irAEs	n	frequency	Time (months)	Treatment	Discontinuation of immunotherapy	Response to treatment
Gastrointestinal tract	17	13.6%	4	23% steroid	58% no	17% steroid
Colitis	8			5% Infliximab	29.4% definitive	83% improvement
Intestinal perforation	1			72% nothing	11.7% temporary	
Hepatitis	8					
Endocrine glands	11	8.8%	4	18% steroid	90% no	63% stable
Hypophysitis	1			82% Other	10% definitive	37% improvement
Hypothyroidism	7					
Adrenal insufficiency	2					
Other	1					
Skin	10	8%	4	20% steroid	60% no	100% improvement
Rash/Prurito	7			20% topic treatment	30% definitive	
Vitiligo	1			60% other	10% temporal	
Other	2					
Rheumatological	7	5.6%	5	20% steroid	72% no	100% improvement
Arthralgias	3			20% local treatment	28% definitive	
Polymyalgia rheumatic	1			60% other		
Sicca syndrome	1					
Inflammatory myopathy	1					
Tenosynovitis	1					
Haematological	4	3.2%	Not available	25% steroid	50% no	25% death
Thrombocytopenia	2				25% definitive	75% improvement
Neutropenia	1				25% temporal	
Pancytopenia	1					
Lung (Pneumonitis)	3	2.4%	12	100% steroid	66% definitive	33% stable: 33% improvement; 33% death
					33% temporary	
Ophthalmologic	1	0.8%	Not available	Not available	Not available	Not available
Neuropathy	1	0.8%	2	steroid	Not available	Improvement
Cardiac	1	0.8%	Not available	Not available	Not available	Not available

THU0632

IDENTIFICATION OF ABERRANT T-CELL PHENOTYPE IN EPISODIC ANGIOEDEMA WITH HYPEREOSINOPHILIA (GLEICH SYNDROME) IN 30 PATIENTS: FREQUENCY, CLINICAL IMPLICATION AND PROGNOSIS

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Background: Gleich's syndrome or "Episodic Angioedema with eosinophilia"(EAE) is a rare disorder characterised by recurrent episodes of angioedema, concomitant hypereosinophilia and frequent elevated serum Immunoglobulin M (IgM) levels. So far, no series were reported in literature.

Objectives: In this retrospective French study we report the clinical spectrum and therapeutic management of patients with EAE in a large French nationwide retrospective multicenter cohort study, with a particular focus on lymphoid variant of hypereosinophilic syndromes-related EAE.

Results: Thirty patients were included with a median age at diagnosis of 41 years⁵⁻⁸⁴ and a median follow up duration of 53 months.³¹⁻⁹⁹ The median time between two angioedema crises was 30 days⁷⁻¹⁹² and the median duration of each crisis was 5.5 days¹⁻⁹⁰ with swelling affected the face, the neck, the upper limbs, and the lower limbs. Twelve patients (40%) had an abdominal. The median blood eosinophil count at diagnosis was 6.9 G/L [1.44-53.5] and total serum IgM levels were increased in 20 patients (67%). Abnormal T-cell immunophenotypes were detected in 12 patients (40%):CD3-CD4+in 8 patients, CD3 +CD4+CD7 in 2, CD3-CD3ic+CD4 CD8-CD5+CD7 in 1 patient and CD3 +4-8-2+5+7+TCR γδ in 1 patients with presence of clonal TCR γ gene rearrangement in 5 cases (17%). Fourteen patients (47%) had bone marrow cytology and/or histology revealing high eosinophil counts and/or infiltration by non-dystrophic eosinophils in all cases. Eosinophilic perivascular infiltration (without vasculitis) was reported in 2 patients (7%) in which a skin biopsy was performed. An eosinophilic infiltrate was also found in various organs (stomach, gallbladder, liver, ileon, and colon) that were biopsied and/or surgically removed.

All 30 patients were initially treated with glucocorticoid with a median initial dose of 40 mg of daily prednisone.⁵⁻⁸⁰ After first line treatment and a median time of 15.2 months (95% CI: 9.4-50.1), disease was considered as uncontrolled in 24 patients (80%) with relapses in 15 patients (50%) or glucocorticoid's dependence in 9 (30%).

Glucocorticoid-sparing agents were used in 14 cases (47%) for relapses (n=8) or glucocorticoid- dependence (n=6). Associated treatments consisted of interferon-α (n=8, 27%), mepolizumab (n=2, 7%), ciclosporin A (n=5, 17%), methotrexate (n=4, 13%), hydroxycarbamide (n=2, 7%).

The presence of an abnormal T-cell population was the sole factor associated with a shorter time to relapse (hazard ratio 4.15 [CI 95% 1.18-14.66; p=0.02). Two deaths occurred during follow-up (7%) due to lymphoma evolution for one and unexplained sudden death for the other.

Conclusions: EAE could be classified as a lymphoid variant of hypereosinophilic syndrome but that it is an heterogeneous condition. Although patients usually respond well to glucocorticoids, those with a circulating T-cell clonal population are at higher risk of both relapse and lymphoma suggesting necessity to long-term treatment and close monitoring.

Disclosure of Interest: None declared

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THU0633

ACUTE FORM OF SARCOIDOSIS (LÖFGREN SYNDROME) IN RHEUMATOLOGY PRACTICE

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Background : Löfgren syndrome (LS) is the acute form of sarcoidosis, characterised by erythema nodosum (EN), joints involvement, fever and intrathoracic lymphadenopathy. LS clinical polymorphism leads to diagnostic errors.

Objectives: To study the clinical, laboratory and radiological features of early stages of sarcoidosis in a cohort of patients referred to rheumatology centre.

Methods: The study included 125 patients (104 females and 21 males, mean age 42±12 y) with clinical and radiological features of LS. All patients were referred to rheumatology centre with EN diagnosis. The median duration of disease was 1 (0,5-2,0) months. All patients were subjected to comprehensive clinical and laboratory-instrumental examination, including biochemical panel and immunological parameters, chest X-ray or CT, as well as (15 cases) histopathology examination of nodular biopsy specimens of the skin and subcutaneous fat.

Results: In 97% pts EN involved the lower legs, mostly the anterior surface, in 35% - the hips, in 25% - the upper limbs and in 3% - the trunk. Symmetric lesions were documented in 50% of patients. Confluence of nodules forming conglomerates was registered in 48% pts. The involvement of more than 50% of lower leg surface (68%) was directly associated with the number of nodules (p<0.001; r=0.60) and C-reactive protein level (p=0.006; r=0.38). There was a direct correlation between the number of nodules and EN duration (p=0.04; r=0.20), and also the tendency to nodules confluence (p<0.001; r=0.39). Joint involvement was documented in 106 (85%) patients, with predominantly ankle (66,4%) and knee (40%) joints affected. Asymmetry of joint involvement was documented in 8% pts. Articular manifestations preceded the emergence of EN in 35 (28%) patients by mean 12±9 days. There was a significant direct correlation between the duration of articular syndrome and appearance of nodules and their number (p=0.02; r=0.45). Joint involvement after EN manifestation – in an average 12±7 days – was documented in 10% of cases. Male gender (odds ratio (OR) 6.5; confidence

interval (CI) 1.2–35; $p=0.026$) and presence of nodular conglomerates (OR 4.8; CI 1.4–16.1; $p=0.01$) were the key predictors of ground glass opacity (GGO) CT phenomenon. In 90% of patients EN did not relapse, and articular syndrome almost completely regressed during 1 year follow-up.

Conclusions: Patients with an acute form of sarcoidosis require coordinated action of different medical specialties, including rheumatologists, to determine the scope of further examination and adequate therapeutic regimen.

Disclosure of Interest: None declared

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THU0634 RISK OF SUDDEN CARDIAC DEATH IN PATIENTS WITH SARCOIDOSIS: A POPULATION-BASED RETROSPECTIVE COHORT STUDY

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Background: Sarcoidosis is an inflammatory, non-caseating, granulomatous disorder of unknown etiology which can affect any body system including the heart and can be associated with increased risk of cardiovascular disease including sudden cardiac death (SCD). However, the risk and incidence of SCD are unknown.

Objectives: We sought to determine whether the risk of SCD in patients with sarcoidosis is higher than in the general population.

Methods: A population-based cohort of 345 incident cases of sarcoidosis (50% female; 90% Caucasian, 5% African-American; mean age 45.6 years) among Olmsted County, Minnesota residents in 1976–2013 was identified from a comprehensive medical record-linkage system. Medical records of those cases were individually reviewed to confirm the diagnosis of sarcoidosis which required physician diagnosis supported by histopathology, compatible clinical presentation and exclusion of other granulomatous diseases. A total of 345 sex and age-matched comparators (50% female; 95% Caucasian, 1% African-American; mean age 45.4 years) were also identified from the same underlying population. Mortality, including time, place and cause of death of cases and comparators were individually reviewed for SCD events. SCD incidence rates are reported per 1 00 000 person-years and Cox proportional hazards models were used for comparisons between groups.

Results: The median length of follow-up was 12.9 (6.0–23.4) years and 15.8 (6.8–25.5) for cases and comparators, respectively. Of the 58 deaths in patients with sarcoidosis, 10 were due to definite/probable SCD, versus 57 all-cause and 9 definite/probable SCDs in comparators. Incidence rate of SCD in sarcoidosis was 192 per 1 00 000 person-years (PY) (95% confidence interval (CI), 92–352) versus 155 per 100,000 PY (95% CI, 71–294) in comparators, corresponding to the hazard ratio of 1.28 (95% CI, 0.52–3.17, $p=0.59$). Analysis by time of SCD, sex, age, calendar year of incidence/index date also did not reveal a significantly different rate of SCD between the 2 groups as demonstrated in table 1.

Category	Number of deaths in sarcoidosis/non-sarcoidosis	Rate per 100,000 PY in sarcoidosis (95% CI)	Rate per 100,000 PY in non-sarcoidosis (95% CI)	Hazard Ratio (95% CI)	p-value
SCD at night (22:00–06:00)	3/1	57 (12–168)	17 (0.4–95)	3.76 (0.39–36.47)	0.25
SCD at day	6/6	115 (42–250)	103 (38–224)	1.16 (0.37–3.60)	0.80
SCD an unknown time	1/2	NA	NA	NA	
Females	6/6	217 (79–471)	205 (75–447)	1.12 (0.37–3.47)	0.85
Males	4/3	163 (44–418)	103 (21–302)	1.49 (0.33–6.69)	0.60
Age: 18–39 years	0/0	0	0	NA	
Age: 40–59 years	2/0	76 (9–275)	0	NA	
Age: 60+ years	8/9	450 (194–886)	470 (215–895)	NA	
1976–1994	3/3	259 (54–756)	228 (47–666)	NA	

1995–2004	1/2	62 (2–345)	110 (13–397)	NA
2005+	6/4	244 (90–532)	149 (41–382)	NA

Conclusions: In this first ever population-based evaluation of SCD in sarcoidosis, patients are not at increased risk for SCD (all sub-types). These findings may reflect actual risk, but estimates may be affected by low statistical power. Future studies may further elucidate the risk and nature of cardiac death among patients with sarcoidosis.

Disclosure of Interest: None declared

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THU0635 PREGNANCY OUTCOMES IN MIXED CONNECTIVE TISSUE DISEASE: RESULTS FROM A MULTICENTRE COHORT STUDY

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Background: Mixed connective tissue disease (MCTD) is characterised by signs and symptoms of a combination of disorders, primarily systemic lupus erythematosus (SLE), scleroderma and polymyositis and is characterised by the presence of high titre antibodies to U1-ribonucleoprotein (RNP).

When planning a pregnancy in patients with connective tissue diseases, ENA profiling is suggested but generally refers to testing for maternal antibodies specifically to components of the SSA/Ro-SSB/La ribonucleoprotein complex since these have been associated with foetal cardiac conduction abnormalities and neonatal skin rashes. Nevertheless, little is known about the maternal and foetal pregnancy outcomes in women with the presence of anti-U1RNP antibodies absent reactivity to SSA/Ro-SSB/La.

Objectives: We aimed to investigate foetal and maternal pregnancy outcomes from a large multicentre cohort of MCTD women.

Methods: Data was retrospectively collected from S. Giovanni Bosco Hospital and Sant' Anna University Hospital, Turin, Italy, the Lupus Unit, Department of Rheumatology at St Thomas' Hospital, London, UK, Hospital das Clinicas da Faculdade de Medicina da Universidade de Sao Paulo, Sao Paulo, Brazil, Hospital Reina Sofia de Córdoba, Spain, ASST Spedali Civili di Brescia, Brescia, Italy.

Inclusion criteria included: Women ever pregnant who fulfilled the established criteria of MCTD with confirmed anti-U1RNP positivity.

Results: This multicentre retrospective cohort study describes the foetal and maternal outcomes of 203 pregnancies in 94 consecutive women ever pregnant (mean age at data collection 45.1 years old, S.D. 10.9; mean disease duration at data collection 12.9 years, S.D. 8.5). Demographic, clinical and laboratory characteristics are summarised in table 1. Of the 203 pregnancies analysed the foetal outcomes were as follows: 146 (71.9%) resulted in live births, 38 (18.7%) in miscarriages, 18 (8.9%) in stillbirths (after 20 weeks gestation) and eleven (5.4%) cases showed intrauterine growth restriction (IUGR). Maternal pregnancy outcomes were as follows: eight (3.9%) cases developed pre-eclampsia, two (0.9%) cases developed eclampsia, 31 (15.3%) women developed gestational hypertension and three (1.5%) cases were diagnosed with gestational diabetes. Moreover, we report a case of complete congenital heart block (0.45%) and a case of skin rash in consecutive offspring born to a mother with anti U1RNP antibodies in the absence of anti-Ro/SSA-SSB/La antibodies.

Patients Characteristics		All (94)	%
Age at data collection, mean (S.D.), years		45.1 (10.9)	
Ethnicity			
	Caucasians, n	64	68.1
	Blacks, n	9	9.6
	Asians, n	4	4.3
	Others, n	17	18.1
Diagnosis			
	MCTD, n	94	100
Disease duration at data collection, mean (S.D.), years		12.9 (8.5)	
	MCTD and aPL, n	13	13.8
	MCTD and APS, n	6	6.4
Clinical manifestations			
	Hematological, n	36	38.3
	Skin, n	57	60.6
	Joints, n	65	69.1
	Cardiac, n	10	10.6
	Renal, n	9	9.6
	Muscular, n	31	33
	Raynaud's, n	66	70.2
	Pulmonary, n	27	28.7
	Neurological, n	6	6.4
Cardiovascular risk factors			
	History of smoking, n	10	10.6
	Arterial Hypertension, n	13	13.8
	Hyperlipidemia, n	11	11.7
	Diabetes, n	2	2.1
Laboratory testing			
	Hypocomplementemia (C3), n	28	29.8
	Hypocomplementemia (C4), n	25	26.6
	anti-dsDNA positive, n	12	12.8
	Hypergammaglobulinemia, n	47	50

Conclusions: The observed live-birth-rate was as high as 72%, with poorer foetal outcomes observed in MCTD women with antiphospholipid antibodies and