SATURDAY, 17 JUNE 2017

Outcome in juvenile idiopathic arthritis

OP0338 FREQUENCY OF COMORBIDITIES IN JIA PATIENTS – RESULTS OF AN OBSERVATIONAL COHORT STUDY

K. Minden[1], N. Betenstehl[2], J. Klotsche[1], E. Seipelt[3], S. Tatsis[4], I. Foeldvari[5], G. Ganser[6], G. Horneff[7]. *[1]Epidemiology Unit, German Rheumatism Research Centre, Berlin; [2]Oberhavelkliniken, Hennigsdorf; [3]Immanuel Krankenhaus Berlin-Buch, Berlin; [4]Kath. Marienkrankenhaus; [5]Zentrum für Kinder- und Jugendrheumatologie, Hamburg; [6]St. Josef-Stift, Sendenhorst; [7]Asklepios Kinderklinik, Sankt Augustin, Germany*

Background: Juvenile idiopathic arthritis (JIA) is a chronic inflammatory disease that often persists into adulthood. In addition to disability and poorer quality of life, JIA is associated with increased long-term morbidity and mortality. The long-term risk of comorbidities in JIA patients is uncertain and guidance on risk assessment is not currently available.
Objectives: To determine the frequency of comorbid conditions in adult JIA patients.
Methods: Patients with JIA transferred from the biologic registry BIKER to the follow-up (FU) registry JuMBO were included in this analysis. All comorbidities, except for serious infections, prospectively recorded by physicians to BiKeR or JuMBO were considered. Comorbidity rates among the various JIA categories were assessed. The Medical Dictionary for Regulatory Activities (MedDRA) was used for disorder coding. Differences in the occurence of comorbidities between JIA categories were analyzed by multinomial logistic regression.
Results: A total of 1,022 young adults (67% female) with JIA and a mean FU of 7.8 (SD=3.5) years (ys) were included in this analysis. The patients' mean age was 22.5 ys (SD=3.7), and disease duration was 12.9 ys (SD=5.9) at the last FU. The majority were classified as polyarticular JIA (36.4%) at BiKeR enrollment. Patients had received a mean of 2.9 (SD=1.3) DMARDs, 77% were ever treated with biologics.
Comorbidities were reported for more than half of the patients (54%), 24.5% of the conditions were stated for the first time in adult age. Eye disorders were the most common comorbid condition group (15.1%), followed by skin and subcutaneous tissue disorders (9.3%), and psychiatric disorders (5.5%). The most frequently reported single diseases were uveitis in 14.4%, chronic secondary pain syndrome in 4.4%, hypertension in 3.6%, and psoriasis in 3.3%. In addition, inflammatory bowel diseases were reported in 2.5% of cases, other immune-mediated disorders, namely autoimmune thyroiditis in 2.5%, type1 diabetes in 0.7% and celiac disease in 0.3%, depression in 2.3%, anxiety in 0.3%, osteoporosis in 1.6%, and amyloidosis in 0.4%. Among the reported comorbidities, there was one case with a cerebrovascular accident, but none with ischemic heart disease, heart failure or diverticulitis. The rate of comorbid condition accrued in the various JIA categories (table 1) differed significantly, with the highest rate in patients with extended oligoarthritis.

Table 1: Frequency of major comorbidities (in %) in the various JIA categories in young adult age

Comorbid condition	Sys JIA	OA, persist.	OA, ext.	PA, RF-	PA, RF+	ERA	PsA	P value
	N= 48	N=97	N=169	N=278	N=94	N=205	N=97	
Any comorbid condition	58.3	47.2	64.1	45.7	47.9	51.7	62.9	0.007
Uveitis	4.2	14.4	34.9	7.9	0	16.6	10.3	<0.001
Psoriasis	2.1	1.0	0.6	1.1	0	3.4	19.6	<0.001
IBD	4.2	0	3.6	1.4	1.1	3.4	5.2	0.233
Hypertension	10.4	2.1	4.1	2.5	2.1	3.4	3.1	0.032
Osteoporosis	10.4	0	1.8	1.8	1.1	0	1.0	<0.001
Amyloidosis	4.2	0	0	0.4	0	0	0	0.001
Chronic secondary pain syndrome	2.1	5.2	4.7	6.1	3.2	4.9	1.0	0.394
Depression	4.2	1.0	2.4	2.2	1.1	2.4	3.1	0.927
Autoimmune thyroiditis	2.1	1.0	1.8	2.2	5.3	1.5	6.2	0.156
Type 1 diabetes	0	0	0	1.1	2.1	1.0	0	0.445
Celiac disease	0	0	0.6	0	1.1	0	0	0.202

Sys JIA - Systemic JIA; OA persist. – Oligoarthritis persistent; OA, ext. – Oligoarthritis extended; PA - Polyarthritis; RF- - Rheumatoid factor negative; RF+ - Rheumatoid factor positive; ERA - Enthesitis-related arthritis; PsA - Psoriatic arthritis; IBD – inflammatory bowel disease

Conclusions: Young adults with JIA have a high rate of comorbidity overall, with extraarticular JIA manifestations being the most frequently reported comorbid conditions. Comorbidity rates vary among the various JIA categories. Patients with systemic JIA have the highest rate of cardiovascular risk factors and osteoporosis, while patients with extended OA have the highest rate of uveitis. An underreporting or unawareness of comorbidities by rheumatologists is possible, guidance on risk assessment in adults with JIA is needed.
Acknowledgements: The authors thank all rheumatologists for contributing patients to the JuMBO registry. BiKeR is funded by unconditional grants from Abbvie, Germany, Novartis, Germany, and Roche, Germany, JuMBO by unconditional grants from Abbvie, Pfizer, and Roche.
Disclosure of Interest: K. Minden Speakers bureau: Pfizer, Roche, Pharm-Allergan, N. Betenstehl: None declared, J. Klotsche: None declared, E. Seipelt: None declared, S. Tatsis: None declared, I. Foeldvari: None declared, G. Ganser: None declared, G. Horneff Speakers bureau: Abbvie, Pfizer, Roche, Novartis, MSD
DOI: 10.1136/annrheumdis-2017-eular.5858

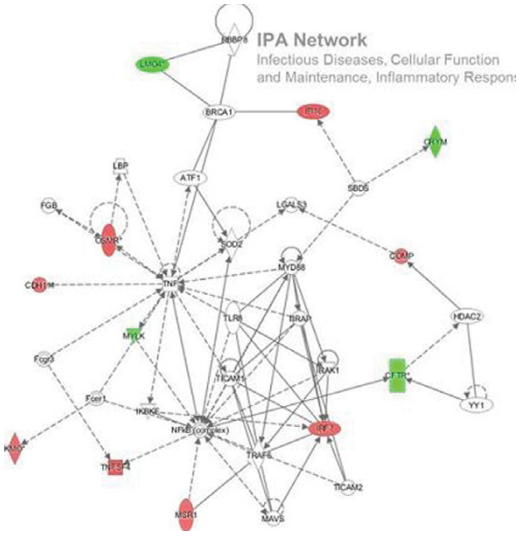
SATURDAY, 17 JUNE 2017

Systemic sclerosis

OP0339 IDENTIFICATION OF A TRANSCRIPTOMIC SIGNATURE CORRELATED WITH MODIFIED RODNAN SKIN SCORE (MRSS) IN PATIENTS WITH DIFFUSE CUTANEOUS SYSTEMIC SCLEROSIS

I. Agueusop[1], S. Illiano[2], C. Rocher[2], E. Boitier[3], J. Murphy[4], Y. Allanore[5], C.P. Denton[6], O. Distler[7], D. Khanna[8], F. Benderitter[2]. *[1]Sanofi-Aventis Deutschland GmbH, Frankfurt am Main, Germany; [2]Sanofi R&D, Chilly-Mazarin; [3]Sanofi R&D, Alfortville, France; [4]sanofi, Bridgewater, United States; [5]Paris Descartes University, Paris, France; [6]Centre for Rheumatology, Royal Free Hospital, London, United Kingdom; [7]Department of Rheumatology, University Hospital Zurich, Zurich, Switzerland; [8]Scleroderma program, University of Michigan, Ann Arbor, United States*

Background: To support internal compound development in systemic sclerosis, a study was performed to identify an mRSS signature in a longitudinal approach by analyzing skin biopsies.
Objectives: Identification of a gene signature that could be used as a quantitative surrogate marker for the mRSS independent of any treatment.
Methods: 77 forearm skin biopsies from 32 patients at baseline, and from the same patients after 8 weeks of treatment with SAR100842 (a LPA1 antagonist) or placebo (N=30) and after an additional 16 weeks of treatment with SAR100842 (N=15) in a phase 2 trial, were collected. Total RNA was extracted with the RNeasy® Fibrous Tissue Mini kit according to the manufacturer's instructions. Total RNA was quantified by spectrofluormetry and qualified by capillary electrophoresis using Agilent Bioanalyzer 2100. Whole transcriptome analysis was performed using Affymetrix chips. Genes highly correlated (Pearson's correlation) with the mRSS were identified at each treatment visit. A signature was identified as a set of genes whose expression levels correlated consistently either positively or negatively with the mRSS at all study visits regardless of treatment group. The correlation value between the genes and the mRSS at baseline had to be >0.5 or $<$ -0.5.The association between mRSS and the single composite marker obtained was investigated. A multivariate analysis of the correlation between the identified genes was performed using the median polish algorithm and PCA. The gene signature underwent pathway analysis using QIAGEN's Ingenuity Pathway Analysis (IPA).
Results: This methodology led to the identification of 64 genes considered for the signature and viewed as a single composite marker that was highly correlated to the mRSS. A principal component analysis was computed and the first component explaining the maximum variance in the signature was highly correlated to the mRSS at baseline and week 8. This correlation was confirmed with the median polish algorithm (Pearson's correlation coefficient of -0.75 and -0.73 respectively). The most significant disease and disorder biological functions associated with the mRSS signature genes were related to immunological diseases. A significant enrichment was also detected for genes associated with inflammatory response and connective tissue disorders with p-values from 2.98E-05 to 2.47E-02.



Conclusions: An mRSS signature was identified using skin biopsies in SSc patients. Some of these genes (i.e. IRF7, THBS1, COMP or BANK1) have been published using similar approaches in other sets of SSc patients (1), which supports our results. The functional categories of this signature are characteristic