THU0565 MACROPHAGE ACTIVATION SYNDROME IN ADULTS WITH INFLAMMATORY RHEUMATIC DISEASES

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Background: Macrophage activation syndrome (MAS) is a rare hyperinflammatory condition characterised by macrophage activation and infiltration resulting in a multi organ damage. MAS is considered to be a type of secondary hemophagocytic lymphohistiocytosis. It is a life threatening complication of various autoimmune or autoinflammatory rheumatic diseases, particularly systemic juvenile idiopathic arthritis (sJIA). Clinical manifestations include hepatosplenomegaly, increase of liver function tests, pancytopeny, neurolological manifestations etc. High doses of glucocorticosteroids (GC), cyclosporine A (CyA) and etoposide are a treatments of choice. In refractory cases biologicals may be an option, too.
Objectives: To point out this very rare but severe complication may occur also in adult patients with rheumatic diseases.
Methods: We report 4 successfully treated cases of adult MAS in rheumatic patients seen in our clinic during the years 2009 – 2016. A review of the literature regarding the efficacy of biologics in MAS treatment is also presented.
Results: We have observed four patients with MAS, two with adult onset Still disease (AOSD), one with rheumatoid arthritis (RA) and one with sJIA. All of the patients were young (20 -33 years, mean age 27,0±5,61 years) with the duration of the primary disease ranging from 9 months to 11 years (mean 4,18±4,01 years). Three patients were in remission of the primary diseases prior to MAS manifestation, only in the last and most severe patient (AOSD) the activity of the underlying disease was not controlled. A demographic and clinical characteristic of the patients is summarized in the table.
All 4 patients were successfully treated, one with high doses of glucocorticosteroids (GC), two with combination GC plus CyA. The last and most severe one had MAS refractory to the combination GC + CyA and must have been added biological therapy (tocilizumab). We reviewed also another cases of MAS treated with biologics which have been published.
Conclusions: Our cases illustrate that MAS may develop also in adult patient with various rheumatic diseases (JIA, AOSD, RA) despite the low activity or remission. It occurs particularly in younger subjects. As the MAS symptoms may overlap with the symptoms of the primary disease (JIA, AODS) the diagnosis may be difficult. MAS must be suspected in inflammatory rheumatic diseases patients with sudden increase of CRP, extreme increase of ferritin, liver function tests and decrease of platelets. An immediate treatment with GC, CyA and etoposide is essential; biologicals (anakinra, canakinumab or tocilizumab) may be benefitial in refractory cases.
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THU0566 CLINICAL AND GENETIC PHENOTYPES OF CHINESE PATIENTS WITH ADULT AUTOINFLAMMATORY DISEASES: REPORT FROM AN ADULT REFERENCE CENTER

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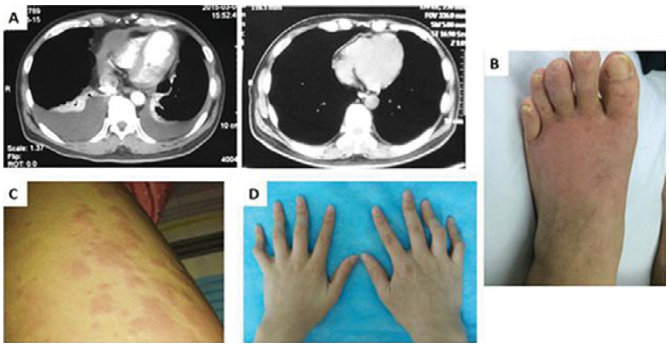
Background: Autoinflammatory diseases (AUID) is a group of disorders characterized by dysfunction of innate immunity which caused by gene mutations leading to coded proteins changes, finally causing uncontrolled systemic inflammation. AUID are usually diagnosed during pediatric age. However, adult-onset disease or diagnosis during adulthood has been occasionally described. Moreover, AUID have been hardly reported in the Chinese population.
Objectives: We aimed to characterize the clinical and genetic phenotypes of Chinese adult patients with AUID.
Methods: We prospectively evaluated clinical and genetic features of adult patients (≥16 years) suspected monogenic AUID in the period April 2015 to May 2016, at the adult AUID center, Department of Rheumatology, Peking Union Medical College Hospital. The definite diagnosis of each disease was deemed to be present if both clinical phenotypes and genetic confirmation were met.
Results: During the study period, a total of 37 adult patients with clinical phenotypes suspicious of monogenic AUID requested for a genetic study. A final diagnosis of monogenic AUID was achieved in 16 patients (43.2% of patients tested). Two additional patients were diagnosed with periodic fever, aphthous stomatitis, pharyngitis and adenitis (PFAPA) syndrome. Finally, a total of 18 patients with AUID were diagnosed and follow-up in our center, including 7 (38.9%) familial Mediterranean fever (FMF), 2 (11.1%) tumor necrosis factor-receptor associated periodic syndrome (TRAPS), 3 (16.7%) cryopyrin-associated periodic syndrome (CAPS), 3 (16.7%) NLRP12-autoinflammtory disease (NLRP12-AD), 1 (5.6%) Blau syndrome (BS), and 2 (11.1%) PFAPA. Disease onset during adulthood was observed in 15 (83.3%) patients, and the final diagnosis was delayed with a mean time of 10 years. Adult AUID patients usually carried low-penetrance mutations and gene variants were presented as heterozygosis or compound heterozygosis.



Conclusions: Adult AUID is not uncommon. FMF, CAPS, and NLRP12-AD are relatively common monogenic AUID in Chinese adult patients. Adult-onset AUID may be related to the presence of low-penetrance mutations, being characterized by nonspecific, incomplete or atypical disease patterns, leading to a delay of diagnosis. The interpretation of gene analysis in adult suspected AUID should be performed with caution, and if possible, should be referred to expert physicians in the field in adult AUID center.
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THU0567 RAPID IMPROVEMENT WITH TOCILIZUMAB IN REFRACTORY AND SEVERE UVEITIC CYSTOID MACULAR EDEMA

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Background: In uveitis, remission-inducing therapy with even more vigor than does rheumatology is mandatory. Since the eye is so much less forgiving of chronic inflammation than is the joint, with profound life-altering consequences. Cystoid macular edema (CME) is the leading cause of blindness in uveitis.
Objectives: To evaluate the rapid efficacy of Tocilizumab (TCZ) in refractory CME.
Methods: Multicentre study of 25 patients with CME due to non-infectious uveitis who had inadequate response to traditional treatment with corticosteroids and at least one conventional immunosuppressive drug including in most cases biological therapy (n=22). CME was defined as OCT >300 μm.
The outcome variables were the degree of inflammation, visual acuity, macular thickness. The results are expressed as mean±SD for normally distributed variables, or as median [IQR] when are not. Comparison of continuous variables was performed using the Wilcoxon test.
Results: 25 patients (17 women/8 men), mean age 33.6±18.9 years were studied. The associated diseases were: juvenile idiopathic arthritis (9), Behçet's (7), Birdshot (4), idiopathic (4), sarcoidosis (1). The ocular pattern was: panuveitis (9), anterior uveitis (7), posterior uveitis (5) and intermediate uveitis (4). Most patients had bilateral involvement (24). Prior to TCZ they received: intraocular corticosteroids (22), iv. methylprednisolone (7), methotrexate (MTX) (19), cyclosporine A (CSA) (17), mycophenolate (4), azathioprine (2), leflunomide (2), cyclophosphamide (1), sulfasalazine (1), acetazolamide (1) and thalidomide (1). The biological used before TCZ were infliximab (8), adalimumab (19),

Abstract THU0565 – Table 1

Patient	Age (years)	Primary disease			Clinical manifestations of MAS	Treatment
		Dg.	Duration	Treatment prior to MAS		
L.H., female	23	JIA	11 years	MTX	hepatosplenomegaly, increase of ALT, AST, pancytopenia, serositis	GC high doses (i.v. pulses), cyclosporine
P.V., male	20	RA	2 years	MTX, SAS	fever, pancytopenia, hepatosplenomegaly, increase of ALT, AST, pericarditis	GC high doses (oral), cyclosporine
P.D., male	32	AODS	3 years	MTX	fever, hepatosplenomegaly, increase of ALT, AST, pancytopenia,	GC high doses (oral)
V.N., female	33	AODS	9 months	MP, AZA	fever, pancytopenia, hepatosplenomegaly, increase of ALT, AST, alveolar hemorrhage	GC high doses (i.v. pulses), cyclosporine, tocilizumab

	Baseline	1st week	2nd week	1st month
OCT (microns), mean±SD	415.7±177.15	413.3±162.9*	388.06±158.1*	330.8±104.2*
Visual acuity, mean±SD	0.39±0.31	0.4±0.31	0.45±0.3*	0.51±0.3*
Anterior chamber cells, median [IQR]	1 [0–1]*	0.5 [0–1]*	0 [0–1]*	0 [0–0]*
Vitritis, median [IQR]	1 [0–2]	1 [0–1.5]	0 [0–1]*	0 [0–0.5]*

*$p<0.05$ compared with basal data.

etanercept (2), golimumab (2), rituximab (2), abatacept (3), anakinra (1) and daclizumab (1).

TCZ administration schedule was 8 mg/kg/4 weeks iv. (n=23), every 2 weeks (1) and subcutaneously 162 mg/2 weeks (1). TCZ was used in monotherapy (13) or combined with conventional immunosuppressive drugs (12). Most of intraocular inflammation parameters showed a rapid improvement after TCZ onset (Table), with corticosteroid-sparing effect (15.9±13.6 to 8.5±5.17 mg; p=0.001). Remission was achieved in 8 patients and improvement in 17. After one month of therapy, no side effects were observed.

Conclusions: TCZ seems a rapid effective treatment in refractory uveitic CME.

Disclosure of Interest: None declared

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THU0568 PREVALENCE AND AUTOIMMUNE RHEUMATIC DISEASE IN PATIENTS WITH AUTOIMMUNE/INFLAMMATORY SYNDROME INDUCED BY ADJUVANTS ASSOCIATED TO SILICONE BREAST IMPLANT

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Background: Autoimmune/inflammatory syndrome induced by adjuvants (ASIA) has been associated with previous exposure to various agents such as silicone implants, which elicit chronic stimulation of the immune system against the prosthetic material and clinical manifestation of autoimmune disease. This is particularly the case in genetically susceptible hosts.

Objectives: The aim is to describe de prevalence, family background and main autoimmune rheumatic disease (ARD) associated to silicone breast implant (SBI).

Methods:

We study a cohort of 150 patients with diagnosis of ASIA associated injection of mineral oil and silicone breast implant (SBI) in a tertiary Hospital, from 2011 to 2016. All patients were evaluated for the fulfilment of ASIA criteria. We only included patients with ASIA criteria associated with SBI plus criteria for an autoimmune rheumatic disease according to The American College of Rheumatology or EULAR. We excluded patient with ASIA and without ARD.

Results: There were 17 women patients with mean age 42.4±15.3 years, mean disease duration of disease 8±3. The clinical manifestation post SBI appeared 8±2 years later.

The ARD were systemic sclerosis (SSc) 5, systemic lupus erythematosus (SLE) 3, rheumatoid arthritis (AR) 3, overlap syndrome 2 (SSc plus SS and SLE plus SSc, Sjogren syndrome 1, Takayasu arteritis 1, Still disease 1, antiphospholipid syndrome 1, and 3 patients also had secondary fibromyalgia. Five Patients had more than 2 autoantibodies, 4 patients had relatives with an ARD. All patients are being treated according to the ARD (steroids plus immunosuppressive 8 patients, immunosuppressive 7, and only steroids 2), in 4 patients the prosthesis were withdrawn with improvement of clinical manifestations.

Conclusions: We found a prevalence of ASIA associated to SBI of 11%. The main ARD were SSc, SLE and RA. In these cases of ASIA associated with SBI some had genetic predisposition to ARD. The use of SBI is not recommended in women who have a family history of ARD.

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THU0569 TREATMENTS OF UVEITIS IN A REFERRAL MULTIDISCIPLINARY UNIT IN NORTHERN SPAIN

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Background: Intraocular inflammation is one of the leading causes of visual impairment and blindness. Early and appropiate treatment is mandatory for avoiding complications.

Objectives: To describe the treatments prescribed in a cohort of patients with uveitis in a referral multidisciplinary unit from northern Spain.

Methods: Retrospective analysis of clinical records of patients evaluated in the Uveitis Multidisciplinary Unit of the Complejo Hospitalario of Navarra since January 2010 until March 2015. We analyzed the demographic characteristics and treatments received in the following 3 months after first visit.

Results: We identified 500 patients, 50% women with a mean age of 47.9 +/- 16.4 years. The most frequent type of uveitis was anterior uveitis (65,4%), followed by posterior uveitis (17,6%), panuveitis (15,2%), and intermediate uveitis (1,8%). Considering the etiology, 31.2% were unclassifiable, followed by non-infectious systemic disease in 29.2%.During the 3-month follow-up, 904 treatments were prescribed. The most frequent treatment was ocular topical (39%), followed by immunosuppressive treatment (27%), antimicrobial (14%), other treatments (10%) and less biological (3%), surgical (3%) and finally periocular (2%) and intravitreal (2%) treatment.Topical ocular treatment: 350 patients received topical ocular treatment, which accounts for 70% of patients. Among topical ocular treatments, 15% of the samples were treated with topical steroids, 54% were topical steroids associated with another topical treatment, 2% were topical antiglaucomatous, 2% received other topical treatments and 27% of the sample did not receive topical treatment.Immunosuppressive treatment: 249 immunosuppressive treatments were prescribed. 50% of the patients received immunosuppressive treatment. Among the immunosuppressive treatments, 25% of the patients received oral steroids, 6% salazopyrine, 4% methotrexate, 5% azathioprine, 2% mycophenolate mofetil, 5% oral steroids associated with another immunosuppressant, 15% salazopyrine associated with another immunosuppressant, 1% other immunosuppressive treatment and 49% of patients did not receive any immunosuppressive treatment.Biological Treatments: 25 patients in the cohort received biological treatment, this represents 5% of patients. The biological treatment types were distributed as follows: 3% of the patients received adalimumab treatment, 1% received infliximab, 1% received other biological treatments, and 95% of the patients did not receive biological treatments.The number of treatments received per patient was analyzed and 50 patients (10%) received no treatment, 152 patients (30%) received 1 treatment, 189 patients (38%) received 2 treatments, 75 patients (15%) Had received 3 treatments, 23 patients (5%) had received 4 treatments, 9 patients (2%) had received 5 treatments and lastly 2 patients had received 6 treatments.

Conclusions: The majority of patients received the combination of two treatments. Topical steroids and oral steroids were the most frequent treatments used.

Disclosure of Interest: None declared

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THU0570 ANAKINRA AS A SUCCESSFUL TREATMENT OF IDIOPATHIC RECURRENT PERICARDITIS: TAPER OR NOT TO TAPER? CASE SERIES AT THE UNIVERSITY OF SOUTHERN CALIFORNIA

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Background: Idiopathic Recurrent Pericarditis can be challenging to treat in patients unresponsive to NSAIDs, aspirin, colchicine and immunosuppressive drugs. Patients become steroid dependent and tapering precipitates recurrences.

Objectives: Report 2 adult cases of idiopathic recurrent pericarditis treated successfully with Anakinra.

Methods: Chart review of 2 patients with idiopathic recurrent pericarditis treated with anakinra at the Keck Medical Center of USC. Literature review on treatment of idiopathic recurrent pericarditis with anakinra.

Results: Case 1: 60-year-old Caucasian male had five episodes of idiopathic pericarditis in 2011. Serologic workup including ANA, anti-dsDNA, malignant and infectious workup was negative. Initially, patient responded to prednisone 0.4 mg/kg/day. Adding colchicine, azathioprine and methotrexate failed to prevent recurrence. Pericarditis developed whenever prednisone was tapered below 20 mg/day with bursts of CRP to 78 mg/dl. In 2012, Anakinra 100 mg sq daily resulted in immediate clinical response and normalization of CRP (1mg/dl). Prednisone and methotrexate were tapered with no recurrence. Gradually Anakinra was tapered to 3 times/week, then once a week, with no recurrence. Case 2: 37-year-old African American male had four episodes of recurrent pericarditis. He had positive ANA 1:320, but negative anti-dsDNA, anti-smith, negative infectious and malignancy workup. Initially, patient responded to prednisone 0.6 mg/kg/day and colchicine. Tapering steroids below 40 mg/day resulted in recurrent pericarditis. Sequential addition of hydroxychloroquine, methotrexate, mycophenolate mofetil, and azathioprine failed to prevent recurrence. Anakinra 100 mg sq daily resulted in prompt resolution of symptoms, normalization of acute phase reactants and allowed successful tapering of steroids. Anakinra is being slowly tapered over the past year, with no recurrence.

Conclusions: Idiopathic recurrent pericarditis, which requires chronic corticosteroids, should be treated by adding another immunosuppressive agent. European Society of Cardiology guidelines recommend azathioprine, cyclophosphamide, methotrexate, hydroxychloroquine, cyclosporine or mycophenolate mofetil. Anakinra has demonstrated success in treating autoinflammatory and autoimmune diseases including FMF, TNF receptor associated periodic syndrome, rheumatoid arthritis and in patients with TRAPS mutation TNFRSF1A. This represented the possibility to decrease inflammation by blocking interleukin-1. Using this rationale we treated our patients. Picco et al reported three pediatric cases treated with anakinra, where its discontinuation resulted in recurrence.