O17

IMMUNOLOGICAL INDICATORS OF POOR OUTCOME IN OLIGOARTICULAR JUVENILE IDIOPATHIC ARTHRITIS

F. Raggi[1,*], S. Pelassa[1], C. Rossi[1], F. Antonini[2], C. Trincianti[3], G. Filocamo[4], A. Civino[5], M. Gattorno[1], A. Ravelli[6], A. Consolaro[7], M. C. Bosco[1]

[1]Unit of Autoinflammatory Diseases and Immunodeficiencies, Pediatric Rheumatology Clinic, [2]Core Facilities, Department of Research and Diagnostics, IRCCS Istituto Giannina Gaslini, [3]Department of Neurosciences, Rehabilitation, Ophthalmology, Genetics and Maternal-Infantile Sciences (DiNOGMI), University of Genova, Genova, [4]SC Pediatric Immunorheumatology, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milano, [5]Pediatric Rheumatology and Immunology, Ospedale Vito Fazzi, Lecce, [6]Scientific Direction, [7]Pediatric Rheumatology Clinic, IRCCS Istituto Giannina Gaslini, Genova, Italy

Introduction: In Oligoarticular Juvenile Idiopathic Arthritis (OJIA), the mechanisms underlying the inflammatory processes within the joints and leading to polyarticular extension are poorly understood. However, the pathogenetic role of immune cells infiltrating the synovial environment is well known, and the involvement of extracellular vesicles (EVs) released by immune cells is being increasingly recognized. Many studies have focused on the effects of EVs released in synovial fluid (SF) of patients affected by adult rheumatic arthritis on disease progression. Immunologically active EVs are mainly released by macrophages (Mf) and T cells, participating in antigen presentation and immune regulation. A better understanding of the immunophenotypic profile of circulating and in situ infiltrated inflammatory cells in OJIA patients and of the surface protein cargo of released EVs may help earlier disease diagnosis and new therapeutic approaches.
Objectives: This study aimed at identifying specific immune cell subsets from samples of OJIA patients at disease onset, their activation markers, and expression of specific EV surface molecules, which could be used as indicators to predict polyarticular extension.

Methods: A total of 50 treatment-naïve OJIA patients was enrolled at the onset and followed-up for two years. Plasma (PL) and SF samples from 10 patients who presented an oligoarticular course (oOJIA) and 10 who developed a polyarticular course (pOJIA) were considered for the analysis. Mf and T cell subsets from PBMCs and SF mononuclear cells (SFMCs) were characterized by cytofluorimetry. Characterization of surface molecules of EVs isolated from SF and PL was carried out.
Results: SF-derived Mf in active joints of patients who developed pOJIA exhibit polarization toward the M1-like phenotype, as shown by predominance of the CD80 and the coexpressing CD80+/CD206+ or CD80+/CD163+ subsets respect to oOJIA patients associated with higher expression of the immunoregulatory receptor TREM1. No differences were observed in the M2 subsets between the groups of patients presenting the oOJIA and pOJIA course. PBMCs displayed the same percentage of M1 and M2, but higher presence of the $CD206^{+}/CD163^{+}$ subset in patients who developed pOJIA. A different state of T cell activation ($HLADR^{+}$) in both PBMCs and SFMCs and a different ratio of Treg in the SMFCs were also observed in oOJIA and pOJIA patients providing discrimination between outcome groups, whereas no differences were detectable in the percentages of naive, central memory, effector memory, and terminally differentiated effector memory $CD4^{+}$ and $CD8^{+}$ subsets derived from SFMCs and PBMCs. Interestingly, analysis on EV surface cargo showed higher expression in pOJIA of the glycoproteins CD9, CD44, and CD11c whose relevance was demonstrated in adult arthritis where their targeting is proposed as drug delivery strategy in disease treatment.
Conclusion: These data suggest that the number of CD80+/TREM-1+ Mf and the Treg subset in the SF of OJIA patients at disease onset might be helpful for early prediction of persistent/extended-to-be patients. Similarly, the expression levels of specific surface markers on SF-derived EVs might have a potential predictive value. These data provide novel mechanistic insights into OJIA pathophysiology and an important contribution in the search of new indicators for improving disease diagnostic accuracy.
Patient Consent: Not applicable (there are no patient data)
Disclosure of Interest: None declared