Conclusion: CZP seems to be effective and safe in female patients with uveitis during pregnancy and neonates.

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AB1056

SYMPOMATIC SCLEROSING MESENTERITIS REVEALING ERDHEIM-CHESTER DISEASE: A RARE CONDITION MEDIATED BY BRAF

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Background: Sclerosing Mesenteritis (SM) refers to an entire spectrum of digestive inflammatory disorders. Diagnosis is based on imaging showing an increase of fat attenuation displacing bowel loops and is in most cases non-symptomatic. Several conditions (abdominal trauma/surgery, neoplasia, infectious and inflammatory diseases) are responsible for SM (1). Among neoplasia, Erdheim-Chester disease (ECD) is a rare clonal histiocytosis characterized by long bone involvement, peri-nephric fat infiltration and cardio-vascular involvement associated with compatible histology (2). Biopsy is mandatory to confirm tissue infiltration by histiocytes and detect somatic mutation. Almost 80% of ECD patients harbor mutation in mitogen activated protein (MAP) kinase pathway especially *BRAF*^{V600E}

gene mutation in about 60% of cases (3). No series of patients presenting both pathologies has been reported. Furthermore, no correlation with *BRAF* mutation status has been described in patient harboring SM and ECD.

Objectives: To describe the clinical, radiological and mutational status of patients harboring SM and ECD.

Methods: We reviewed the database of patients with histiocytic disorders in Besancon University Hospital. Patient required one abdominal computed tomography showing sclerosing mesenteritis and clinical/histological features of ECD to fulfill the inclusion criteria. All biopsy samples were investigated for mutation of MAP kinase pathway gene.

Results: Four patients suffered from SM and ECD. The median age at the diagnosis of ECD was 68 years old (61-72). All patients described abdominal pain and the mean duration between first symptoms and diagnosis of ECD was 12 months (4-19). The mean CRP level at diagnosis was 40.75 mg/L (5-117). Two patients were found to have myeloid neoplasms (chronic myelomonocytic leukemia (#2) and essential thrombocythemia (#4)) concurrent with ECD diagnosis.

Regarding abdominal computed tomography, all patients had a mesenteric mass associated with hyper-attenuated mesenteric fat and a "fat halo sign". One patient (#2) had ascites and one had splenomegaly (#4) but no patient had enlarged lymph nodes. CT also demonstrated peri-nephric fat infiltration ("hairy kidney") (4/4), vascular sheathing of aortic branches (3/4), adrenal hypertrophy (1/4) or ureter dilation (1/4). The mean SUV_{max} of the mesentery was 7.5 (4.1-10.9) at diagnosis on ¹⁸F- fluorodeoxyglucose-PET. Three patients underwent mesenteric fat biopsy and all samples exhibited ECD histology. Regarding mutational status, 75% (3/4) patients had *BRAF*^{V600E} mutation.

After initiation of therapies for ECD (targeted therapies for 3/4 patients), all patients had improvement of digestive symptoms and decreased of SUV_{max} on evaluation ¹⁸ FDG-PET during the follow up.

Conclusion: ECD should be investigated in patient with symptomatic SM especially if it is associated with peri-nephric fat infiltration. This condition is rare and might be driven by *BRAF* gene.

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AB1057

SCHNITZLER'S SYNDROME IN THE DIFFERENTIAL DIAGNOSIS OF ADULT STILL'S DISEASE

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Background: Schnitzler's syndrome (SchS) and adult onset Still disease (AOSD) are currently considered as multifactorial autoinflammatory diseases (MAIDs) and are classified as systemic inflammation with urticarial rash. Clinical similarities between SchS and AOSD (fever, urticarial rash, arthralgias), increased ESR and CRP and the efficacy of IL-1 inhibitors may lead to the diagnostic delay in SchS pts. Testing for monoclonal gammopathy helps establish the diagnosis in SchS pts but is not routinely used in AOSD pts.

Objectives: to examine demographic, clinical and laboratory characteristics, and the therapy of SchS pts in a single rheumatology center.

Methods: 5 SchS patients (2 females, 3 males), aged 32 to 68, underwent inpatient and outpatient examinations in the rheumatology center. All pts underwent a standard rheumatology examination, including ESR, CRP and M-gradient. 4 pts underwent genetic testing for mutations in *NLRP3*, *TNFRSF1A* genes to exclude MAIDs, such as CAPS and TRAPS.

Results: All pts were initially diagnosed with AOSD. The age at onset ranged between 28 and 66 years. Time to diagnosis varied from 2 to 22 years, being within 4 years in 4 of 5 pts. Patients presented with fever (4), urticarial rash (5) and musculoskeletal manifestations (5) (arthralgia in 3, bone pain in 4). Of 2 pts with serositis one presented with pericarditis and another – with pleuritis. Only 1 demonstrated a sore throat and polyneuropathy of the lower extremities. ESR and CRP were increased in all pts, leukocytosis was noted in 4 (Table 1). The

Table 1. Demographic, clinical and laboratory characteristics of patients with Schnitzler's syndrome

Pts	The age (y)	The age at onset (y)	Diagnosis delay (y)	ESR (<15 mm/h)	CRP (<6g/l)	M-gradient (g/l)	Anakinra	Canakinumab	The treatment duration (y)
1	51	40	4	31	107	7,1	0	1	5
2	53	28	22	40	29	5,7	0	0	0
3	36	29	3	140	44	7,8	0	1	3
4	58	53	3	100	192	7,6	1	1	0,5
5	69	66	2	49	96	5,1	1	1	0,5

Abbreviations: Pts – patients, y- years, ESR – erythrocyte sedimentation rate, CRP – C-reactive protein

monoclonal IgMk secretion was revealed in 5 pts, IgMk and IgM λ – in 1 and IgG κ and IgG λ - 1. No *NLRP3*, *TNFRSF1A* gene mutations were identified. Prior to the diagnosis, all pts were treated with glucocorticoids with a transient partial clinical response and a disease relapse after reducing the dose or stopping the treatment. 2 pts failed to respond to methotrexate and 1 – to hydroxychloroquine. 4 pts were prescribed with 150 mg canakinumab, a monoclonal antibody targeting IL-1, subcutaneously once every 8 weeks. The treatment duration varied from 6 months to 5 years. 2 pts, who initially received daily 100 mg anakinra subcutaneously for 2 to 3 months with a positive response, were further treated with canakinumab. During the treatment with canakinumab, all pts rapidly responded with a complete resolution of fever, rash, arthralgias and bone pains, an overall health improvement and a normalization in ESR and CRP levels. The therapy was well tolerated. In 1 patient, the intervals between canakinumab injections were prolonged to 5 months without any evidence of relapse. During this period, the male patient became a parent to a healthy child.

Conclusion: In rheumatology practice SchS can be misdiagnosed with AOSD. AOSD patients should be tested for monoclonal gammopathy. IL-1 inhibitors are a highly effective and well-tolerated treatment option for SchS. In SchS patients with a complete response to canakinumab, injection intervals can be individualized.

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AB1058 JOINT HYPERMOBILITY SYNDROME AND PRIMARY OPEN-ANGLE GLAUCOMA

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Background: Eye symptoms: myopia, prolapse of the upper eyelid, epiblepharon in the upper eyelid are small diagnostic criteria for joint hypermobility syndrome (JHS).

There are few publications in the literature on the relationship between JHS and primary open-angle glaucoma (POAG).

It is known that in the development of JHS, the distribution of collagen of types I and III with the predominance of collagen of type III is important, the latter is encoded by the COL3A1 gene. When using POAG in the connective tissue of the middle and deep layers of the sclera by the immunohistochemical method, intense focal accumulation of type I and III collagen was previously revealed, and in the layers of the sclera's own substance, type III collagen, unusual for it.

Objectives: To study articular and extraarticular clinical manifestations, instrumental, laboratory signs, as well as to conduct molecular genetic studies on the carriage of the Col3A1 gene in patients with a diagnosis of POAG and compare them.

Methods: Nine consecutive patients with an established diagnosis of POAG (burdened heredity by glaucoma) with arthralgia were sent for consultation to the V.A. Nasonova Research Institute of Rheumatology from the Moscow Helmholtz Research Institute of Eye Diseases. All patients are women, the average age is 56.7 $\pm$ 10.5 years, the average Beighton score - 4.86 $\pm$ 1.7, the mean value of the Westergren ESR - 11,8 $\pm$ 5.1 mm/h, CRP_{hs} - 4.9 $\pm$ 9.4 mg / l, all of them were seronegative for rheumatoid factor (RE) and ACCP. All patients responded to the JHS diagnosis according to the 1998 Brighton diagnostic criteria. DNA was isolated from the leukocyte fraction of venous blood using the Wizard DNA Purification Kit (Promega) according to the manufacturer's instructions. The study of gene polymorphisms was performed by the method of minisequencing with subsequent time-of-flight mass spectrometry of a sample on a matrix (MALDI-TOF) in the clinical diagnostic laboratory of NPF L1TEX LLC using a standard protocol (Wise C.A., 2003).

Results: 9 patients had arthralgia, 8 - vertebralgia, 3 - myalgia. 2 had a history of wrist joint dislocation, 7 had flat feet (3 of them had Hallucis valgus), 5 had spondylosis and spondylolisthesis (protrusions and disc herniation according to MRI of the spine), and 4 had excessive skin and / or striate atrophy of skin. Extraarticular manifestations: mitral valve prolapse was detected in 3 patients (in 1 of them + atrial septal defect) with ultrasound of the heart, in 3 - descent of

the internal organs (nephroptosis, uterine prolapse), in 4 - pronounced varicose veins of the lower extremities. All patients had a carrier state of the A allele identified by marker C.2092G> A and C allele c.2244T> C of the COL3A1 gene, and a family history of glaucoma. Identification of compliance with JHS diagnostic criteria and the presence of genetic factors (COL3A1 gene) in patients with POAG is of great scientific importance, since it confirms not only clinical associations, but also the genetic proximity of these two conditions. It is also difficult to overestimate the practical value, since patients with POAG need the help of a doctor in the treatment of their articular and other non-ophthalmological manifestations of JHS, and establishing a diagnosis of JHS will require a more thorough examination of the eyes in terms of detecting POAG, its treatment or prevention.

Conclusion: The association of JHS, POAG and COL3A1 gene necessitates further study of the association of JHS and POAG: POAG as a clinical manifestation of JHS, on the one hand, and the role of JHS as a possible risk factor for the development of POAG - on the other hand.

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AB1059 A RANDOMIZED, PLACEBO-CONTROLLED STUDY OF ANAKINRA IN PATIENTS WITH STILL'S DISEASE

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Background: Adult-onset Still's disease (AOSD) and systemic juvenile idiopathic arthritis (SJIA) are rare autoinflammatory disorders associated with an activated IL-1 pathway, characterized by spiking fever, rash, arthritis, lymphadenopathy, hepatosplenomegaly and serositis. There is a growing understanding that SJIA and AOSD are one disease with different ages of onset, i.e. Still's disease. The anaSTILLS study (anakinra in Still's disease) was designed to further evaluate efficacy and safety of anakinra in patients with Still's disease across all age groups.

Objectives: The primary objective was to demonstrate efficacy of anakinra versus placebo as assessed by ACR30 response with absence of fever at Week 2. Secondary objectives included: early onset of efficacy, sustained efficacy, time to study drug discontinuation, safety, pharmacokinetics, clinical signs and biomarkers.

Methods: 'anaSTILLS' was a randomized, double-blind, placebo-controlled, 12-week study including patients with active and newly diagnosed (6 months) Still's disease according to adapted ILAR criteria if <16, or Yamaguchi criteria, if ≥ 16 years of age at disease onset. Patients were randomized to anakinra 2 mg/kg (max 100 mg/day), 4 mg/kg (max 200 mg/day) or placebo.

Results: 12 patients were randomized and received study drug: 6 anakinra (2 mg/kg n=2, 4 mg/kg n=4) and 6 placebo, the study was terminated early due to slow recruitment. 1 patient on placebo had lymphoma, not Still's disease, and was excluded; thus in total 11 patients were analyzed for efficacy, 8 were children [median (range) age=4.0 (1-11) years] and 3 were adults [median (range) age=32.0 (25-51) years]. 55% were male and the mean symptom duration was 74.2 days. All patients on anakinra but none on placebo achieved ACR30 response with absence of fever at Week 2 (p-value=0.0022). The efficacy of anakinra was further demonstrated by superiority to placebo in ACR50/70/90 responses with absence of fever at Week 2. All placebo patients discontinued the study within 6 weeks, 2 due to progressive disease, 2 due to lack of efficacy and 1 due to withdrawal by patient. There was a numerically higher proportion with early onset of efficacy (Week 1) in the anakinra group compared to placebo. The