean C4 14.8 ± 11.5 mg/dL; and mean CH50 37.0 ± 23.1 U/mL). Fifteen patients had at least one episode of hypocomplementemia, and 19 patients did not. Most patients had multiple organ lesions. The details of dominant lesions were as follows: Dacryoadenitis and/or sialadenitis (Mikulicz disease), 36/57 patients (63.2%); biliary or pancreatic lesion, 29/57 (50.1%); retroperitoneal fibrosis, 22/57 (38.6%); and renal lesion 16/57 (28.1%). All patients were given prednisolone and gradually reduced (mean induction dose 31.7 ± 9.8 mg/day). No patients received immunosuppressant as induction therapy. During the follow-up period, 6 patients relapsed, and the dose of prednisolone was increased immediately. Relapsed lesions were as follows: Mikulicz disease, 3/6 patients (50.0%); biliary or pancreatic lesion, 1/6 (16.7%); retroperitoneal fibrosis 1/6 (16.7%); and pulmonary lesion 1/6 (16.7%). Patients with hypocomplementemia had significantly shorter relapse-free survival than those without ($p=0.039$, Figure 1). Patients with decreased serum C4 or CH50 (less than the lower limit of normal) also had significantly shorter relapse-free survival than those without, but those with decreased serum C3 did not. Such a tendency was not seen in other blood markers (IgG4, IgG, IgE, anti-nuclear antibody, rheumatoid factor, C-reactive protein, soluble interleukin-2 receptor, eosinophils).

Conclusion: Hypocomplementemia at baseline in patients with decreased serum C4 or CH50 may predict relapse of IgG4-RD after prednisolone therapy.

REFERENCES:

- [1] Stone JH, et al. N Engl J Med 2012; 366: 539-51.

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THU0593

CLINICAL AND GENETIC FEATURES OF CHINESE ADULT PATIENTS WITH TUMOR NECROSIS FACTOR RECEPTOR-ASSOCIATED PERIODIC SYNDROME

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Background: Tumor Necrosis Factor Receptor-Associated Periodic Syndrome (TRAPS) is an autosomal dominant autoinflammatory disease, associated with the mutation of tumor necrosis receptor superfamily member 1A (*TNFRSF1A*) gene,

located on chromosome12p13. TRAPS is usually diagnosed during pediatric age. However, adult-onset disease or diagnosis during adulthood has been occasionally described. Moreover, TRAPS has been hardly reported in the Chinese population. Herein, we aimed to characterize the clinical and genetic features of Chinese adult patients with TRAPS.

Objectives: Adult patients (≥ 16 years) suspected monogenic autoinflammatory diseases during the period April 2015 to October 2018, at the adult autoinflammatory disease center, Department of Rheumatology, Peking Union Medical College Hospital (PUMCH).

Methods: Clinical data were evaluated. Gene sequencing was performed in each patient to support the diagnosis and exclude other monogenic autoinflammatory diseases. Finally we compared the data with those from Japan and Europe.

Results: During the study period, 8 patients with TRAPS were diagnosed and follow-up. The ratio of male to female was 3: 1. The median age of disease onset was 4 (0.5–38.5), and adult-onset was observed in 2 (25%) patients. The median time of diagnosis delay was 17.8 (1.5–50.5) years. There were seven Chinese Han and one Manchu patients. One patient had a family history of TRAPS. The most frequent symptom was fever (8, 100%). The attacks of 5 (62.5%) patients lasted more than 1 week, and the intervals of 7 (87.5%) patients were longer than 2 weeks. Skin involvement occurred in 6 (75%) patients, with maculopapular mentioned in 6 and erythema annulare presented in 3. Four (50%) patients had arthralgia, while one had polyarthritis. 4 (50%) patients complained respectively of myalgia or headache. 4 (50%) patients experienced abdominal pain and one (12.5%) had vomiting. One (12.5%) patient had periorbital edema, while 3 (37.5%) had conjunctivitis. Up to 5 (62.5%) patients got nonspecific pharyngitis. No patient suffered from chest pain or amyloidosis. Eight gene variants were detected in *TNFRSF1A* gene. Heterozygous gene variants were found in 7 Chinese Han patients, and homozygous (c.769-23, T>C) happened to the Manchu patient. The variants included C58 (exon 2), G65E (exon 3), F89L (exon 3), C99G (exon 3), V202G (exon 6), c.769-23T>C (IVS8), S290I (exon 9) and m.1735A>G (non-coding region). NSAIDs were given to 2 patients, glucocorticoid or immunosuppressive agents given to 3 patients respectively, and etanercept to 5 patients. A complete response was found in all the 5 patients received etanercept. The effectiveness of other drugs were 50% in NSAIDs, 66.7% in glucocorticoid and immunosuppressive agents.

Conclusion: This is the first and largest case series of TRAPS in Chinese adult patients. It highlights the importance of screening *TNFRSF1A* gene in patients with unexplained periodic fever syndrome. Four novel *TNFRSF1A* variants, S290I, F89L, V202G and m.1735A G in non-coding region, have been identified. The atypical clinical manifestations of our patients compared to those from Europe might be related to their low-penetrance *TNFRSF1A* variants. Further studies are needed to explore the more accurate phenotypes and genotypes of the Chinese patients with TRAPS.

Figure legends: clinical manifestations of Chinese adult patients with TRAPS. A. Periorbital edema; B. erythema annulare; C. Maculopapular rash; D. Radiology showed intestinal obstruction.