were defined according to the type and the duration of symptoms (Hyperacute painful shoulder, subacute inflammatory symptoms and chronic mechanical pain). Short-term response (up to 6 weeks) to treatment was also analyzed for the two first subgroups

Results: 25% of the patients consulting for shoulder pain had evidence of RCC as demonstrated by ultrasound. Hyperacute and subacute inflammatory symptoms were not linked to calcification (Hyperacute: 16 pts with 13pts without (p value : ns), subacute: 32 pts in both groups). The mean age (54 years) and female predominance (60%) were also similar in patients with or without calcification. However, patients with hyperacute painful shoulder with RCC were younger (mean years: 49 against 58 years; p: 0.007). None were <35 or > 60 years old and 75% of them were females. In 60% of cases of hyperacute painful shoulder linked to calcification, the acute flare was the first shoulder complaint compared to <30% in the overall sample (p: <0.0001).

More than a 1/3 of the patients with RCC (35% in chronic and 43% in acute symptom groups) had no other echographic lesion compared to < 5% of patients without RCC. Calcifications were rarely associated with partial or total rotator cuff rupture (<10% against 25% without, p: 0.007). Steroid infiltrations were mostly performed with rapid short-term response in the acute and subacute groups linked to calcification: 15/16, 24/34 against 4/13 p:0.001, 10/34 p:0.001 without calcification. Surgery was necessary in 7/101 pts with chronic symptoms without calcification against only 1/95 when calcifications were present (p:0.03).

Conclusion: Clinical and demographic data cannot clearly predict the presence of RCC in patients presenting with shoulder pain. However, acutely symptomatic RCC is found preferentially in middle aged women, often with no degenerative or traumatic echographic lesions. Steroid infiltration appears to be the treatment of choice when acute inflammatory symptoms linked to RCC are present

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Basic science in paediatric rheumatology

THU0505 INTRINSIC AND EXTRINSIC B CELL DEFECT IN DADA2 PATIENTS

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Background: ADA2 Deficiency is an autoinflammatory disease characterized by systemic vasculopathy, strokes and mild immunodeficiency. The defect is due to a mutation in ADA2 gene. It regulates the catabolism of extracellular adenosine, which is an important regulator of Class Switch Recombination in B lymphocytes.

Objectives: We addressed if ADA2 mutation affects directly B-cell function and the capacity of helper T cells to support B cells.

Methods: 14 patients carrying LOF mutations in ADA2 were examined. We analyzed immunophenotype by flow cytometry. B cells isolated from DADA patients or HD have been cultured alone or in co-culture with CD4+ T cells and *in vitro* B cell proliferation has been evaluated by CFSE dilution, whereas B cell differentiation to Immunoglobulins secreting cells in response to TLR9 agonist and T cell help has been evaluated by ELISA assay.

Results: Flow-cytometric analysis showed a significant reduction of switched memory B cells and of CD4+/CD8+ T cells. We identified an significant expansion of circulating Tfh cells in DADA2. Then we investigated a role of ADA2 in B cells: we found that it is expressed, secreted but the activity is strongly impaired in DADA2. We also addressed the interaction between B and T cells; we found that proliferation and differentiation of patients' B cells were not sustained from patient's T cells.

Moreover DADA2 T cells showed an impairment in the IL21 production and a downregulation of CD40L.

Conclusion: Our findings suggest that ADA2 mutation could affects directly B cell function and T cell help functions.

REFERENCES:

- [1] Zhou Q, et al. Early-onset stroke and vasculopathy associated with mutations in ADA2. *N Engl J Med* 2014 Mar 6;370(10):911-20.
- [2] Navon EP, et al. Mutant adenosine deaminase 2 in a polyarteritis nodosa vasculopathy. *N Engl J Med* 2014 Mar 6;370(10):921-31.
- [3] Schepp J, et al. Screening of 181 Patients with Antibody Deficiency for Deficiency of Adenosine Deaminase 2 sheds new lights on the disease in Adulthood. *Arthritis and Rheum* 2017 August; Vol. 69, 8:1689–1700.
- [4] Caorsi R, Monogenic polyarteritis: the lesson of ADA2 deficiency. *Pediatr Rheumatol Online J* 2016;14(1):51.
- [5] Caorsi R, et al. ADA2 deficiency (DADA2) as an unrecognised cause of early onset polyarteritis nodosa and stroke: a multicentre national study. *Ann Rheum Dis* 2017; 0:1-9.

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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., Elisabetta Traggiai Employee of: Novartis, Marco Gattorno Grant/research support from: MG has received unrestricted grants from Sobi and Novartis

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THU0506 MAST CELL DEFICIENCY AMPLIFIES INFLAMMATORY RESPONSE IN A MOUSE MODEL OF KAWASAKI'S DISEASE

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Background: Kawasaki's disease is a pediatric medium vessel vasculitis causing coronary arteritis and potentially coronary artery aneurysms. Higher systemic levels of Interleukin-6 (IL-6) in the first week of disease has been shown to be associated with a higher risk of coronary artery aneurysms (1, 2). Mice injected with *Candida albicans* water-soluble fraction (CAWS) develop coronary and aortic arteritis like that seen in Kawasaki's disease. Our prior work has demonstrated that mast cell degranulation can inhibit lipopolysaccharide (LPS)-induced IL-6 gene expression in the aorta and systemic IL-6 production (3).

Objectives: The objective of this study was to determine if mast cells play a role in the IL-6 homeostasis in an established mouse model of Kawasaki's disease (CAWS model).

Methods: 8-10-week-old male wild type controls (WT) and KitW-sh/W-sh mice (mast cell deficient, MCD) of C57Bl/6 background were randomly distributed into four groups (WT-PBS, WT-CAWS, MCD-PBS, MCD-CAWS). They were either injected intraperitoneally with PBS or CAWS (2 mg/mouse) daily for a period of 5 days. Eight animals from each group

were sacrificed at either 7, 14 or 30 days after the last injection and blood, aorta and heart specimens were harvested. A pathologist (OT), blinded to treatment groups, examined aortic root and adjacent myocardium specimens and assigned a score for the degree of inflammation (0-6).

Results: Seven MCD-CAWS mice died unexpectedly within 24 hours of the first CAWS injection. Autopsies reviewed marked liver sinusoidal dilation in all and patchy necrosis of the liver in 4. Similar, liver findings were seen in 75% of MCD-CAWS after 7 days, but not in other groups. MCD-CAWS mice had higher systemic IL-6 compared to WT-CAWS at both 7 days (208 ± 21 vs 152 ± 12 pg/ml; $p < 0.001$) and 14 days (226 ± 49 vs 169 ± 19 pg/ml; $p = 0.04$), but not at 30 days. By 14 days mice in MCD-CAWS had significantly higher serum INF γ compared to WT-CAWS mice (97 ± 4 vs 87 ± 7 pg/ml, $p = 0.0086$) which remained persistently elevated even at 30 days (103 ± 8 vs 91 ± 4 pg/ml; $p = 0.002$). TNF α was higher in MCD-CAWS compared to WT-CAWS at 7 days (258 ± 8 vs 243 ± 6.5 pg/ml, $p = 0.0016$), 14 days (266 ± 14 vs 239 ± 6 pg/ml, $p < 0.001$) and 30 days (326 ± 52 vs 256 ± 8 pg/ml, $p = 0.002$). The average aortic root inflammatory score was non-significantly higher in the MCD-CAWS group compared to WT-CAWS at both 7 days (1.5 vs 1.3) and 14 days (3.7 vs 2.4).

Conclusion: Mast cell deficiency resulted in higher systemic levels of IL-6, TNF α and INF γ in the CAWS mouse model of Kawasaki's disease. Similarly, mast cell deficiency resulted in more intense inflammation at the root of the aorta in this model. These results support the novel concept that mast cells play a protective role in reducing the initial systemic inflammatory response in Kawasaki's disease.

REFERENCES:

- [1] Ueno Y, Takano N, Kanegane H, Yokoi T, Yachie A, Miyawaki T, et al. The acute phase nature of interleukin 6: studies in Kawasaki disease and other febrile illnesses. *Clinical and experimental immunology*. 1989;76(3):337-42.
- [2] Chow YM, Lin CY, Hwang B. Serum and urinary interleukin-6 (IL-6) levels as predicting factors of Kawasaki disease activity. *Zhonghua Minguo xiao er ke yi xue hui za zhi [Journal] Zhonghua Minguo xiao er ke yi xue hui*. 1993;34(2):77-83.
- [3] Springer J, Raveendran V, Smith D, Maz M, Dileepan K. OP0138 Novel Role of Mast Cells in the Regulation of Large Vessel Vasculitis. *EULAR Paris, France: Ann Rheum Dis*; 2014. p. 112-3.

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THU0507

TYPE I INTERFERON SCORE AND INTERFERON INDUCED MEDIATORS CXCL10 AND NEOPTERIN ARE CORRELATED WITH DISEASE ACTIVITY IN JUVENILE DERMATOMYOSITIS

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Background: Interferons (IFNs) seem to play an important role in the pathogenesis of juvenile dermatomyositis (JDM). Our group previously reported that expression of both type I and type II IFN related genes is increased in muscle biopsies of JDM patients and correlates with histological and clinical features of the disease.

Objectives: The aim of this study was to investigate expression of interferon regulated genes (IRGs), as well as serum levels of two type I and type II IFN induced chemokines (CXCL9, CXCL10) and neopterin in peripheral blood of JDM patients and to assess their correlations with clinical and laboratory findings.

Methods: We collected 189 blood samples from 39 JDM patients at different time points during follow-up. In 11 patients we obtained the first blood sample at time of muscle biopsy. We measured expression of type I IRGs (IFI27, IFI44L, IFIT1, ISG15, RSAD2, SIGLEC1), IFN γ and type II IRGs (CXCL9, CITA, IDO1) by quantitative PCR (qPCR) and calculated a type I and type II IFN score for muscle and blood samples; serum

levels of CXCL9, CXCL10 and neopterin were analyzed by ELISA. Ten healthy subjects were used as controls (HC). At each visit, the following clinical data were recorded: physician's global assessment (PGA) of disease activity VAS (Visual Analogue Scale), cutaneous VAS, Cutaneous Assessment Tool (CAT) activity score, Childhood Myositis Assessment Score (CMAS), serum levels of creatine phosphokinase (CK, IU/l), presence of myositis specific or myositis associated antibodies (MSA/MAA), prednisone (or equivalent) dose (mg/kg/daily), ongoing immunosuppressive medications.

Results: Serum levels of CXCL9 were significantly correlated with muscle expression of IFN γ and type II IFN score. The correlation of CXCL10 levels with muscle type I and type II IFN score was weaker. Muscle expression of CXCL9 and CXCL10 correlated with serum levels of these chemokines. Type I IFN score in blood of JDM patients was increased compared to HC and significantly correlated with PGA, cutaneous VAS, CAT activity score. Serum levels of CXCL9 and CXCL10 were significantly higher in JDM patients compared to HC. MSA positive JDM patients showed higher levels of CXCL9 and CXCL10 compared to MSA negative patients. CXCL10 levels correlated with PGA and CMAS, but not with cutaneous disease activity. CXCL9 showed no significant association with the evaluated clinical features. Neopterin levels significantly correlated with PGA, cutaneous VAS, CAT activity score and CMAS.

Conclusion: Our findings indicate that expression of IRGs, measured as type I IFN score, and serum levels of CXCL10 and neopterin reflect specific features of disease activity in JDM, supporting their role as valuable disease biomarkers.

REFERENCES:

- [1] Moneta GM, Pires Marafon D, Marasco E, Rosina S, Verardo M, Fiorillo C, Minetti C, Bracci-Laudiero L, Ravelli A, De Benedetti F, Nicolai R. Muscle Expression of Type I and Type II Interferons Is Increased in Juvenile Dermatomyositis and Related to Clinical and Histological Features. *Arthritis Rheumatol*. 2018 Dec 15. doi: 10.1002/art.40800.

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THU0508

CHANGES IN MIR-17-92 CLUSTER EXPRESSION LINK SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS, MONOCYTE-TO-MACROPHAGE DIFFERENTIATION, AND INTERFERON REGULATION

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Background: MicroRNAs (miRNAs) are small noncoding RNAs which post-transcriptionally regulate gene expression. The miR-17-92 cluster is well studied in cancer biology and cellular differentiation; its overexpression has been found to serve a major oncogenic role in the targeting and downregulation of tumor-suppressive pathways, such as PTEN or TGF β . Our previous work identified several members of the cluster – miR-18, miR-19a/b, miR-20a, and miR-92a – with significantly higher levels in monocytes from patients with active Systemic Juvenile Idiopathic Arthritis (SJIA). SJIA is a chronic inflammatory disease of childhood with features of autoinflammation, and innate immune cells including monocytes have important roles in disease pathogenesis. Children with SJIA are at risk for life-threatening complications including Macrophage Activation Syndrome (MAS), an episode of overwhelming inflammation characterized by macrophage proliferation and driven by IFN γ .

Objectives: Characterize the regulation of the miR-17-92 cluster, define key targets, and determine the cluster's role in inflammation and SJIA.