AB0541

LUPUS MANIFESTATIONS IN A PATIENT WITH SPONDYLOARTHRITIS TREATED WITH TUMOUR NECROSIS FACTOR-ALPHA ANTAGONIST: SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) OR DRUG-INDUCED LUPUS ERYTHEMATOSUS (DILE)?

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Background: Systemic lupus erythematosus (SLE) is a multisystem autoimmune inflammatory disease. Drug-induced lupus erythematosus (DILE) is defined as the development of lupus-like symptoms that is temporarily related to continuous drug exposure which resolves with cessation of the offending drug. It is usually accompanied by serologic findings of a positive antinuclear antibody (ANA) and anti-histone antibodies. Tumour necrosis factor- α (TNF α) antagonist-induced lupus-like syndrome (TAILS) is a well-known side effect of this class of substances. A retrospective study reported twenty two cases whose lupus manifestations abated within a few weeks (median eight weeks) in all patients except one with longer-lasting evolution of six months.

Objectives: We reported a case which posed a diagnostic challenge to us, a patient with spondyloarthritis (SpA) who presented with lupus-like features during treatment with Golimumab.

Methods: Case report

Results: A 36-year-old lady was diagnosed as spondyloarthritis when she presented with peripheral arthritis, plantar fasciitis, right eye anterior uveitis and bilateral chronic sacroiliitis confirmed via sacroiliac magnetic resonance imaging. Investigations revealed raised erythrocyte sedimentation rate (ESR) and negative HLA-B27. She developed allergic reaction to sulfasalazine and non-steroidal anti-inflammatory drugs (NSAIDs), thus intravenous Golimumab was initiated. Although she responded to this therapy and ESR had reduced during assessment at 24 weeks, Golimumab was stopped due to funding issue. It was restarted after six months but had to be discontinued again after four months because she developed recurrent fever and malar rash. During this presentation, investigations revealed leukopenia of 2.46×10^9 , ESR of 93 mm/hr, low complements and positive direct coombs' test. ANA, anti-double stranded DNA, anti-histone antibody and anti-smith antibody were all negative. Infective screening was negative. TAILS secondary to Golimumab was diagnosed. Apart from discontinuation of Golimumab, 0.5mg/kg/day of prednisolone was started which resulted in improvement of the malar rash and leukopenia. However, four months after the last dose of Golimumab, recurrent fever and leukopenia recurred when the prednisolone dose was reduced to 5mg on alternate-days. At this time, we considered diagnosis of SLE rather than TAILS because of persistent SLE manifestation despite cessation of Golimumab and improvement with oral corticosteroid. Furthermore, although not pathognomonic, the anti-histone antibody was negative.

Conclusion: This case posed a diagnostic challenge as both SLE and DILE can present similarly. The approach to managing this patient with coexisting SpA and SLE is also a challenge since there is a dilemma as to what can be offered after failure of NSAIDs and conventional disease-modifying antirheumatic drugs since anti-TNF α is contraindicated in SLE.

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AB0542

PREGNANCY OUTCOMES IN ANTIPHOSPHOLIPID SYNDROME: 8 YEAR-EXPERIENCE FROM A MULTIDISCIPLINARY UNIT

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Background: Women with antiphospholipid syndrome (APS) are at increased risk of recurrent miscarriage, fetal death, placental insufficiency, preeclampsia and fetal growth restriction. Although treatment improves fetal-maternal outcomes, there are still some unsuccessful pregnancies. A multidisciplinary approach with strict monitoring is essential in order to attain obstetrical success.

Objectives: To assess pregnancy outcomes in portuguese women with APS who were surveilled at a multidisciplinary unit.

Methods: Pregnant women fulfilling the Sydney classification criteria for definite APS, who attended our specialized Rheumatology and Obstetrics outpatient clinic between 2010 and 2018, were included in this retrospective observational study. Cases of suspected APS not meeting the classification criteria were excluded. All pregnancies were followed by a multidisciplinary team (rheumatologists, obstetricians and nurses). Data was collected from medical records. Adverse Pregnancy Outcomes (APO) were defined as: spontaneous abortion (<10w), fetal death ($\geq 10w$), neonatal death, fetal growth restriction (FGR) and delivery prior to 36 weeks of gestation with or without preeclampsia (PE).

Results: A total of 35 pregnancies were identified in 25 women with APS. Twelve (48%) patients had thrombotic APS, 9 (36%) had obstetric APS and 4 (16%) had mixed APS. Primary APS was seen in 56% of patients, while systemic lupus erythematosus was found in 44%.

The average maternal age at conception was 32.8 ± 5.2 years. Mean duration of disease prior to pregnancy was 6.4 ± 5.5 years. In regard to antiphospholipid antibody (APL) profile, 28.6%, 25.7% and 28.6% of patients were triple, double and single positive, respectively. Although they had fulfilled laboratorial criteria in the past, 17% of patients were negative for all APL. All patients were instructed to receive prophylactic or therapeutic low-molecular-weight heparin combined with low dose aspirin for the duration of pregnancy.

Regarding fetal outcomes, there were 2 (5.7%) cases of first-trimester miscarriage, 1 (2.9%) medical abortion due to exposure to teratogenic drugs at the time of conception and 4 (11.4%) fetal deaths. Among the cases of fetal death, one concerned a patient who suspended heparin on her own initiative and another one who became pregnant under warfarin and whose fetus had trisomy 18. The other cases occurred at 11 and 18 weeks of gestation, under regular therapy. There were no cases of neonatal death or other fetal malformations. The rate of live births was 80%, with a mean gestational age of 37.3 ± 1.5 weeks and mean birth weight of 2796.4 ± 462 g. Most women delivered by cesarean section (54.3% of cases). There were 6 (17.1%) cases of preterm birth, three (8.6%) corresponding to fetus with FGR. Concerning maternal outcomes, there was one single case (2.9%) of PE. There were no cases of eclampsia or HELLP syndrome.

Table 1. Clinical and serological features of adverse pregnancy outcomes and successful pregnancies.

	APD, n=11 (32.4%)	Successful pregnancies n=23 (67.6%)	p-value *	OR (CI 95%)
Maternal age, mean	32.3 $\pm$ 5.8	33.2 $\pm$ 4.2	0.244 *	-
Disease duration, mean	7.7 $\pm$ 6.6	5.8 $\pm$ 5.0	0.358 *	-
History of thrombosis	9 (81.8%)	14 (60.9%)	0.271	-
History of previous APOs	7 (63.6%)	12 (52.2%)	0.715	-
Concomitant SLE	8 (72.7%)	11 (47.8%)	0.270	-
Lupus anticoagulant	11 (100%)	11 (47.8%)	0.003	25 (1.32 – 474.08)
IgG aCL	6 (54.5%)	8 (34.8%)	0.458	-
IgM aCL	0 (0%)	5 (21.7%)	0.150	-
IgG anti-B2GPI	7 (63.6%)	8 (34.8%)	0.151	-
IgM anti-B2GPI	2 (18.2%)	4 (17.4%)	0.999	-
Single Positivity	2 (18.2%)	7 (30.4%)	0.682	-
Double Positivity	3 (27.3%)	6 (26.1%)	0.999	-
Triple Positivity	6 (54.5%)	4 (17.4%)	0.045	5.7 (1.15 – 28.33)
Negative APL	0 (0%)	6 (26.1%)	0.145	-
Low complement levels *	4 (50%)	5 (23.8%)	0.209	-
Anti-dsDNA Φ	3 (37.5%)	2 (18.2%)	0.603	-

The only patient who had a medical abortion was excluded from this analysis.

* Fisher's exact test, except otherwise indicated.

Φ Independent t-test.

*Data available for 29 pregnancies.

Φ Applied only to patients with SLE (n=19).

Lupus anticoagulant ($p = 0.003$, OR 25, CI 95% 1.32 – 474.0) and triple APL ($p = 0.045$, OR 5.7, CI 95% 1.15 – 28.33) positivity were associated with adverse pregnancy outcomes. In this cohort, no association was

found between poor obstetric outcomes and history of thrombosis, presence of SLE or low complement levels (table 1).

Conclusion: In our study, most pregnancies were uneventful. Despite the small sample size, we reinforce the importance of a multidisciplinary evaluation and surveillance before, during and after pregnancy in women with APS in order to implement early treatment and to optimize fetal-maternal outcomes.

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AB0543

FEATURES ASSOCIATED WITH RENAL DAMAGE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS DECEASED OVER A 10-YEAR PERIOD

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Background: Renal damage (RD) is one of the most important contributors to morbidity and mortality in patients with systemic lupus erythematosus (SLE).

Objectives: We aimed to assess features associated with RD in a group of 90 deceased SLE patients routinely followed-up at our institution, which serves as a national referral center for SLE.

Methods: We retrospectively analyzed 90 SLE patients (68 females) deceased from 2002 to 2011. All patients were ≥ 18 years of age at death, fulfilling $\geq 4/11$ classification criteria of the American College of Rheumatology (ACR). We identified patients with RD, as defined by the Systemic Lupus International Collaborating Clinics (SLICC)/ACR index. An extensive set of variables was compared between patients with and without RD (RD and RD-N, respectively): demographics, ACR criteria at diagnosis and cumulatively at death, total damage and its components one year following diagnosis and non-renal damage and its components cumulatively at death, as well as components of the metabolic syndrome, smoking, sicca and Hughes syndrome. Frequencies were compared using the chi-square and Fisher's exact test, and continuous variables using the t-test and Mann-Whitney U test. Variables associated with RD were analyzed using multivariate logistic regression.

Results: We identified 25/90 patients who accrued RD over the course of their disease. In the univariate analysis, we found no difference between RD and RD-N patients in any of the following parameters: demographics, total count of ACR criteria at diagnosis and death, as well as damage at one year after diagnosis and cumulative non-renal damage at death. Compared to RD-N patients, RD patients had a higher proportion of malar rash at diagnosis (11/25 vs. 13/65, $p=0.021$) and a higher cumulative proportion of renal disorder (19/25 vs. 30/65, $p=0.011$), including proteinuria and urinary casts (17/25 vs. 23/65, $p=0.005$, for both). RD patients also had a higher proportion of myocardial infarction as an item of cumulative damage (7/25 vs. 6/65, $p=0.023$) and were more frequently obese (11/25 vs. 15/65, $p=0.049$). Conversely, hematological disorder and leukopenia at diagnosis were less frequent in RD compared to RD-N patients (4/25 vs. 30/65, $p=0.008$ and 1/25 vs. 21/65, respectively). In the final multivariate model (adjusted for gender, age at diagnosis and disease duration), malar rash at diagnosis and the cumulative presence of renal disorder (classification criteria of the ACR) were positively associated with RD. Conversely, leukopenia at diagnosis was inversely associated with RD (Figure 1).

Variable	OR	95% CI	p
Malar rash (dg)(yes/no)	27.416	3.586-209.620	0.001
Leukopenia (dg)(yes/no)	0.016	0.001-0.273	0.004
Renal disorder (cum)(yes/no)	7.141	1.091-46.760	0.040
Myocardial infarction (cum)(yes/no)	6.117	0.319-117.197	0.229
Obesity (cum)(yes/no)	1.917	0.425-8.638	0.397
Male gender (yes/no)	1.913	0.335-10.916	0.465
Age (dg)(years, cont)	1.018	0.969-1.070	0.481
Disease duration (cum)(years, cont)	0.940	0.826-1.070	0.352

dg - at diagnosis, cum - cumulatively, yes/no - binary variable, cont - continuous variable

Figure 1. Features associated with renal damage (multivariate logistic regression model)

Conclusion: More than a quarter of deceased patients accrued RD. While malar rash at diagnosis may be associated with a higher likelihood of developing RD, early leukopenia may be associated with its lower likelihood in deceased patients.

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ECHOCARDIOGRAPHIC CHANGES IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS BEFORE TO INITIATION OF IMMUNOSUPPRESSIVE THERAPY

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Background: Cardiovascular diseases are becoming the leading cause of death among SLE patients due to increasing life-spans. Transthoracic echocardiography (TTE) is a routine and widely available modality in everyday clinical practice useful to identify specific pathological cardiac changes and predictors of heart failure (HF).

Objectives: Obtaining of specific TTE findings in SLE patients prior to initiation of pathogenic immunosuppressive therapy was the objective in this study.

Methods: Thirty four pts (91% females, aged 30[26-34]years (median [interquartile range 25%-75%]) with "non-treated" SLE (ACR 1997 and SLICC 2012 criteria) were included. None of pts was treated either with prednisone or cytotoxic drugs at the moment of inclusion.

Results: Median SLE duration was 18[6-60]months, SLEDAI-2K - 13[8-19], SLICC/DI - 0[0-0]scores. Leading SLE clinical manifestations included: hematological changes (74%), kidney involvement (59%), joints (50%) and skin involvement (50%). Immunological abnormalities were detected in all patients and were as follows: ANA positivity - in 100%, anti-dsDNA antibodies - in 76% of SLE patients. Concurrent antiphospholipid syndrome was found in 2(6%) patients. Valve insufficiency with varying degree of regurgitation was the commonest pathology found in "non-treated" SLE patients based on TTE data: mitral valve insufficiency - in 31(91%), tricuspid valve - in 31(91%), pulmonary valve insufficiency - in 21(62%), aortic valve insufficiency - in 4(12%) patients. Endocarditis was a rare pathology found in 5(15%) patients, while mitral and tricuspid valves prolapse was seen more often - in 16(47%), while not a single case of valve stenosis was found. Pericardial pathology was detected in 16(47%) patients: exudative - in 9(26%), and adhesive (thickening, hardening and separation of leaflets) - in 7(21%).

There were no cases of CAD or MI, although there were 2(6%) documented cases of cerebral stroke in past history, and 1(3%) case of confirmed CHF. Most common TRF were dyslipidemia and hypertension - in 15(44%) and 11(32%) SLE patients respectively.

Median LVEF was 64[59-67]%, LV end-systolic dimension- 30[27-32]mm, LV end-diastolic dimension - 48[45-51]mm, pulmonary artery systolic pressure - 24[22-32]mm Hg. LV diastolic dysfunction (LVDD) was found in 10 (29%), systolic dysfunction (LVSD) - in 4(12%), LV myocardial hypertrophy (LVH) - in 5(15%); left atrium dilatation (LAD) was found in 4(12%), and increased dimensions of right atrium was detected in 3(9%) SLE patients.

Conclusion: Most common cardiac abnormalities in "non-treated" SLE patients with high activity (SLEDAI-2K 13 scores) were valve dysfunction (insufficiency with regurgitation), mitral and tricuspid valve prolapse and pericarditis. Of importance is the presence of early subclinical features of HF almost in 1/3 of naive to treatment SLE patients: LVDD (29%), LVH (15%), and LAD (12%). SLE patients should be thoroughly monitored both for adequate control of SLE activity, and cardiac pathology with correction of TRF, regular assessments by a cardiologist, TTE, and early administration of cardio-protection therapy in view of increased HF risk in SLE patients, predetermining unfavorable prognosis.

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