Genomics, genetic basis of disease and functional genomics

AB0001

PLASMA miRNA PROFILE IN PATIENTS WITH HAND OSTEOARTHRITIS

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Background: MicroRNAs (miRNA) are short non-coding RNAs that can be involved in diverse physiological processes¹. Aberrant miRNA profiles have been shown in various diseases including osteoarthritis (OA)²; for instance, miR-21-5p or miR-140 are known for their altered expression in osteoarthritic cartilage^{3,4}. However, no screening of circulating miRNAs has been done in patients with hand OA (HOA) so far.

Objectives: Our aim was to profile circulating miRNAs in plasma of patients with HOA in screening and validation cohort.

Methods: We screened the expression of miRNA profiles in 4 patients with erosive (3 females, mean age=63.7±7 yrs) and 4 patients with non-erosive (3 females, mean age=62.4±6 yrs) HOA, and 4 control subjects (3 females, mean age=63.5±7 yrs). The validation cohort included 10 patients with erosive (7 females, mean age=67.5±7 yrs) and 10 patients with non-erosive (6 females, mean age=67.6±8 yrs) HOA, and 10 control subjects (8 females, mean age=64.3±8 yrs). Circulating miRNA screening were performed using TLDA and selected miRNAs were validated by qRT-PCR.

Results: Profiling circulating plasma discovered 42 miRNAs from 754 analysed miRNAs with different concentration among subjects, including miR-23a-3p (1.7 fold), -222-3p (2.0 fold), and -30e-3p (13.0 fold) to be elevated in patients with HOA compared to control subjects. In addition, six miRNAs were distinctive between erosive and non-erosive HOA, e.g. hsa-miR-24-3p was 2.3 times lower and hsa-miR-576-5p was 3.4 times higher in erosive compared to non-erosive disease.

Out of these selected miRNAs, qRT-PCR validated 42 miRNAs and confirmed 11 miRNAs (e.g., miR-23a-3p or -222-3p) with different concentration between patients and controls. However, no miRNAs distinguished between erosive and non-erosive HOA, although miR-101-3p (4.5 fold) and -320b (13.7 fold) almost reached statistical significance.

Conclusion: Based on our study, we identified 11 miRNAs that may have a potential as biomarkers of HOA. However, further studies on larger cohorts are needed.

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Acknowledgments: This work was supported by the project AZV no. NV18-01-00542 and MHCR No. 023728.

Disclosure of Interests: Jiří Baloun: None declared, Aneta Pekacova: None declared, Tereza Kropackova: None declared, Veronika Horvathova: None declared, Klára Prajzlerová: None declared, Mária Filková: None declared, Karel Pavelka Consultant of: Abbvie, MSD, BMS, Egis, Roche, UCB, Medac, Pfizer, Biogen, Speakers bureau: Abbvie, MSD, BMS, Egis, Roche, UCB, Medac, Pfizer, Biogen, Jiří Vencovsky: None declared, Ladislav Šenolt: None declared
DOI: 10.1136/annrheumdis-2020-eular.1938

AB0002

CONGENITAL DEFECTS IN A COHORT OF PREGNANT WOMEN FROM A CLINIC OF RHEUMATIC DISEASES AND PREGNANCY

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Background: Some studies have suggested an increased risk of adverse health outcomes for the child of patients with Rheumatic Diseases (RD), including neurodevelopmental disorders, congenital heart defects, hematological malignancies and autoimmune diseases. It is well known that 2 to 3% of

live births have a congenital defect. About 7 % of all newborn deaths are due to birth defects.

Objectives: Describe Genetical Evaluation in a cohort of pregnant patients with RD

Methods: We included 22 women from February to December 2019 from a Clinic of Pregnancy and Rheumatic Diseases in Hospital Universitario in Monterrey, Mexico. All spontaneous pregnancies (21 singletons, 1 double twin), with adequate prenatal control. Ten Rheumatoid Arthritis, Antiphospholipid Syndrome in 4 cases; 5 Systemic Lupus Erythematosus, 2 Sjögren's Syndrome and a case of Dermatomyositis. In the perinatal genetics approach, medical and familial history was obtained, and pedigree was developed; ultrasound information of 12 and 22 weeks of gestation was integrated, risks for aneuploidies were adjusted according to maternal age. At birth, the dysmorphological description was made, somatometry is performed, and the newborn screening were evaluated (metabolic, hearing, cardiac). Thus, giving genetic counseling for each case.

Results: Two patients were excluded, so 20 women with follow-up, 12 (60%) were born without complications or birth defects; in 3(15%) there were adverse events (a spontaneous abortion at 12 weeks-of-gestation [wg]; a fetal death in the case of twin pregnancy, at 34.1 wg, with facial asymmetry, intrauterine growth restriction; and a premature delivery, at 36.5 wg; no defects; there were 5(25%) congenital defects: a preauricular appendix, with normal renal ultrasound. A congenital heart disease (transposition of large vessels, tricuspid stenosis). A case of macrosomia (diabetic fetopathy); a heart block with perinatal pacemaker placement (mom with lupus). And in the latter case, Krabbe disease, even without confirming it. Table 1.

Table 1.

Maternal diagnosis	Effects on fetus/neonate	N (%)
Congenital Defects		5 (25%)
Antiphospholipid syndrome	Congenital Heart Disease	
Lupus erythematosus systemic	Heart Block with Perinatal Pacemaker Placement	
Rheumatoid arthritis	Krabbe Disease	
Rheumatoid arthritis	Preauricular appendix	
Sjögren Disease	Diabetic Fetopathy	
Adverse events		3 (15%)
Rheumatoid arthritis	Spontaneous Abortion	
Antiphospholipid syndrome	Fetal death	
Rheumatoid arthritis	Premature delivery	

Conclusion: One out of every 4 pregnancies of women with rheumatic diseases presented a congenital defect, of which, the heart diseases (CHD) have been described as of greater presentation in these groups.

It is very important that women with rheumatic diseases are well attached to a comprehensive clinic in which, in addition to receiving proper attention of their rheumatic disease, they have adequate preconception and prenatal control of their pregnancies, since there is a greater risk of congenital alterations and of perinatal adverse events, as shown by this cohort. Further research is needed to fully elucidate the potential disease-related factors that might lead to the increased risk of adverse health outcomes in offspring, as well as to improve the monitoring and control of their rheumatic diseases.

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Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2020-eular.4537

AB0003

SINGLE-NUCLEOTIDE POLYMORPHISMS (RS28493229 AND RS2290692) IN ITPKC GENE IN CHILDREN WITH KAWASAKI DISEASE

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Background: Kawasaki disease (KD) is an acute medium vessel vasculitis manifesting with mucocutaneous lesions and cardiac complications especially coronary artery lesions (CALs). Inositol 1,4,5-triphosphate 3-kinase C (ITPKC) gene polymorphisms are have been shown to be associated with susceptibility to KD and CAL.

Objectives: This study was designed to investigate the association of single nucleotide polymorphisms (SNPs) of the ITPKC gene with KD and CAL in Indian children.

Methods: Two SNPs of the ITPKC gene (rs28493229 and rs2290692) were studied in 50 cases of KD and 50 healthy controls. The Deoxyribonucleic acid