AB0975 **INCIDENCE OF INFECTIONS WITH BIOLOGICAL THERAPIES IN PARAGUAYAN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS: BIOBADAGUAY (BIOLOGICAL THERAPIES ADVERSE EVENTS PARAGUAYAN-URUGUAYAN REGISTER)**

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Background: Biological Therapies (BT) are important in the therapeutic arsenal of rheumatic diseases; however there is an increased risk of infections with their use.
Objectives: To determine the frequency and type of infections in Paraguayan patients with Juvenile Idiopathic Arthritis (JIA), included in the BIOBADAGUAY Register.
Methods: A prospective observational study of patients with JIA treated with BT, included in the BIOBADAGUAY Register. Patients at the onset of BT were included. The change and/or discontinuation of BT and the occurrence of adverse events (AEs) were recorded. Infectious events as affected organ, type, severity, outcome and need of temporary or permanent suspension of the biological agent were analyzed.
Results: 59 patients with JIA and 69 BT were identified between May 2012 and December 2016. Female: 63% (37), Men: 37% (22). The mean age was 10 (3–18) years old. Mean disease progression of 2.8 (0.2–12) years from the diagnosis to BT beginning. JIA subtypes: poliarticular negative RF (27%), oligoarticular (27%: extended 22% and persistent 5%), enthesitis related arthritis (21%), systemic (12%), poliarticular positive RF (7%), psoriatic (3%), other (indeterminate) (3%). Biologic treatments: Adalimumab (ADM) 41 (59%), Etanercept (ETN) 19 (28%), Tolicizumab (TCZ) 9 (13%). There were 83 AEs of all treatments, 80 (96%) no serious and 3 (4%) severe with 1 death. Infections and infestations 54 (65%) of AEs were recorded. Of all TB infections: the 94% (51) were not serious and the 63% (34) required temporal discontinuation. Most infectious recovered without sequelae, except one death due to pneumonia (Table 1).

Type	Number AA	Agent	Suspension	Complete recovered
Respiratory Infection	33	18 ADM	21 Temporal	Yes
Infection		9 ETN		
		6 TCZ		
	1	1 TCZ	Yes	No (Death)
Pulmonary Tuberculosis	1	1 ETN	1 Temporal	Yes
Dengue	3	2 ADM	3 Temporal	Yes
		1 ETN		
Infectious Diarrea	3	1 ADM	3 Temporal	Yes
		1 TCZ		
		1 TCZ		
Urinary Infection	2	1 ETN	2 Temporal	Yes
		1 ADM		
Chickenpox	1	1 ADM	Temporal	Yes
Herpes	2	2 ADM	No	Yes
Toxoplasmosis	1	1 ADM	1 Temporal	Yes
Vulvovaginitis	1	1 ADM	No	Yes
Skin Infection	5	1 ADM	2 Temporal	Yes
		3 ETN		
		1 TCZ		
Scabies	1	1 TCZ	No	Yes
Total	54	28 ADM	34 Temporal	
		16 ETN		
		10 TCZ		

Conclusions: 1) Infections and infestations (65%) were the AEs more frequently observed. 2) Of al Infections, respiratory tract iwere the most frequently observed. 3) Most of the infections were not serious and recovered without sequela. 4) The most frequently agent involved in infectious events was ADM (52% of all infections); even so it is most frequently administered agent. 5) Increased number of patients, greater diversity of treatment as well as a longer data to corroborate the observation period is required.
Disclosure of Interest: None declared
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Other orphan diseases

AB0976 **REMISSION OF MULTICENTRIC RETICULOHISTIOCYTOSIS WITH COMBINATION TOCILIZUMAB AND ZOLEDRONATE**

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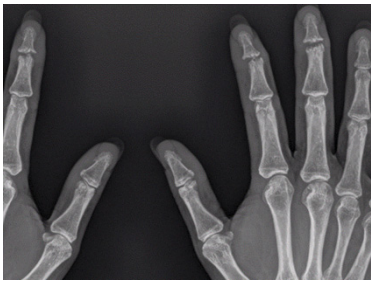
Background: Multicentric reticulohistiocytosis (MRH) is a rare non-Langerhans cell histiocytosis. It can affect any organ but predominantly skin and joints. Joint involvement usually precedes skin involvement and can be very destructive. Early diagnosis and treatment is therefore important but can be difficult.We describe a woman with MRH and severe erosive joint disease who responded to combination tocilizumab and zoledronate.
Objectives: A 43 yr old woman presented in 2012 with a 3 mth history of rash on her face, chest and ears and fingers, and arthralgia affecting shoulders, wrists, fingers and knees. On examination she had diffuse hand swelling, right knee effusion and erythematous eruption affecting her face, chest and ears with papules on the sides of her fingers.
Investigations: normal FBC, CRP, U+Es, LFTs. ESR 12 mm/hr. ANA +ve at 1:1280 (finely speckled). Ro +ve; ENA including Jo-1, ANCA and dsDNA antibodies -ve, C3/4, Igs all normal/-ve. Hand XR: periarticular DIP erosions. Skin biopsy: large multinucleate cells with abundant cytoplasm staining positive with CD68 (histiocytic marker); CD1a negative (Langerhans cell marker), consistent with MRH. PET-CT body: incidental finding of thymic remnant.
Methods: Initial Rx:prednisolone 20 mg od + HCQ 200mg bd with initial good response of joint and skin symptoms, but recurrence of symptoms on reducing steroid dose. Nov 2012: MTX up to 20mg /week added. Stopped after 4 mths because of a linear rise in P3NP levels to 11.2. Fibroscan showed slightly raised stiffness of 7.4kPa. AZA 75mg od introduced in Feb 2013, then etanercept 50mg weekly. This led to good control of symptoms for approximately 4 mths on single agent therapy. March 2014: relapse of joint and skin symptoms. June 2014: tocilizumab 8mg/kg iv 4 weekly started. After 5 infusions, her skin cleared for the first time. December 2014: relapse of joint and skin symptoms. Tocilizumab was adjusted to 650mg per mth from 620mg in view of slight weight gain. Annual iv zoledronate 5mg was started. She has had no further joint or skin exacerbations. July 2015: prednisolone was down to 1mg daily and stopped completely by May 2016. From July 2015 there appears to have been no progression in DIP joint erosions, and possibly some healing of the DIP changes. She has remained off any steroids.
Results: Picture shows X ray hands July 2015



Conclusions: The pathogenesis of MRH is poorly understood. The overexpression of cytokines including TNFα, IL-1 and IL-6 in inflammatory lesions gives a number of logical drug options, including tocilizumab. The observation that mononuclear cells in both skin nodules and synovium in MRH exhibit some properties of osteoclasts might explain the mechanism behind reported success using bisphosphonates. To our knowledge, this is only the second case to report success with using tocilizumab in the treatment of MRH and the first to report on concomitant treatment with a bisphosphonate. No adverse effects have been observed throughout treatment, and remission appears to be sustained. Without withdrawing treatment we cannot know if the remission is natural or drug induced, though the relatively short timescale suggests a drug effect.
Disclosure of Interest: None declared
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AB0977 **DETERMINATION OF A CUT-POINT BETWEEN LOW/HIGH ANTI RNP ANTIBODIES TITRES, IN PATIENTS WITH MIXED CONNECTIVE TISSUE DISEASE**

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Background: Sharp described Mixed Connective Tissue Disease (MCTD) in 1972[1]. MCTD is characterised by the presence of Raynaud phenomenon, puffy hands, synovitis, acrosclerosis, myositis and positive anti-ribonucleoprotein (RNP) antibodies. Classification criteria for MCTD except for Kasukawa's criteria demand the presence of high titres of anti-RNP antibodies (measured by hemagglutination). As a result, the cut-point between low and high anti-RNP titres must be well defined. In best of our knowledge, this cut-point have not been established for modern laboratory techniques.
Objectives: Determinate a cut-point between low/high anti-RNP titles measured by ELISA, for the diagnosis of Mixed Connective Tissue disease. Describe the clinical and immunological characteristics of patients with positive titres of anti-RNP antibodies.
Methods: It was a Retrospective cohort study of patients with positive anti-RNP antibodies (>10) measured by ELISA. We had identified all patients with positive antiRNP antibodies titres in the last five years, using our laboratory base date. Clinical histories were reviewed, we recollected clinical and paraclinical data. We performed descriptive analysis and ROC curves for diagnostic tests with STATA software.
Results: We detected 75 patients with positive antiRNP antibodies, we obtained 65 clinical records. 89,23% (58) of patients were women and 10,77% (7) men.

The mean age at diagnosis was 45,01 years (SD 16,71 ± years), The median of tracing was seven yeas (P25 de four years/P75 de 14 years). The mean initial antiRNP titre was 239,33 the median was 144 (P25 58/P75 400). The initial diagnosis were Mixed Connective Tissue Disease 6,25% (4), Undifferentiated Connective Tissue Disease 31,25% (20), systemic erythematosus lupus 45,31% (29) and Others 14,06% (9). MCTD diagnosis was made in 29,69% (19) of patients at the end of follow-up. Patients with MCTD as final diagnosis presented in their first visit Raynaud phenomenon 73,68% (14), puffy hands 31,58% (5), acrosclerosis 10,56% (2), myositis 21,05% (4), Arthralgias 68,42% (13), arthritis 57,89% (11), Pulmonary arterial hypertension 5,26% and Interstitial lung disease 10,53% (2). The initial RNP titre was evaluated using the number of times over the laboratory cut point. The area under the ROC curve for the initial RNP was 0,70. Looking for the highest specificity with and adequate sensitivity, we selected the cut-point with highest LR +. The selected cut-point was ≥24,4 times the laboratory cut-point, with s specificity of 77,78 and a sensitivity of 57,89.

Conclusions: The cut-point for low/high RNP titres measured by ELISA in our cohort of patients with MCTD as a final diagnosis was ≥24,4 times the laboratory cut-point.

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AB0978 ASSOCIATION OF INFLAMMATORY ARTHRITIS WITH VOGT-KOYANAGI-HARADA SYNDROME (VKHS)

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Background: VKHS is a rare cause of granulomatous uveitis leading to significant visual loss in patients who develop it, usually accompanied with extraocular manifestations that include meningismus, vitiligo, poliosis, and hearing loss. In our country is responsible for 13% to 27% of all uveitis, affecting mainly young women.

Objectives: To describe the presence of inflammatory arthritis in patients with VKHS at a third level hospital.

Methods: A cross-sectional study of 4 patients with established VKHS that fulfilled the 2001 revised diagnostic criteria for Vogt-Koyanagi-Harada disease (1) was rolled out. Ultrasonography was performed to all patients by a trained rheumatologist in carpal, metacarpophalangeal (MCP) and proximal interphalangeal (PIP) joints evaluating presence of power Doppler (PD) signal, bone erosions, and cartilage changes.

Results: We included 3 women and 1 man, mean age was 34.7±10.3 years, and they all had characteristics of complete VKHS. Mean disease duration (since first manifestation of ocular symptoms) was 5.2±3.5 months. One patient had synovitis on physical examination. Out of the 4 patients with PD signal, 4 had involvement of both wrist, MCP and PIP joints consistent with polyarthritis pattern, and bone erosions were detected in one patient (Table)

Table. Characteristics of patients with VKHS and inflammatory arthritis

	Sex	Age	Complete VKHS	Serous retinal detachment	PD in carpal joints	Number of MCP joints with PD	Number of PIP joints with PD	Number of erosions	ESR/CRP elevation	Reumatoid Factor/ACCP
Patient 1	F	21	Yes	Yes	Yes	4	3	0	Yes	No
Patient 2	F	36	Yes	Yes	Yes	7	3	0	Yes	No
Patient 3	M	36	Yes	Yes	Yes	6	4	0	Yes	No
Patient 4	F	46	Yes	Yes	Yes	7	1	2	Yes	No

VKHS: Vogt-Koyanagi-Harada syndrome; PD: power Doppler signal; MCP: metacarpophalangeal joint; PIP: proximal interphalangeal joints, ESR: erythrocyte sedimentation rate; CRP: C reactive protein; ACCP: anti-cyclic citrullinated peptide

Conclusions: The presence of inflammatory arthritis in patients with VKHS has only been described in one case (2). Despite the exceptionality, we propose that polyarthritis and probably erosive arthritis can represent part of the spectrum of the disease, processes that share some features of the genetic susceptibility with rheumatoid arthritis as HLA-DR4, CTLA-4 and STAT4.

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AB0979 EOSINOPHILIC FASCITIS: CLINICAL EXPERIENCE IN A SERIES OF 21 PATIENTS

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Background: The Eosinophilic fascitis (EF) is a uncommon sclerodermiforme síndrome with unknown etiology and poorly understood pathogenesis and natural evolution. The published series are short, with a total of 280 cases described in the literature from 1974.

There is neither clinical tests nor consensus on the EF treatment.

Objectives: To describe a series of 21 patients with EF.

Methods: Multicentric, retrospective Case Series Study.

We reviewed 21 patients diagnosed of EF (cutaneous induration+consistent biopsy) between January 1998 to January 2015. A total of 13 males and 8 females.

Results: The mean age at diagnosis was 41 years 8range between 28 and 66).

Trigger factor was suspected in 8 patients (intense exercise in 7).

The zones of cutaneous affectation were fundamentally the upper and low extremities.

The hyperesonophilia was present in 100% of the patients. The average of the % more high of hyperesosinophilia was 21.2% (range 4–45.4%).

11 patients presented artralgias and 5 patients presented arthritis (4 polyarticular/1 oligoarticular).

The MRI was used for diagnosis and/or follow-up in 8 patients, especially in the diagnosed ones in the last 5 years.

The average initial dose of prednisone was 40 mg/día, the average maximum dose of prednisone was 40 mg/dia and the mean steroid treatment duration was 22 months (range 9–47 months). Other immunomodulatory agents were: methotrexate 11, hydroxychloroquine 2, azatioprina 2 and D penicillamine 1.

5 years after follow-up, the evolution was the complete resolution in 13 patients and the partial improvement in 6.

Other clinical and analytical manifestations (N=21).	YES, n (%)	NO, n (%)
Hypergammaglobulinemia	13 (63)	8 (37)
Elevated ESR	4 (16)	17 (84)
Elevated CRP	8 (37)	13 (63)
Elevated CK	0	21 (100)
Systemic symptoms	7 (32)	14 (68)
Visceral affectation	3 (11)	18 (89)
Autoimmune thyroid	2 (5)	19 (95)
Peripheral neuropathy	4 (16)	17 (84)

Conclusions: In our series, the EF prevails in males, in the decade of the 40 and in the majority one did not find trigger factor. There was presence of arthritis in a significant percentage of patients. In the last years the use of the RMN has been added to the diagnosis and to the follow-up. Though there are no clinical tests that support it the use of the metotrexato has been generalized as adjuvant treatment to the steroids.

Disclosure of Interest: None declared

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AB0980 EPIDEMIOLOGICAL PROFILE OF THE PULMONARY DISEASES IN MIXED CONNECTIVE TISSUE DISEASE: ABOUT 55 CASES

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Background: Mixed connective tissue disease (MCTD) are a systematic autoimmune disease that the aetiopathogeny remains misunderstood. This disease is often associated with systemic involvement which sometimes is very serious, such as pulmonary diseases.

Objectives: To describe the characteristics of the pulmonary diseases among a sample of MCTD.

Methods: We conducted a retrospective study including patient's cases diagnosed with a MCTD between the period of 10 years in the departement of internal medicine. The demographic, clinical, treated in the immunological, biological and radiological data were collected then analysed.

Results: In total we had 55 patients. 87% of them were female. The mean age of the sample was 50, 64±15 years. Major types of MCTD were: Rheumatoid polyarthritis (45.5%), sarcoidosis (18.2%), scleroderma (12.7%), and the lupus erythematosus (10. 9%). These causes were diagnosed after a mean delay of 686, 18 days. A lung disease was found in 50.9% of the cases. It was either present without symptoms in 52.8% of the cases or revealed by dyspnoea (22.6%), a cough (18.9%)or hemoptysie isolated or associated to thoracic pains (1.9% each).The most frequent type of respiratory diseases were adenopathies (26.9%). Pleurisy, fibrosis, and interstitial lung diseases were described among 11.5% of the cases. Bronchiectasis, Lung arterial high blood pressure, pleural nodules, bronchi dilatation were reported in 7.7%. In only 3.8% we had patients with cancer and emphysema. Chest radiographs were normal in 65.5% of the