Genetic association with articular damage in patients with juvenile idiopathic arthritis (JIA)

ArticleInfo		
ArticleID	:	2185
ArticleDOI	:	10.1186/1546-0096-12-S1-P25
ArticleCitationID	:	P25
ArticleSequenceNumber	:	422

ArticleCategory	:	Poster presentation
ArticleFirstPage	:	1
ArticleLastPage	:	
ArticleHistory	:	RegistrationDate : 2014–9–17 OnlineDate : 2014–9–17
ArticleCopyright	:	Radziszewska et al; licensee BioMed Central Ltd.2014 This article is published under license to BioMed Central Ltd. This is an Open Access article distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/4.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited. The Creative Commons Public Domain Dedication waiver (http://creativecommons.org/publicdomain/zero/1.0/) applies to the data made available in this article, unless otherwise stated.
ArticleGrants	:	
ArticleContext	:	129691212S1S1

Anna Radziszewska,[Aff1]
Corresponding Affiliation: Aff1

Annette Bryant,[Aff1]

Karen Rosendahl,[Aff2]

Lil-Sophie Ording Müller,[Aff2]

Abdul Hassan,[Aff2]

Clara Malattia,[Aff3]

Sandrine Lacassagne,[Aff4]

Pierre Quartier,[Aff4]

Alberto Martini,[Aff3]

Patricia Woo,[Aff1 Aff2]

Aff1 University College London, UK
Aff2 Great Ormond Street Hospital for Children, London, UK
Aff3 Istituto Giannina Gaslini, Genoa, Italy
Aff4 Hôpital Necker, Paris, France

Introduction

Bone loss in inflammatory arthritis such as rheumatoid arthritis is partly due to aberrant expression of cytokines and bone homeostasis regulatory molecules, leading to excess bone resorption.

Objectives

To investigate if genetic factors affect the degree of cartilage and bone loss in JIA, irrespective of disease duration and treatment.

Methods

DNA was extracted from saliva samples from 80 JIA patients from Great Ormond Street Hospital, UK, 98 from Hôpital Necker, France, and 54 from Istituto Giannina Gaslini, Italy. Genetic variation was investigated using the tagging single nucleotide polymorphisms (tSNPs) approach. 17 candidate genes were selected for analysis: RANK, RANKL, osteoprotegerin (OPG), osteopontin, DKK-1, IL-1α, IL-1β, IL-1R1, IL-1R2, IL-1RN, IL-1RAP, IL-6, TGFβ1, IL-10, IL-19, IL-20, IL-24. 391 tSNPs were genotyped using the Illumina GoldenGate assay genotyping platform and KBioscience, UK. JADI-A scores, wrist MRI bone erosion scores, and X-ray Poznanski scores were taken at presentation (baseline) and after 1 year followup.

Results

At baseline patients were divided into those with no damage (JADI or MRI score of 0) or with

damage (any score>0). At 1 year follow-up patients were divided into those who had improved, unchanged, or worsened. Significant tSNPs from genetic association analysis using PLINK are presented below. Table 1.

Table 1

	JADI				MRI			
	Gene	**P**	**OR**	**n**	**Gene**	**P**	**OR**	**n**
Baseline (associated with damage)	upstream RANKL	0.0004	1.98	n=110 vs n=119	upstream DKK1	0.0022	NA	n=109 vs n=24
	RANKL promoter	0.0009	1.91		upstream DKK1	0.0037	NA	
	upstream RANKL	0.0036	0.57					
	OPG intronic	0.0094	1.68					
Followup (associated with improvement)	IL1R2 intronic	0.0024	0.48	n= 55 vs n=118	IL6 promoter	0.0047	5.19	n=32 vs n=53
	IL1R2 promoter	0.0043	2.05		IL19 intron	0.0065	3.52	
	upstream IL1R2	0.0050	0.50		between IL1R2 and IL1R1	0.0076	0.38	
	RANK intronic	0.0090	9.21	n= 55 vs n=17				
Followup (associated with no change)	downstream OPG	0.0081	3.16	n=101 vs n=17	IL20 promoter	0.0084	3.38	n=23 vs n=29

We observed weak correlations between JADI-A and MRI scores (Spearman's r = 0.298, p<0.0001), JADI-A and Poznanski scores (Spearman's r = -0.288, p=0.012), and Poznanski and MRI scores (Spearman's r = -0.381, p=0.001). Disease duration, activity, and treatment were varied and were not significantly associated with the damage parameters in this cohort.

Conclusion

Our findings suggest that polymorphisms in cytokine and bone remodelling genes such as RANKL or OPG may be associated with the degree of articular damage in JIA. Given the weak correlations we found between JADI-A and MRI scores, it is not surprising that different tSNPs were found to associate with MRI damage than with JADI-A damage. Further studies including a larger cohort of patients are needed to validate these findings.

Disclosure of interest

None declared.