and a systematic search was carried out specifically for identification of deleterious genetic variants in genes involved in novel inflammatory pathways.

Results: The index case was coming from a consanguineous family of Assyrian origin, who is now 22-year-old male. He presented to our outpatient clinic with recurrent attacks of fever, urticarial rash on the extremities and trunk, conjunctival injections and arthralgia, without a trigger or more frequently following an infection. His attacks started when he was 13, and two to three days lasting attacks recurred more frequently during warm weather conditions or following hot baths. He had highly elevated CRP and ESR during attacks, but his acute phase response did not return to normal values in between the flares. Low C3 and C4 values were also observed during asymptomatic periods. His ANA test became positive during the course of his disease, with an increasing titer in the last year. He responded partially to corticosteroids as well as canakinumab and anakinra treatments, and he is currently on low dose steroids and 100 to 200 mg/day anakinra. Whole exome sequencing revealed a deleterious homozygous c.769C>T mutation in AGLB3 (ATP/GTP binding protein-like 3) gene, which results in early termination of the protein (p.Gln257Ter) and deletion of the functional carboxypeptidase domain. This protein belongs to metalloproteases that mediate both deglutamylation and deaspartylation of target proteins. AGLB3 is suggested to catalyse the deglutamylation of polyglutamate side chains, especially in proteins such as tubulins. Also, STRING search revealed the interaction of AGLB3 with complement regulatory proteins, such as CD46, CD55, and CD59, which are potent inhibitors of the complement membrane attack complex. We searched databases from Turkey and other sources including 1000 Genomes Project data, and we could not identify this variant in other individuals.

Conclusions: This study identifies the AGLB3 metalloprotease gene as a potential autoinflammatory gene involved in a novel pathway and possibly associated with hypocomplementemic urticarial vasculitis phenotype. Previously, DNASE1L3 mutations have been associated with hypocomplementemic urticarial vasculitis and systemic lupus erythematosus phenotype. The loss of function mutation in the AGLB3 may result in a potent innate inflammatory response as well as autoimmunity through a new pathway, which is resulting in lower complement levels and ANA positivity along with recurrent inflammatory episodes. This complex phenotype explains a partial response to the IL-1 blockade, and further studies in patients/families with a similar phenotype are needed.

Disclosure of Interest: None declared

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SAT0598

SYSTEMATIC LITERATURE REVIEW ON THE EFFICACY AND SAFETY OF IMMUNOMODULATORY DRUGS IN PATIENTS WITH NONINFECTIOUS INTERMEDIATE AND POSTERIOR UVEITIS, PANUVEITIS AND MACULAR OEDEMA

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Background: Posterior segment uveitis (PSU) is a sight-threatening condition

Objectives: To perform a systematic review of the literature on the use of immunomodulatory drugs in adult patients with non-infectious and non-malignant PSU including intermediate (IU) and posterior uveitis (PU), panuveitis (PanU) and macular oedema (ME).

Methods: Search strategies were designed for Medline, Embase, and Cochrane Library for articles with clinical, safety or cost-effectivity data up to, Jan 2017 followed by secondary search from their bibliography. Quality was assessed (Jadad/Oxford)

Results: From 1103 articles, 31 moderate quality clinical trials (CT) were selected, prospective/retrospective, with variability in mean duration, No. and patients' characteristics. PSU was treated with synthetic DMARDs methotrexate (MTX), azathioprine (AZA), cyclosporine A (CsA), cyclophosphamide (CyC), tacrolimus, sirolimus, micophenolate (MMF) and interferon β , and biologic DMARDs ranibizumab, dexamethasone, rituximab (RTX), secukinumab, adalimumab (ADA), bevacizumab and infliximab (IFX) at usual dosages. Most common measures: visual acuity (VA), macular thickness and vitreous haze. MTX vs.MMF, was effective in IU, PU and PanU, with no differences in efficacy and adverse events (AEs), neither in Vogt-Koyanagi-Harada. MTX was effective with RTX, and SC was inferior to IFN β with lower rate of AEs in IU with cistoid ME (CME). CsA did not show efficacy vs. placebo (pbo), with more neurological AEs. Tacrolimus vs. CsA was safer with similar efficacy, and CsA was useful with no differences vs.

prednisone (pred) or vs.CsG, and similar vs.CYC at 2 y in Behçet PSU. CsA +pred + ketoconazole combined showed additional benefits. CYC+AZA were effective in PU, except for VA and retinal vasculitis, with no differences vs. RTX +MTX. CYC was useful in serpinoid choroiditis $\pm$ dexamethasone. ADA was useful in IU, PU and PanU vs. pbo. IFX in Behçet PSU, was more effective vs. prednisone +CsA + AZA/MTX. Intravitreal ADA and IFX did not show any benefit. Secukinumab vs. pbo did not prevent recurrences. In another RCT, IV route showed a higher response rate vs.SC for 30 mg/kg, with similar rate of EAs. Intravitreal bevacizumab was effective in multifocal choroiditis and CME. Intravitreal ranibizumab was useful in pigmentary retinitis +CME. Dexamethasone in Behçet PSU did not show benefit vs. pbo. Tacrolimus as 2nd line in PU was effective $\pm$ pred. Intravitreal and subconjunctival sirolimus were effective in IU, PU and PanU in vitreal haze but not VA and ME, improving functional scores

Studies flow chart

Conclusions: 1 Moderate quality of evidence

2 Variability in patients, definitions and outcomes

3 Systemic DMARDs MTX, MMF, CsA, CyC, tacrolimus, sirolimus, MMF and IFN β were useful in PSU;AZA in combination

4 Biologic DMARDs ADA, IFX (systemic), ranibizumab, bevacizumab (intravitreal) were useful, dexamethasone did not show efficacy. Possible efficacy of secukinumab

5 Intravitreal anti-TNF (ADA,IFX) were not useful

Disclosure of Interest: None declared

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SAT0599

IDIOPATHIC GRANULOMATOUS MASTITIS MAY RESPONSE WELL TO COMBINATION OF IMMUNOSUPPRESSIVES AND GLUCOCORTICOIDS

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Background: Idiopathic granulomatous mastitis (IGM) is a rare inflammatory disease of breast. Corticosteroids (CS) and immunosuppressive agents constitute treatment alternatives other than surgery.

Objectives: To evaluate the clinical characteristics and treatment responses of IGM patients followed up in our clinic.

Methods: The medical records of 70 IGM patients who were referred to Hacettepe University Rheumatology Clinic were examined. Forty-four patients who had at least one visit in the last 2 years were included in the analysis. Demographic, clinical and laboratory characteristics of the patients, treatments, clinical and/or ultrasonographically measured lesion sizes at the time of diagnosis and at the last follow-up were recorded. Complete and partial response in the last control visit were defined as $\geq 50\%$ and $<50\%$ decrease in the lesion size, respectively. Lesions which are stable or increasing in size was accepted as unresponsive. Increase in the drug dose by the clinician or increasing of the lesion size during follow-up were considered as relapse.

Results: Median age was 35.7 (24.3–57.2) years and median symptom duration was 2.5 (0.2–54.1) months at baseline. Palpable mass (90.9%) and breast pain (88.1%) were the most common symptoms. Skin fistules and axillary lymphadenopathy were present in 16 (37.2%) and 15 (34.1%) patients, respectively. Erythema nodosum was seen in 5 (11.4%) patients during follow-up. The median follow-up duration was 10.5 (1.05–99.6) months. CS monotherapy and combination of CS and immunosuppressive were used in 3 (7.8%) and 38 (86.4%) patients, respectively. Three patients were followed up without treatment. The first immunosuppressive agent was methotrexate (MTX) in 32 patients (84.2%) and

azathiopurine (AZA) in 6 patients (15.7%). In one patient, MTX was switched to AZA due to hepatotoxicity. Treatment regimens and responses of the patients are summarised in table 1. IGM lesions disappeared in 24 patients at the end of follow-up. In two patients who were on MTX and KS, surgical excision was required because of unresponsiveness. Among relapsed patients (n=5), 2 patients were on MTX and KS, 1 patient was on AZA and KS and 2 patients were on KS at the time of relapse. In one patient, relapse was observed 1 year after cessation of MTX and KS.

Abstract SAT0599 – Table 1. First line treatments and responses at last follow-up visit*

	MTX+CS (n=32)	AZA+CS (n=6)	CS (n=3)	Observation (n=3)
Age*, years	36.1 (25.6-50.3)	33.8 (28.2-39.9)	28.9 (24.3-57.2)	29.4 (29.4-37.1)
Follow-up duration*, months	8.3 (1.5-54.4)	26.0 (13.8-99.5)	9.6 (3.0-35.8)	8.6 (1.0-13.4)
Duration of immunosuppressive treatment*, months	7.3 (0.9-28.2)	12.9 (8.2-27.3)	-	-
Immunosuppressive dose**	15 (10-15)	150 (100-150)	-	-
Duration of CS treatment*, months	7.0 (0.9-25.8)	13.7 (1.9-99.5)	2.5 (2.0-9.6)	-
Initial CS dose*,mg	30 (10-40)	20 (10-30)	20 (10-30)	-
CS dose at last control visit*,mg	7.5 (0-30)	0 (0-10)	10 (10-15)	-
Patients who discontinued CS, n (%)	12 (37.5)	3 (50.0)	-	-
Response to treatment				
Unresponsive, n (%)	5 (17.2)	1 (16.7)	-	-
Partial response, n (%)	1 (3.4)	-	1 (33.3)	-
Complete response, n (%)	23 (79.2)	5 (83.3)	2 (66.7)	2 (66.7)

* Lesion size at last follow-up visit was available in 40 patients

*Values are given as median (min-max)

*Treatment doses are presented as mg/week for MTX and mg/day for AZA.

Conclusions: In a case series previously published by our study group, the efficacy of the combined use of KS and immunosuppressant's in IGM treatment was retrospectively studied.¹ In this study, the efficacy of immunosuppressive therapy has been demonstrated with prospective approach.

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Disclosure of Interest: None declared

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SAT0600 MULTICENTRIC RETICULOHISTIOCYTOSIS (1980–2017): CLINICAL CORRELATES, TREATMENT OUTCOMES & ASSOCIATION WITH AUTOIMMUNITY & MALIGNANCY

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Background: Multicentric reticulohistiocytosis (MRH) is a rare systemic disease characterised by papulo-nodular skin eruptions and a rapidly progressive, deforming arthritis. It can mimic rheumatic disorders such as rheumatoid arthritis or dermatomyositis. Immunosuppression is often helpful, but challenging due to the association of MRH with malignancy.

Objectives: To examine the clinical correlates and outcomes of MRH and its association with malignancy and other autoimmune conditions

Methods: A retrospective review of all patients with MRH treated at our institution between 01/01/1980 and 04/30/2017 was performed. Demographics, clinical features, laboratory tests, imaging findings, histopathology, treatments and outcomes were abstracted. Data on autoimmune disorders and malignancies before and after MRH diagnosis were collected.

Results: We identified 24 patients with MRH (58% female, 75% Caucasian, mean age at diagnosis 52 y). Median length of follow up was 2.3 y. All patients had confirmed diagnosis by histopathology (23 skin, 7 synovial). All patients had cutaneous and articular involvement. Nodular skin lesions were noted in 96% patients (periungual area and dorsal hand in 87%, periarticular 61% [around DIP 42%, PIP 25%, MCP 8%], face 54%, arms 42%, back 29%, neck 21%, legs 21%, ears 12%, scalp 12%). Mucosal nodules were noted in 30%. Regarding articular involvement, 22 (92%) had arthralgia, 21 (88%) patients had joint swelling, and 13 (54%) had synovitis. Frequency of joint involvement was upper extremity PIP (29%) > upper extremity DIPs, MCPs, wrist > MTPs, Toes > Knees > Elbows. Radiographic erosions were noted in 67% patients. Constitutional symptoms included fatigue,¹⁵ unintentional weight loss,¹⁰ lymphadenopathy⁴ and pruritis.¹¹ Systemic features included dysphagia,⁵ photosensitivity,⁴ dry eyes,³ pericarditis² and pleuritis.¹ Several patients had positive autoimmune serologies: ANA,⁸ RF,⁵ Anti-CCP,³ SS-A,³ SS-B,² Anti-DsDNA.¹ A third of patients had concomitant autoimmune disorders: inflammatory arthritis,³ Sjögrens,¹ chronic focal granulomatous nephritis,¹ JRA,¹ psoriasis,¹ myasthenia gravis and ITP.¹ A third of patients (8/24) had malignancy: malignant melanoma,³ basal cell carcinoma,² and 1 each with ovarian carcinoma, squamous cell carcinoma lung, peritoneal

adenocarcinoma, and endometrial carcinoma. Most patients were treated with systemic glucocorticoids¹⁵ and oral DMARDs¹³: methotrexate,⁸ cyclophosphamide,¹⁰ chlorambucil² and cyclosporine.¹ Biologics were used in 4 patients (1 infliximab, 2 etanercept, 1 adalimumab). Only 2 patients had complete resolution of their symptoms, while majority showed only partial improvement. 10 (44%) patients developed joint deformities involving: wrist,⁴ MCP,⁴ PIP,⁷ DIP,⁴ knee² and MTP.³ None had arthritis mutilans. 75% patients were alive at last follow up.

Conclusions: To our knowledge, this is the largest series of MRH patients from a single institution, highlighting the rarity of the condition, and an unmet need for treatment options that can allow sustained disease remission. We emphasise the need for histopathology to distinguish it from mimicking rheumatic conditions and initiating early aggressive treatment to potentially prevent deforming joint disease. A high vigilance for malignancy and other autoimmune diseases is necessary.

Disclosure of Interest: None declared

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SAT0601 ANTI-IL6-RECEPTOR TOLICIZUMAB IN GRAVES' ORBITOPATHY. MULTICENTER STUDY OF 29 PATIENTS

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Objectives: To assess the efficacy of Tocilizumab (TCZ) in refractory thyroid associated orbitopathy (TAO) due to Grave's disease.

Methods: Multicenter study of 29 patients with TAO refractory to conventional immunosuppressive therapy.

Results: We studied 29 patients (58 eyes) (23 women/6 men); mean age at diagnosis 48.79±12.39 years. Besides oral corticosteroids and before the onset of TCZ, patients had been treated with pulses of intravenous methylprednisolone (n=24), methotrexate (n=2) and other drugs (methimazole in 4 cases, leflunomide in 1, selenium in 9). Urgent decompressive surgery had to be performed in 2 patients.

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 (n=14 eyes) or moderate