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FRI0618 (2019)

ANALYSIS OF NEW REFERRALS TO A SPECIALIST UK ADULT AUTOINFLAMMATORY DISEASE SERVICE

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Background: Diagnosis of the systemic autoinflammatory diseases (SAIDs) requires a high index of suspicion and previous series has suggested that there are often long diagnostic delays, particularly in TRAPS and MKD.

Objectives: To look at the case mixed referred to a single adult clinic in London specialising in assessment of potential SAIDS over the course of the year of 2017.

Methods: All new referrals were accepted for clinical assessment. At the first visit patients had a full history and examination, genetic testing – varying from single gene to a 20 gene panel depending on clinical features, and laboratory testing including fortnightly blood draws for serial analysis of the hepatic acute phase response proteins, CRP and SAA over a 3 month period.

Patients with a non suggestive history, non contributory genetic testing and no evidence of inflammation accompanying symptoms were felt not to have SAIDS and referred back to their local hospitals for further management. Other cases were diagnosed based on full clinical assessment, other investigations – for example ferritin in AOSD, genetic testing results, serial monitoring of CRP and SAA and therapeutic trials, for example colchicine in presume FMF and anti IL-1 therapies in CAPS and Schnitzler's syndrome

Results: 273 new patients were referred. Median age at referral was 37.4 years, the oldest patient was 84.3 years old and 59% were female. 174 (64%) were of northern European ancestry, 68 (25%) were eastern Mediterranean, west Asian or southern European ancestry, 19 (7%) were of south or east Asian ethnicity and 4% were of African or Afro-Caribbean ancestry. 76% of referrals were from hospital specialities. The referral source was: rheumatology 38%, general practitioner 24%, dermatology 8%, immunology 8%, gastroenterology 6%, infectious diseases 3%, clinical genetics 3%, nephrology 2%, haematology 2%, gynaecology 2%, emergency department 1%, respiratory 1%, other 2%.

After work up 135 (49.5%) were felt not to have a SAID as the cause of their symptoms. Of the remaining 138 patients who did have evidence of a SAID the diagnoses made were: FMF 33%, uncharacterised SAID 26%, CAPS 9%, AOSD 8%, recurrent idiopathic pericarditis 6%, Schnitzler's Syndrome 5%, TRAPS 4%, variant PFAPA 4%, DADA2 1%, MKD 1%, crmo 1%, Behcets 1%, Cattleman's disease 1%.

The median interval between reported symptom onset and diagnosis were as follows: 16 yrs for FMF, 28.1 yrs for CAPS, 5.0 years for recurrent idiopathic pericarditis, 4.5 yrs for Schnitzler's Syndrome, 5.7 yrs for TRAPS, 20.5 yrs for variant PFAPA, 12.5 yrs for DADA2, 17 yrs for MKD and 2 years for crmo.

Conclusion: This series suggests that recognition and diagnosis of the SAIDS remains a challenge. More than 1/3 of referrals were from rheumatology, referrals from primary care were almost exclusively from patients with a known family history of one the inherited syndromes. The wide variety of referring specialities reflects the diverse nature of SAIDS and the importance of almost all specialities considering the possibility of SAIDS. Only just over

recognised SAID spectrum and 26% of these have
netic testing. Of those in whom a diagnosis could be
(https://www.eular.org) treatment no patients had

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AB1011 (2019)

APPLICATION OF AUTOINFLAMMATORY DISEASE DAMAGE INDEX (ADDI) TO AUTOINFLAMMATORY DISEASES IN A TERTIARY REFERRAL HOSPITAL

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Background: Autoinflammatory diseases (AIDs) cause chronic systemic inflammation that can damage multiple organs. Recently, the autoinflammatory disease damage index (ADDI) has been developed and validated in the four most common monogenic AIDs, Cryopyrin-associated Periodic Syndrome (CAPS), Familial Mediterranean Fever (FMF), Mevalonate Kinase Deficiency (MKD) and Tumor Necrosis Factor Receptor-associated Periodic Fever Syndrome (TRAPS). The use of ADDI index could also be of great value in other AIDs.

Objectives: The aim of this study is to assess the application of ADDI in patients with the four most common monogenic diseases and other AIDs. To accomplish this objective a detailed cohort of patients with different AIDs is presented.

Methods: All patients with AIDs followed in the Pediatric Rheumatology Unit comprising the Transitional Care and specialized AIDs outpatient clinics from Hospital Universitari Vall d'Hebron were identified. A cross-sectional, descriptive study was performed applying ADDI by two pediatric rheumatologists (EM, ML). Laboratory test including C-reactive protein (CRP) mg/dl, amyloid protein (AP) mg/L, erythrocyte sedimentation rate (ESR) mm/h and protein/creatinine rate (mg/g Cr) were performed at the moment ADDI was applied. Variables related with disease duration, current treatment and accumulated corticosteroids treatment were assessed. The continuous variables are presented as mean and standard deviation (mean ± SD) and categorical variables are presented by percentages.

Results: A total of 41 patients with AIDs were included, 61% were female, with a median age of 20 ± 11.9 years at inclusion. Disease duration was 11 ± 8.2 years. AIDs included were 11 patients with FMF (26.8%), TRAPS n=4 (9.8%), MKD n=3 (7.3%), CAPS n= 2 (4,9%), Blau syndrome n= 7 (17.1%), SAVI syndrome n=3 (7.3%), crmo n=4 (9.8%), PFAPA n=2 (4.9%), APLAID n=1 (2.4%), Stickler syndrome n=1 (2.4%), and 3 unknown AIDs with genetic test negative n=3 (7.3%). Current treatment is variable among patients, 6 (15.8%) are taking disease-modifying antirheumatic drugs (DMARDs), 9 (23.7%) Colchicine, 8 (21.1%) Anakinra, 13 anti-TNF therapy (34.2%), 1 (2.6%) Ruxolitinib and 1 (2.6%) Abatacept. Only 6 patients were receiving corticoids with mean prednisone dose of 7.5 mg/day. The global ADDI mean score was 2.3 ± 2.2. Regarding the eight different items included in the item, musculoskeletal domain shown the highest score with 1.02, followed by the ocular domain with 0.42. The patient with APLAID syndrome had the highest score of 6 followed by BLAU syndrome with 4.71. FMF has the lowest score with 0.83. Laboratory test results were mean ESR 27.2 ± 26.7mm/h, CRP 0.7 ± 1.3 mg/dl, AP 13.9 ± 18.6mg/L. Proteinuria was present in 2 patients with mean 286.5 ± 246.1mg/g. EM and ML applied ADDI in 5-10 minutes average.

Conclusion: ADDI is a feasible index suitable to measure damage in a single patient. Despite it was performed to the four most common AIDs it could be applied to other diseases. In our cohort the mean ADDI index was low and musculoskeletal item has the highest score. This result could be explained by the tight control of the disease and successful targeted therapy. Laboratory tests also support this finding. Nevertheless, some organ

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FRI0600 (2019)

FIRST SINGLE-CENTERED COHORT OF CHINESE PATIENTS WITH PEDIATRIC SAPHO

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Background: The SAPHO syndrome (Synovitis, Acne, Pustulosis, Hyperostosis and Osteitis) is an disease entity with chronic inflammatory osteoarticular symptoms and typical dermatological lesions. Pediatric SAPHO is regarded as equivalent of Chronic Recurrent Multifocal Osteomyelitis (crmo) or Chronic Non-bacterial Osteomyelitis (CNO). There have already been several pediatric SAPHO cohorts about Caucasian populations. No Chinese cohorts have been reported.

Objectives: The aim of this study was to evaluate clinical features and treatment for all pediatric SAPHO patients admitted to Peking Union Medical College Hospital (PUMCH, Beijing, China)

Methods: We conducted a single-centered non-intervention retrospective study of 24 pediatric SAPHO patients who were diagnosed with Khan's modified criteria in PUMCH from April 2014 to August 2018 [1]. The demographic (sex, age, onset age, follow-up years), clinical (bone and skin symptoms), laboratory (ESR, CRP, HLA-B27, ANA, IL-6, IL-8, TNF-α), imaging (CT, MRI, bone scintigraphy), histologic (lymphocytic, granulocytic) and treatment (medications and effect) data were collected.

Results: Detailed information of 15 male and 9 female was available. The mean ± SD age at onset of bone and skin symptoms was 11.7 ± 3.8 and 14.4 ± 2.7 years, respectively. The duration of follow-up was 19.2 ± 15.2 months. 17 (71%) patients had skin manifestations (46% Severe Acne, all male; 21% Palmoplantar Pustulosis, all female; 4% psoriasis). Involvement of bone lesions varied (42% anterior chest wall, 29% mandible, 50% peripheral bones, 21% spinal bones). ESR, CRP, IL-6, IL-8, IL-10 was elevated in 88%, 96%, 50%, 71%, 70% patients, respectively. 11 did bone biopsy (6 dominantly lymphocytic, 3 granulocytic, 2 both). CT, MRI and bone scintigraphy were performed in 79%, 96%, 96% patients, respectively. A total of 6 patients have been treated with NSAIDs, 10 with bisphosphonate, 10 with TNF-α antagonist, 1 with Glucocorticoids, with a variable response. 70% patients showed complete remission after bisphosphonate or TNF-α antagonist therapy.

Table 1

Clinical characteristics of 24 pediatric SAPHO patients

Skin manifestation	**17/24 (71%)**
Severe acne (M/F)	11/0
PPP (M/F)	0/5
None (M/F)	3/4
Psoriasis (M/F)	0/1
Nonspecific rash (M/F)	1/0
Bone manifestation	**24/24(100%)**
Pain	24 (100%)
Swelling	17 (71%)
Restricted function	19 (79%)

patients

			sponse	Total
				6/24
				10/24
TNF-α antagonist	7	3	0	10/24
Glucocorticoids	0	1	0	1/24

Conclusion: This is the first Chinese cohort of pediatric SAPHO patients. Their bone lesions could be divided into 4 types, anterior chest wall, mandible, peripheral bones and spinal bones. We also provide evidence that bisphosphonate and TNF-α antagonist are useful for pediatric SAPHO treatment.

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OP0342 (2019)

IDENTIFYING CANDIDATE ITEMS TOWARDS THE DEVELOPMENT OF CLASSIFICATION CRITERIA FOR CHRONIC NONBACTERIAL OSTEOMYELITIS (CNO) AND CHRONIC RECURRENT MULTIFOCAL OSTEOMYELITIS (crmo)

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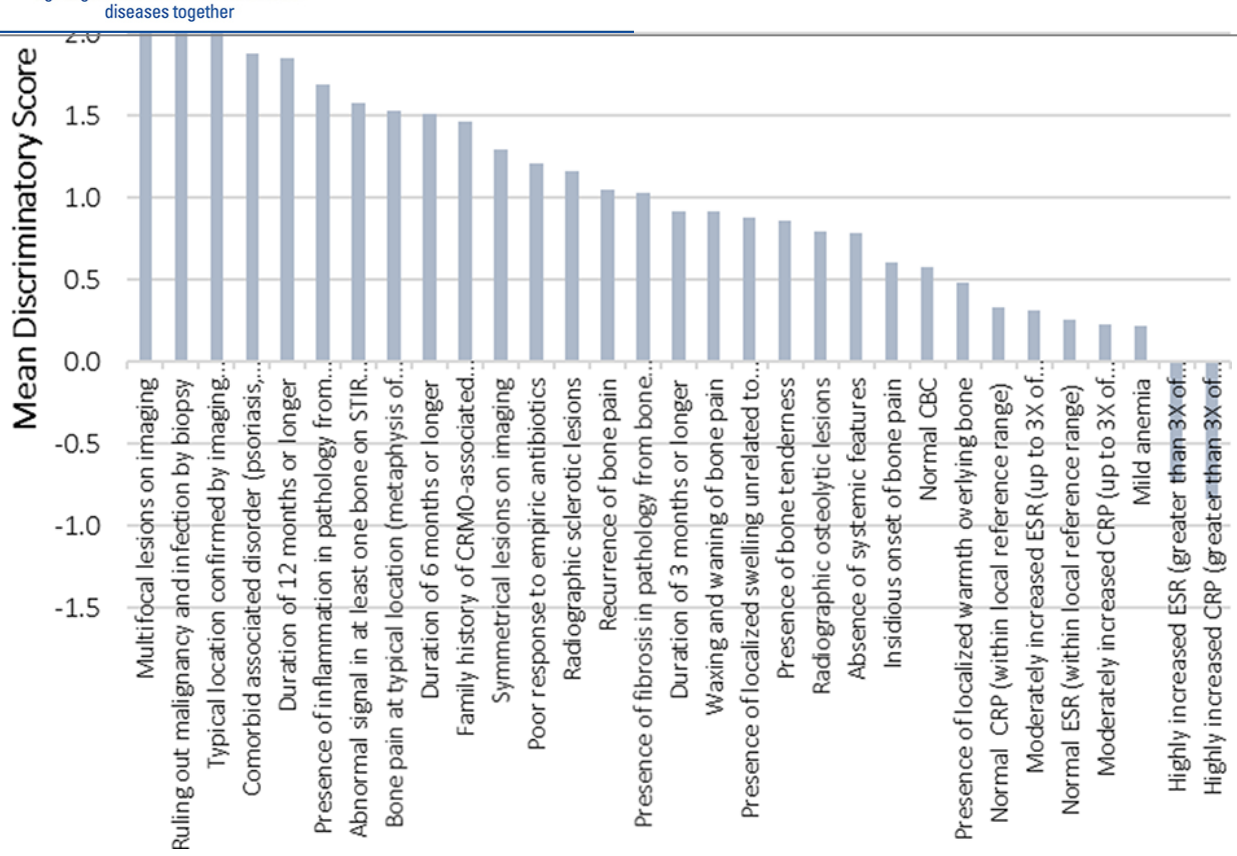
Background: Chronic nonbacterial osteomyelitis (CNO) is a severe and occult autoinflammatory bone disease of unknown cause. Early diagnosis is challenging, and CNO may debilitate affected children when left untreated. Currently, evidence-based and validated diagnostic and classification criteria for crmo/CNO are lacking. The insidious disease course, increasing disease incidence, and significant delay in diagnosis highlight the need for the development of classification criteria that leads to more precise and early selection of patients for clinical trials [1,2].

Objectives: To identify candidate items towards developing classification criteria for CNO using anonymous survey and nominal group technique.

Methods: An international collaborative effort was formed within the pediatric and adult rheumatology communities to conduct the following phases: 1) to generate candidate criteria items by a Delphi survey among international rheumatologists; 2) to reduce candidate criteria items through consensus processes involving physicians managing CNO and patients or caregivers of children with CNO. This study was approved by Seattle Children's Hospital Institutional Review Board.

Results: In Phase 1, 259 pediatric rheumatologists (30%, N=865) participated in an online questionnaire about features most relevant to the classification of CNO. Of those, 77 (30%) practiced in Europe, 132 (51%) in North America, and 50 (19%) in other continents. A total of 138 (53%) responders had >10 years of practicing experience and 108 (42%) had managed >10 CNO patients. There were 33 candidate criteria items initially identified. In Phase 2, candidate items were presented to 39 rheumatologists and 7 parents and items were refined or eliminated through item reduction techniques. Seventy-seven (94%, N=82) workgroup members then participated in a second survey to rank the remaining items by their distinguishing power of CNO from mimicking conditions. Figure 1 shows the mean score for the remaining 31 candidate criteria. Multifocal lesions, ruling out malignancy and infection and typical location on imaging had the greatest means. CRP and/or ESR greater than 3x the normal upper limit had the greatest negative means.



Discriminatory Score: +3/-3 (increases/decreases the likelihood of crmo the most)

+2/-2 (increases/decreases the likelihood of crmo moderately)

+1/-1 (increases/decreases the likelihood of crmo slightly)

0 (no difference)

Conclusion: Through surveys and consensus technique, candidate items towards developing classification criteria for CNO were identified. This list of items will guide the design of a feasible patient data collection form towards weighting of each item in the classification criteria.

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Acknowledgement: CNO/crmo Work Group, Childhood Arthritis and Rheumatology Research Alliance

Disclosure of Interests: Melissa Oliver: None declared, Eveline Wu: None declared, Raymond Naden Speakers bureau: Was a speaker at conferences paid by pharmaceutical companies several times in the past, but not in the last 7 years., Matthew Hollander: None declared, Polly Ferguson: None declared, Fatma Dedeoglu

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SP0187 (2019)

PATHOPHYSIOLOGY AND THERAPEUTIC CONSEQUENCES AUTO-INFLAMMATORY BONE DISORDERS

Christian Hedrich

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Chronic nonbacterial osteomyelitis (CNO) is an autoinflammatory bone disorder, covering a clinical spectrum with asymptomatic inflammation of single bones at the one end, and chronic recurrent multifocal osteomyelitis (crmo) at the other end. Bone inflammation, however, can also be a symptom of other autoimmune/inflammatory conditions. Rare monogenic autoinflammatory diseases with bone involvement have informed research and provide models for the more common and pathophysiologically complex disorder CNO/crmo.

Despite recent efforts, the exact molecular pathophysiology of CNO remains incompletely understood. Profound dysregulation of cytokine responses was demonstrated in CNO/crmo. Failure to produce antiinflammatory cytokines interleukin (IL)-10 and IL-19 contributes to activation of inflammasomes and subsequent IL-1β release. In IL-10-deficient and in CNO-prone chronic multifocal osteomyelitis mice, IL-1β was linked to bone inflammation. Recently, increased inflammasome component expression and inflammasome assembly have been linked with CNO/crmo in humans. Furthermore, alterations to the gut microbiome were suggested in contributing to IL-1β release from innate immune cells in mice, offering an interesting target in the search for molecular mechanisms in CNO.

This presentation will review molecular alterations in autoinflammatory bone disease, focussing on CNO and discuss therapeutic consequences.

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SP0188 (2019)

SAPHO – AN ADULT PERSPECTIVE

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Background: The acronym SAPHO has been introduced to describe a syndrome in adolescents and adults suffering from synovitis (arthritis), acne, pustulosis, hyperostosis, and non-bacterial osteitis preferentially in the sternal region. Currently, this also includes the entity CNO with non-bacterial chronic recurrent multifocal osteomyelitis (crmo) in cases which primarily occur in adult age.

Objectives: The diagnostic certainty of SAPHO syndrome in case of incomplete presentation of the clinical features has been unclear so far. Furthermore, the treatment approach of SAPHO syndrome is difficult because the etiology remains unknown, although a reactive infectious osteitis in genetic predisposed subjects seems appealing.

Methods: Here we present relevant case series of SAPHO patients which should elucidate the relevance of different diagnostic procedures and treatment options. It has been noted, however, that particularly in respect of the use of antirheumatic drugs case series with predominantly small numbers of SAPHO patients suggest different treatment approaches.

Results: The diagnosis of SAPHO syndrome is made not only in the full picture of the disease according to the acronym, but also in non-bacterial and non-malignant osteitis with hyperostosis with simultaneous or delayed onset of acne, psoriasis and/or PPP. In addition, the primary manifestation of CNO in adulthood is nowadays classified as SAPHO syndrome. Recent studies have previously confirmed the usefulness of skeletal scintigraphy in 2 phases as a diagnostic. Imaging with MRI is frequently used preferentially for the assessment of osteitis activity, CT for the assessment of destruction and hyperostosis. The CT-guided biopsy of the lesion should be performed in solitary manifestation of osteitis. Basically, SAPHO syndrome has a high impact on patients' general health resulting in high burden of disease. There are many approaches to drug therapy, but only a few have been investigated in larger case series - none of them as controlled studies. Smaller case series of less than 10 patients reported limited efficacy of DMARD with MTX, azathioprine, or ciclosporin. Studies with larger case numbers show a moderate efficacy of bisphophonates as well as TNF-alpha blockers. A short-term but not sustained effect has been demonstrated for the antibiotic azithromycin, as well as for steroids per os or as infiltration into osteitis. Referring to the treatment approach in SpA newly approved biologicals with IL-17 or IL-12/23 blocking effects demonstrated promising results in individual case reports of SAPHO patients.

Conclusion: Modern diagnostic imaging methods are increasingly being used for SAPHO syndrome. The selection of potentially effective drugs for SAPHO syndrome has increased. However, prospective studies to develop guidelines for the diagnosis and therapy of SAPHO syndrome are still lacking. Until further notice, the therapy is based on the recommendations for psoriatic arthritis or spondyloarthritis.

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AB0960 (2019)

THE HELIOS (HACETTEPE UNIVERSITY ELECTRONIC RESEARCH FORMS) REGISTRY: USE OF BIOLOGIC DRUGS IN AUTOINFLAMMATORY DISEASES

Selcan Demir, Ezgi Deniz Batu, Fuat Akal, Erdal Sag, Ummusen Kaya Akca, Elif Arslanoğlu, Emil Aliyev, Kübra Yüksel, Armağan Keskin, Yelda Bilginer, Seza özen

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Background: Autoinflammatory diseases (AID) are characterized by a dysregulation of innate immunity leading to uncontrolled inflammation. The treatment in AID is critical to control the disease activity, to prevent complications, and to improve the health-related quality of life. Biologic drugs have revolutionized the treatment and outcomes in AID.

Objectives: Herein we aim to present the clinical characteristics of children to whom biologic drug therapy was initiated for the management of AID.

Methods: A web-based registry called the Helios Registry (**Hacettepe univErsity eLectronIc research fOrmS) has been formed to evaluate the data of all children on biologic treatment. We have been enrolling patients since August 2018 retrospectively and prospectively. We have analyzed the data about the general characteristics of the patients, treatment, the biologic drug used, and adverse effects. Only the patients with the following diagnoses were included: systemic juvenile idiopathic arthritis (SJIA), familial Mediterranean fever (FMF),** cryopyrin associated periodic syndrome (CAPS), and chronic recurrent multifocal osteomyelitis (crmo).

Results: Of 60 patients included, 19 had FMF (31.7%), 24 had sJIA (40%), 10 had CAPS, (16.7%), and 7 had crmo (11.7%). Their median age was 10.7 (2-20) years old and disease duration was 2.8 (0-6) years, at the time of biologic drug initiation. 58.3% were currently on canakinumab, 20% anakinra, 10% tocilizumab, 10% etanercept, and 1.7% adalimumab. 63.3% of our patients had previously used at least one other biologic drug. The rate of glucocorticoid use before biologic treatment was 56.6%. The median duration of glucocorticoid treatment after initiating biologic drugs was 7.4 months. 56 (93%) patients achieved remission on biologic therapy. There were 15 patients (25%) who received tuberculosis prophylaxis due to positive tuberculin skin test (diameter≥10 mm) and there was no Quantiferon test positivity. Thirteen adverse events (AE) had been noted. 2 of them were serious events as anaphylaxis due to tocilizumab infusions. The rest of the adverse events were mild thrombocytopenia (n=2), varicella infection (n=1), and local side effects (n=8). The median number of the infections per year was one and there were no death or malignancy.

Conclusion: The most commonly prescribed biologic drugs were IL-1 inhibitors especially for patients with IL-1-mediated AID (FMF, CAPS, and SJIA). The biologic treatment in AID is effective and there were no serious side effects.

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zgi Deniz Batu: None declared, Fuat Akal: None
a: None declared, Elif Arslanoğlu: None declared, Emil Aliyev: None declared, Kübra Yüksel: None declared, Armağan Keskin: None declared, Yelda Bilginer: None declared, Seza özen Consultant for: Seza Ozen is receiving consultancy fees from Novartis, Speakers bureau: Roche

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Session: Paediatric rheumatology *(Scientific Abstracts)*

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THU0517 (2019)

THE LONGITUDINAL EUROFEVER PROJECT: AN UPDATE ON ENROLLMENT

Ilaria Gueli, Martina Finetti, Fabrizio De Benedetti, Jordi Anton, Maria Alessio, Joost Frenkel, Luca Cantarini, Romina Gallizzi, Judith Sanchez Manubens, Marco Cattalini, Efimia Papadopoulou-Alataki, Rolando Cimaz, Donato Rigante, Alma Nunzia Olivieri, Pavla Dolezalova, Alberto Martini, Nicolino Ruperto, Marco Gattorno

IRCCS Istituto Giannina Gaslini, UOSD Centro Malattie Autoinfiammatorie e Immunodeficienze, on the behalf of the Paediatric Rheumatology International Trials Organisation (PRINTO) and the Eurofever Project, Genoa, Italy

Background: In 2008 the Paediatric Rheumatology European Society (PReS) promoted an International Project for the study of Autoinflammatory Diseases (AIDs) named Eurofever, whose main purpose is to create a web-based registry for the collection of information in AIDs patients.

Objectives: To implement the Registry with the new recently described AIDs and to increase the collection of longitudinal data.

Methods: The data were extracted from the Eurofever registry, which is hosted in the PRINTO website (http://www. printo.it). From February 2015 we started the longitudinal collection of follow-up data with particular focus on treatment, modification of the clinical picture, onset of complication/adverse events. We have enrolled patients included in the registry up to 28 September 2018.

Results: Up to date 4175 patients have been enrolled (3843 of them with complete demographic information, 1903 M e 1940 F) from 62 countries. For 3356 (87%) patients also clinical data from onset to diagnosis, collected during the first visit performed at referred pediatric or adult center, are available. For each disease the number of enrolled patients is: FMF 1086 pts (951 with complete clinical data); TRAPS 273 pts (256 complete); CAPS 298 pts (279 complete); MKD 205 pts (190 complete); Blau's disease 49 pts (26 complete); PAPA 42 pts (41 complete); NLRP12 mediated periodic fever 13 pts (11 complete); DADA2 14 pts (9 complete); DIRA 3 pts (all complete); SAVI 3 pts (all complete); CANDLE 1 pt (complete) and Majeed 4 pts (all complete). Among multifactorial autoinflammatory diseases: PFAPA 676 pts (551 complete); CNO 581 pts (540 complete); Behcet 214 pts (186 complete), undefined periodic fever 368 pts (292 complete) and Schnitzler 13 pts (all complete). The median onset age is 4 years (range 1 month – 75 years), the median diagnosis age is 8 years (range 1 month – 78 years). Most of patients (3509, 91%) presented disease onset during pediatric age (<16 years), 334 (9%) during adult age (81 FMF, 31 CAPS, 53 TRAPS, 40 crmo, 12 Schnitzler syndrome e 90 unknown fever). 405 of 3509 (12%) patients with pediatric onset received diagnosis during adult age. The median diagnostic delay is 5 years; diseases with longer diagnostic delay are: NLRP12 (24 years, range 4-76), CAPS (15 years, range 0-77), PAPA (14 years, range 2-57), TRAPS (12 years, range 0-77). 396 patients have been treated with at least one biologic drug, 1031 with DMARDs, 427 with systemic steroid and 686 with others drugs. The most frequent diseases treated with biologic drugs are: CAPS (38%), multifactorial diseases (22%), TRAPS (14%), MKD (11%), rare monogenic (8%: 1 CANDLE, 2 DIRA, 2 NALP12, 3 Majeed, 8 DADA2 and 14 PAPA), and FMF (7%). Since February 2015, longitudinal visits have been inserted for 477 (12%) patients, with detailed data on treatment and safety.

ngoing. The analysis of data will improve our
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I perform consultancy activities on behalf of the Gaslini Institute for the companies listed below:

AbbVie, Biogen, Boehringer Ingelheim, Bristol-Myers Squibb, EMD Serono, Janssen, Novartis, Pfizer, R-Pharm.

The money received for these activities are directly transferred to the Gaslini Institute's bank account. Before March 2016, I was the head of the Pediatric Rheumatology Department at the G. Gaslini Hospital, where the PRINTO Coordinating Centre is located. For the coordination activity of the PRINTO network, the Gaslini Hospital received contributions from the industries listed in this section. This money has been reinvested for the research activities of the hospital in fully independent manners besides any commitment with third parties., Nicolino Ruperto Grant/research support from: The Gaslini Hospital, where NR works as full-time public employee, has received contributions (> 10.000 USD each) from the following industries in the last 3 years: BMS, Eli-Lilly, GlaxoSmithKline, F Hoffmann-La Roche, Janssen, Novartis, Pfizer, Sobi. This funding has been reinvested for the research activities of the hospital in a fully independent manner, without any commitment with third parties., Consultant for: Received honoraria for consultancies or speaker bureaus (< 10.000 USD each) from the following pharmaceutical companies in the past 3 years: Ablynx, AbbVie, Astrazeneca-Medimmune, Biogen, Boehringer, Bristol-Myers Squibb, Eli-Lilly, EMD Serono, GlaxoSmithKline, Hoffmann-La Roche, Janssen, Merck, Novartis, Pfizer, R-Pharma, SanofiServier, Sinergie, Sobi and Takeda., Speakers bureau: Received honoraria for consultancies or speaker bureaus (< 10.000 USD each) from the following pharmaceutical companies in the past 3 years: Ablynx, AbbVie, Astrazeneca-Medimmune, Biogen, Boehringer, Bristol-Myers Squibb, Eli-Lilly, EMD Serono, GlaxoSmithKline, Hoffmann-La Roche, Janssen, Merck, Novartis, Pfizer, R-Pharma, SanofiServier, Sinergie, Sobi and Takeda., Marco Gattorno Grant/research support from: MG has received unrestricted grants from Sobi and Novartis

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VACCINATION SAFETY AND COVERAGE IN AN ITALIAN COHORT OF AUTOINFLAMMATORY DISEASES

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Background: Vaccine-preventable diseases are again emerging in our population after anti-vaccine campaign has started. In autoinflammatory diseases (AID), vaccine triggered-disease is a well known phenomenon for Hyper-IgD/Mevalonate-Kinase Deficiency (MKD). In CAPS, severe flares have been experienced after pneumococcus vaccine, while PFAPA patients did not achieve sufficient and protective levels of antibodies. This evidence has raised doubts in physicians and families about the safety of vaccines.

Objectives: To evaluate, in a cohort of italian AID, the vaccination coverage of the Italian Vaccination Schedule and the prevalence of adverse reactions and disease flares induced by vaccinations.

Methods: An anamnestic questionnaire was applied to AID patients refering to the AID Unit of the Istituto Giannina Gaslini from August 2017 to August 2018. Acquired data were revised for quality of information. Data about disease triggers in AID were obtained from the EUROFEVER registry for statistical reference.

Results: Triggers in AID Eurofever Registry : In august 2018 a total of 3783 patients were enrolled in the EUROFEVER registry (1908 female, 50,43%). The mean age of symptoms at disease onset was 7.04 +/- 9,48 SD yrs, (minimal 0 - maximum 75,92 yrs). The distribution among the periodic hereditary fevers was: 28,75% FMF (n=1081); 17,66% PFAPA (n=666); 9% Undefined inflammatory disease (UND n = 347); 7,85% CAPS (n=297); 7,16% TRAPS (n=271) and 5,39% MKD (n=204). Vaccines triggered the disease in 70% of the MKD, while PFAPA, TRAPS and UND had a rate of reactions of 20%. This was also found in 12.34% of CAPS, whereas FMF and inflammatory bone disorders had a rate of 6% and 3%, respectively. Excluding other causes of reactions, and isolating just vaccines as a cause, MKD had a higher percentage of reactions (7,14%), while PFAPA and UND had 1% and CAPS, TRAPS, FMF and inflammatory bone disorders had less than 1%. Triggers in IGG cohort : 150 questionnaires were distributed with 70% rate of response. Quality of data was 100% for coverage and adverse reactions. 105 patients were identified: PFAPA (n=26); CAPS (n=5); TRAPS (n=6); FMF (n=14); MKD (n=8); Inflammatory Bone Disorders (crmo and PAPA, n=4) and UND (n=41). Rate of coverage was lower than 90% for Hib3 (83,11%), MMR/MMRV (88,9%) and for Rota C (1,85%). For DTP3, Hep3, PCV3 and IPV the rate of coverage was higher than 90% for all vaccines. 11 moderate/severe reactions were observed as following: 5 after DTPA+IPV (1 PFAPA; 2 TRAPS, 1 MKD and 1 UND); 1 after Hib (PFAPA); 1 after P10/13 (PFAPA); 4 after MPR (1 PFAPA, 1 TRAPS, 1 MKD and 1 UND). The general rate of severe reactions/shot was 6,36 for 1000 shots and no severe infection, death, persistent or significant disability or life-threatening condition was observed. Just one MKD patient had a severe disease flare requiring hospitalization following pneumococcal vaccine.

Conclusion: Data show that in AID patients vaccines may more frequently trigger the disease. Therefore, vaccination in AID may be cosidered a peculiar public health problem. Specific recommendations for vaccination in AID are warranted as well as further investigations for immunologic protection.

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