inhibitors (baricitinib and tofacitinib, respectively), one patients with anti-TNF (infliximab) and another one with anti-CD20 (rituximab).
Conclusion: In general, our results match with what it is published in the literature.
For the treatment of AOSD has been used high doses of ASA (4g/day) or NSAID. However, the required doses (with their respective adverse effects), its limited responses and the frequent relapses after its suppression make difficult to maintain it. Nowadays, the systemic glucocorticoids are our first choice (0,5 to 1 mg/kg/day). A high average of our patients have a positive response with it, but in a 54% of the cases were neccesary to add methotrexate or others DMARDs because of a partial response with steroids.
In the physiopathology of the AOSD there is an increase of pro-inflammatory cytokines, as the tumor necrosis factor, IL-1 e IL-6. The use of therapies that inhibit these molecules (anti-TNF, anakinra or canakinumab as anti-IL1 or tocilizumab or sarilumab as anti IL-6) is being a progress. The inhibitors of IL-1 can be more efficient for systemic manifestations, while the inhibitors of IL-6 are for articular and systemic affectation. The TNF inhibitors should being used for the articular affectation only. In our patient cohort there is no patient with anti-IL1, a patient in clinical remission with anti-TNF and another one with anti-IL-6. Prospective studies with a higher number of patients is neccesary to define better the AOSD treatment.
Disclosure of Interests: None declared
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AB1077 ANTI-IL6-RECEPTOR TOCILIZUMAB IN GRAVES' ORBITOPATHY. MULTICENTER STUDY OF 46 PATIENTS IN CLINICAL PRACTICE

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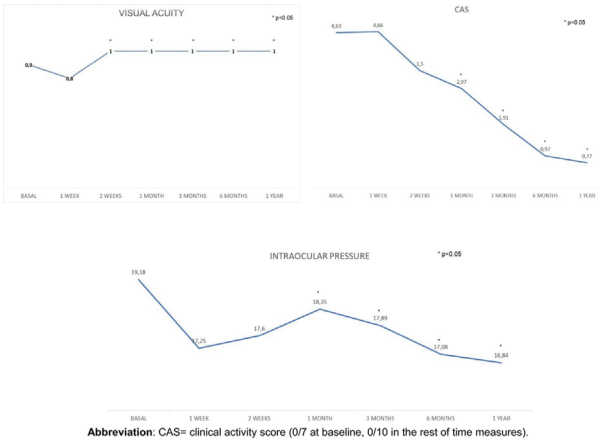
Background: Graves' orbitopathy (GO) is the most common and important extrathyroidal manifestation of Graves' disease. Corticostereoids and conventional immunosuppressors are not always effective or well tolerated. The IL-6 receptor antibody tocilizumab (TCZ) has demonstrated efficacy in the treatment of this pathology.
Objectives: To assess the efficacy of TCZ in refractory thyroid associated orbitopathy (TAO) due to Grave's disease.
Methods: Multicenter study of 46 patients with TAO refractory to conventional immunosuppressive therapy.
Results: We studied 46 patients (85 eyes) (37 women/9 men); mean age at diagnosis 49.2±11.8 years. Besides oral corticosteroids, before the onset of TCZ patients had been treated with pulses of iv methylprednisolone (42), radioactive iodine (4), methotrexate (2) and other drugs (selenium in 11 cases, methimazole in 8, leflunomide in 1 and azathioprine in 1). 7 patients underwent ocular urgent decompressive surgery.
According to the classification of severity of the EUGOGO group (European Group on Graves' Orbitopathy) using the clinical activity score (CAS), before TCZ onset patients whose data were available had severe (27 eyes) or moderate (34 eyes) disease. Moreover, patients presented exophthalmos (53 eyes), strabismus (37 eyes), muscle fibrosis (38 eyes) and dysthyroid optic neuropathy (10 eyes).
TCZ was used in monotherapy (43) or combined with methotrexate (2) or azathioprine (1) at 8 mg/kg/iv/4 w (41) or 162 mg/sc/w (5). TCZ yielded rapid and maintained improvement in all ocular parameters as shown in Figures.

FIGURES 1,2,3. Improvement of ocular parameters with TCZ therapy.
Data are expressed as mean or median.



Abbreviation: CAS= clinical activity score (0/7 at baseline, 0/10 in the rest of time measures).

Figure 1

After a mean of 7.42±6.41 months using TCZ and a mean follow-up of 16.47±11.99 months, all patients experienced ocular improvement, with TCZ withdrawal in 28 cases due to complete remission (10), improvement (12) or stability of ocular inflammation (3), inefficacy (2) and total thyroidectomy (1). Only 5 relevant adverse effects were observed (neutropenia, external otitis, otitis media, costal osteitis and gingival hyperplasia, 1 each).
Conclusion: TCZ appears to be a useful and secure option in GO treatment.

REFERENCES

[1] Bartalena L, et al. Consensus statement of the European group on Graves' orbitopathy (EUGOGO) on management of Graves' orbitopathy. Thyroid. 2008; 18 (3:333-346).
[2] Russell DJ, et al. Tocilizumab as a steroid sparing agent for the treatment of Graves' orbitopathy. Am J Ophthalmol Case Rep. 2017 Jul 8;7:146-148.

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AB1078 RED CELL DISTRIBUTION WIDTH (RDW) – A NEW POSSIBLE DISEASE ACTIVITY PREDICTOR IN RELAPSING POLYCHONDRITIS

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Background: Relapsing polychondritis (RP) is a rare condition defined by recurrent inflammation of cartilaginous tissue and systemic manifestations. Biomarkers for RP diagnosis and assessment of disease activity, damage and prognostic in clinical practice are currently lacking. Red blood cell distribution width (RDW) is an index of erythrocyte size variation depicting

anizocytosis. RDW is routinely assessed, is not influenced by infections and its standard deviation (RDW-SD) does not depend on medium corpuscular volume. Recent studies showed an increased RDW in various autoimmune diseases (systemic lupus erythematosus, Sjogren's syndrome, rheumatoid arthritis, systemic vasculitis), correlating with inflammatory markers and disease activity. Also, the RDW seen in solid tumors and hematological cancers has prognostic value.

Objectives: To asses the RDW-SD in RP patients, its relation with the disease activity and with the presence of neoplasia

Methods: We performed a retrospective study on the patients diagnosed with RP in a tertiary Rheumatology department between January 2017 and January 2019, using the Atlasmed data management system of the institution. The concomitant diseases and the inflammation parameters were recorded. The RP activity was measured using RPDAI (relapsing polychondritis disease activity index). The correlation between variables were calculated using GraphPad Prism.

Results: We identified 20 patients, median age 59.04 years (range 38-81), with a male-to-female ratio of 1: 5.66. An associated autoimune disease (Sjogren syndrome, Hashimoto thyroiditis, systemic lupus erythematosus, rheumatoid arthritis, psoriatic arthritis) was found in 85% of pacients. Moreover, 40% of the pacients had various types of solid or hematologic neoplasia, including myelodysplastic syndrome. An elevated RDW-SD was seen in 90% of RP patients. The average RPDAI was 10.6 points. RDW-SD significantly correlated to RPDAI (p=0.0012). Of the inflammatory parameters, RDW-SD was not found to be related to ESR and CRP. RDW-SD increased with age, but no correlation was found between RPDAI and age. All pacients with neoplasia had abnormally high RDW-SD. Nevertheless, RDW-SD was not significantly different in RP patients with or without neoplasia (Mann-Whitney test, p=0.56).

Conclusion: RP was frequently associated with other autoimune diseases, but also with neoplasia.The positive correlation of RDW-SD and RPDAI in RP suggests a possible new, clinically employable, biomarker of disease activity.

REFERENCES

[1] Arnaud L et al, Autoimmun Rev 2012; 12(2):204-9. doi:10.1016/j.autrev.2012.06.005.
[2] Hu ZD, JLPM 2016, doi: 10.21037/jlpm.2016.10.02

Disclosure of Interests: None declared
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AB1079 **CHECKPOINT INHIBITOR-ASSOCIATED ARTHRITIS: PHENOTYPES AND CYTOKINE ASSOCIATIONS**

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Background: Immune checkpoint inhibitors (CI) have revolutionized cancer management, but can also cause immune-related adverse events. Five percent of CI-treated patients develop inflammatory arthritis, but it is poorly defined phenotypically and immunologically.

Objectives: To characterize phenotypes of CI-associated arthritis, and compare cytokine levels in these patients to rheumatoid arthritis (RA) and osteoarthritis (OA) controls.

Methods: Patients referred for CI-associated arthralgia or arthritis were prospectively enrolled in an institutional registry. Serum was collected when patients underwent phlebotomy for a clinical indication. We used a Luminex Human Magnetic Assay to measure levels of IL-1β, IL-2, IL-6, IL-8, IL-10, IL-12, IL-17, IL-22, TNF, IFN-γ, PD-L1, CCL2, CXCL2, CXCL13, OSM, CCL20, GM-CSF, CXCL-11 in CI-treated patients, and in stored serum from 7 RA patients (matched for medication, age, sex, CDAI) and 4 OA patients (age, sex matched). All comparisons were planned a priori.

Results: Thirty-six patients were enrolled 5/1/18-1/25/19. Median [IQR] age was 67[58-78], 18(50%) were female, 14(39%) were smokers and 13 (36%) had melanoma. Twenty-two (61%) were on anti-PD1 or PD-L1 monotherapy, and the remainder were on combination CI. Phenotypes included 1. Small joint involvement in 17(47%), 2. Exclusively large joint involvement in 6(17%), 3. Arthralgia without arthritis in 9(25%), and 4. Polymyalgia rheumatica in 4(11%). In all, 7(19%) had concomitant tenosynovitis or enthesitis, mostly accompanying large joint arthritis or arthralgia (6/7). Median CDAI at entry was 11[7-23] and median ESR 29[18-44]. The majority (58%) of patients with the small joint phenotype were RF and/or CCP positive and one had erosive disease, compared to none with the large joint phenotype. ANA positivity was common (74%) and did not vary across phenotypes. Median time of symptom onset was 4 [0.8-12] months after CI initiation. Median follow up was 7[3-22] months but only 5(14%) had resolution of arthritis off medication during that period. 22(61%) required CI discontinuation, 5(14%) due to arthritis. 29 (81%) required steroids including 15(42%) who required >20mg prednisone. 19(53%) required a synthetic DMARD and 5(14%) required a biologic DMARD. Of 33 patients with known cancer status, 15(45%) had a complete response, 5(15%) a partial response, 5(15%) "stable" disease, 6 (18%) progression, and 2(6%) died. Cytokines were measured in 22 patients, who were similar to the cohort as a whole except for more CCP positivity (p=0.02). CI patients with the small joint phenotype had higher levels of IL-6 than RA controls (p=0.04) (Figure 1) and IL-6 levels trended higher in the small joint vs. exclusively large joint phenotype (Figure 2). The B cell chemoattractant CXCL13, a factor produced by T peripheral helper cells in RA synovium[1], trended higher in the serum of CI patients (Figure 3). Other cytokine levels did not differ significantly in patients with the small joint vs. exclusively large joint phenotype, or in CI-arthritis patients vs. controls.

Conclusion: Half of patients with CI-arthritis present with an RA-like phenotype with small joint involvement and frequent seropositivity, and have elevated levels of IL-6 compared to RA patients. This small joint phenotype may represent an accelerated form of RA.

REFERENCES

[1] Rao DA, et al. Nature 2017: 542(7639):110-114

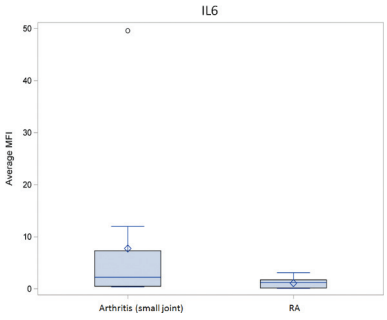

Figure 1. MFI=mean fluorescent intensity

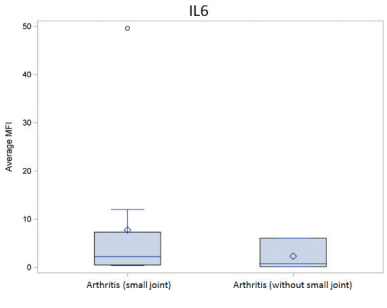

Figure 2

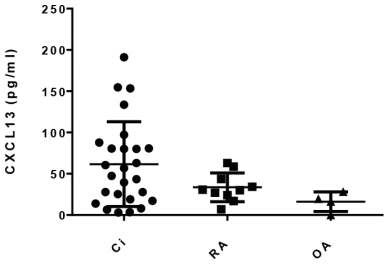

Figure 3