Patients with APS still develop significant morbidity and mortality despite current treatment. It is imperative to increase the efforts in determining optimal prognostic markers and therapeutic measures to prevent these complications.[5]

Learning objectives
- Discuss data that support treatment decisions for APS

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Workshop

01 MANAGEMENT OF REFRACTORY LUPUS: PLACE OF BIOLOGICS

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Case 1: 34-year-old female with acute onset of SLE, clinical and serologically active despite of standard of care

Bernardo Pons-Estel

Previous medical history Hypothyroidism (2015). Silicone breast prosthesis (June 2017). On January 2018, after sun exposure, she developed acute onset fever, asthenia, fatigue, photosensitivity, malar rash, oral ulcers, alopecia, arthritis and myositis (myalgia and muscle weakness). Laboratory tests: RBC 3.6 ($\times 10^{12}$/L), haemoglobin 9.40 g/dl, haematocrit 34%, WBC 2,3 ($\times 10^{9}$/L), neutrophils 81%, lymphocytes 16%, platelets 163 ($\times 10^{9}$/L), ESR 39 mm (1st hr), CRP 23 mg/L, ALAT/ASAT double, BUN 38 mg/dl, serum creatinine 0.7 mg/dl, GFR 67 mL/min, blood sugar level 79 mg/dl, cholesterol 186 mg/dL, HDL-C 47 mg/dl, LDL-C 112 mg/dl, proteinuria 228 mg/24 h, ANA 1/2560, anti-dsDNA 1/160 (IF), anti-Sm (+), anti-U1RNP (+), anti-Ro (-), anti-La (-), C3 43 mg/dl (90–140), C4 10 (20–55). SLEDAI 20. She received diagnosis of systemic lupus erythematosus (SLE) in February 2018, and she was treated with prednisone 50 mg/d (1 mg/k/d), hydroxychloroquine 400 mg/d and IVGG 0.4 g/kg/d for five consecutive days. She received immunisation with influenza and pneumococcal vaccines.

Follow-up From April to June 2018 prednisone was gradually tapered off until 5 mg/d. In August 2018 she experienced a flare with oral/nasal ulcers, arthritis, alopecia, Raynaud, leukopenia, lymphopaenia, anti-dsDNa 1/80 (IF), C3 47 and C4 13 mg/dl. Her SLEDAI score was 13, and she was treated with azathioprine 100 mg/d (but discontinued due to GI intolerance), prednisone 20 mg/d (gradually tapered off until 5 mg/d), and hydroxycloroquine 400 mg/d. In November 2018 she experienced a new flare with fever, oral ulcers, arthritis, cutaneous vasculitis, leukopenia, lymphopenia, ANA 1/2560, anti-dsDNA 1/160 (IF), C3 48 and C4 9 mg/dl, PPD test, HBV antigens and antibodies, anti-HCV and HIV were all negative. At this time her SLEDAI score was 20.

Treatment She was treated with prednisone 50 mg/d (1 mg/k/d), hydroxychloroquine 400 mg/d, and belimumab (IV infusion, 10 mg/k = 520 mg for one hour). It was well tolerated, with no infusion reactions.

After 6 months of belimumab she is in complete clinical remission (SLEDAI 0), without prednisone, and negative anti-dsDNA, and normal values of C3 98 mg/dl (90–140), C4 24 mg/dl (20–55).

Discussion points
- Therapeutic options with non–biological drugs
- Ideal patient for belimumab
- Cost–benefit evaluation with belimumab: short and long term

Case 2: Relapsing-remitting polyarthritis

Andrea Doria

A 21-year-old Caucasian female was diagnosed with SLE in 2005, when she was 14 years old, based on fever, pleurisy, polyarthritis and modest proteinuria. She had positive ANA, anti-dsDNA and even anti-U1RNP/Sm. She responded well to treatment with three pulses of methylprednisolone and then oral prednisone and hydroxychloroquine (HCQ). On May 2009 she stopped prednisone for clinical disease remission. On January, March and May 2013 she had three episodes of lupus flare with skin rash and polyarthritis, which were treated with prednisone 25 mg/day and HCQ with partial response. However, as corticosteroid dosage was reduced clinical manifestations worsened. On June 2013 she experienced a new flare and developed very severe polyarthritis (DAS28 7.16) with myositis, and had positive anti-dsDNA and low C3 and C4. She was taking HCQ and prednisone at high doses. Her SLEDAI score was 12. Thus, she had active clinical disease, active serology, she was taking a standard therapy and, last but not least, she had three flares in the last 6 months. It also should be noted that she had recurrent genital herpes zoster.

We started belimumab also due to the fact that the patient was young, she had a very active serology, a relapsing-remitting polyarthritis and, last but not least, she had refused methotrexate.

We observed a progressive decline in SLEDAI, DAS28, a progressive decrease in prednisone dosage in anti-dsDNA antibody levels and increase of C3 and C4 serum levels.

Discussion points
- In selected cases belimumab can be used before other immunosuppressants
- Early use of belimumab is associated with rapid, marked and sustained response

Case 3: Subacute cutaneous lupus erythematosus

Andrea Doria

A 44-year-old female patient affected with SLE since 2004, when she was 32-years-old.

The diagnosis of lupus was based on subacute cutaneous lupus erythematosus (SCLE) manifestations, hematological abnormalities, multiple positive autoantibodies including anti-dsDNA and anti-P-ribosomal. She was effectively treated with

prednisolone and HCQ. From 2009 to 2012 she experienced three skin flares, all treated with the increase of prednisone dosage and, in addition, HCQ was switched to chloroquine (CQ) at the time of the first flare, methotrexate 15 mg/week was added to CQ in the second fare, and in the third flare she accepted to be enrolled in a RCT of sifalimumab. In May 2013 she experienced a new flare; at baseline evaluation she had SCLE, leucopenia, high levels anti-dsDNA and low C3. She was taking prednisone 10 mg/day, CQ 200 mg/day and methotrexate 15 mg/week. The SLEDAI was 7, SLICC DI 0. Thus she had active skin and hematological manifestations, active serology, despite the standard treatment and she experienced one flare per year during the last 4 years. For all these reasons we decided to start belimumab. Both SLEDAI and CLASI initially decreased and white blood cell count increased. After 10 months she experienced a relapse of skin rash, which required a temporary increase in prednisone dosage.

Discussion points

- Belimumab may reduce SCLE flares although a complete recovery of SCLE manifestations is uncommon
- During belimumab treatment, relapses should be managed with a temporary increase of prednisone dosage or changing background immunosuppressant.

Learning objectives

- Describe therapeutic options for patients with acute onset SLE that remains serologically active despite standard therapy
- Identify patients who would benefit from biologic treatment with belimumab
- Discuss the potential short and long term cost benefits of belimumab

02 MANAGEMENT OF DIFFICULT INFECTIONS IN SLE

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Case 1: 40-year-old African female with lupus flare

Zahir Amoura

A 40-year-old African female was referred for fatigue, weight loss (-5 kg during the last month), fever (39°C) and right paralumbar pain. Physical exam displayed bilateral malar rash and there was no joint pain.

Laboratory tests revealed: Hb: 8.2 g/dL (12.0–16.0), white cell count ($\times 10^9$/l): 2.00 (4.00–10.00), neutrophils: 0.952 (2.00–7.50), lymphocytes: 0.840 (1.50–4.00), platelets: 105 ($\times 10^9$/l) (150–400). Creatininemia: 47 µmol/l (44- 80), ASAT: 188 (17–27), ALAT: 98 (11–26), Gamma-GT: 127 U/l (8–36), Total bilirubin: 12 µmol/l (2–17), albuminaemia: 23 g/l, fasting triglyceridaemia: 3.47 mmol/l (0.4–1.65); CRP: 177 mg/l (<5.00). Procalcitonin: 1.71 µg/l (<0.5), Fibrinogenaemia 4.1 g/l (2.0–4.0), positive ANA: 1/1280, positive anti-dsDNA: 84 UI, low C3: 0.61 g/l.

Blood cultures (X3): negative. Urine cultures: negative, daily proteinuria (g/24h): 2.5.

Kidney biopsy: Lupus nephritis Class III (A: 14%; C: 7%).

Thoracic-abdominal-pelvic CT scan: polyadenopathy: right and left sus-clavicular, axillar, mediastinal lymph nodes. Abscess of the right psoas.

Aspirate of the right psoas abscess displayed numerous Escherichia coli.

The patient was diagnosed with a concomitant lupus flare and a right abscess of the psoas.

Discussion Point

- Management of a severe infection concomitant with a lupus flare

Case 2: 54-year-old Caucasian female with SLE

Zahir Amoura

A 54-year-old Caucasian female was diagnosed with systemic lupus erythematosus (SLE) in 2003 based on psychosis and lupus nephritis Class IV, positive antinuclear antibodies, positive dsDNA antibodies, low C3 level. She had been treated with prednisone, hydroxychloroquine and IV cyclophosphamide. Cyclophosphamide was switched to mycophenolate mofetil 2 g/day for 5 years. She had a renal relapse in 2015 (Class III + V) and was treated with mycophenolate mofetil (MMF) 2 g/day + prednisone 0.5 mg/kg/day). Prednisone was tapered to 5 mg/day and MMF was maintained. In January 2019, she had sudden changes of mood, becoming more irritable and sensitive. Her condition deteriorated over the next few days. She presented manic symptoms with psychomotor excitement, logorrhea, tachypsychia, euphoric state and insomnia. She had delusions and hallucinations with dysmorphophobic and nosophobic thematics. She was hospitalised and received olanzapine (40 mg/day), loxapine (50 mg/day) and clonazepam (3.5 mg/day). Cerebral spinal fluid analysis was normal. An electroencephalogram showed diffuse slow waves (0.5 to 1 wave per second). Antinuclear antibodies were positive (1/320), anti-DNA antibodies were negative; and C3 level was normal. A magnetic resonance imaging scan showed small and non-specific hyperintensities. She then became catatonic showing rigidity, mutism, staring, waxy flexibility and negativism. A diagnosis of SLE-induced psychosis with catatonia was made. Antipsychotic medications were stopped, and a high dosage of lorazepam (15 mg/day) was started together with three IV methylprednisolone pulses (1 g) followed by a month of 1 mg/kg/day oral prednisone, progressively tapered. MMF was stopped and switched to cyclophosphamide (0.7 g/m2; two weekly then monthly pulses) and 13 plasma exchanges. Catatonia as well as psychotic symptoms progressively improved.

In March 2019, she presented with fever (40°C), dyspnea with tachypnea (respiratory rate 28/min), supine blood pressure of 90/50 mmHg, tachycardia (105 BPM). Laboratory test were: Hb: 10.2 g/dL (12.0–16.0), neutrophils($\times 10^9$/l): 11.12 (2.00–7.50), lymphocytes: 0.260 (1.50–4.00), platelets: 355 ($\times 10^9$/l) (150 – 400). Creatininemia: 150 µmol/l (44–80), ASAT: 88 (17–27), ALAT: 68 (11–26), Gamma-GT: 48 U/l (8–36), Albuminemia: 22 g/l,; C-reactive protein: 241 mg/l (<5.00). Procalcitonin 21 µg/l (<0.5), positive anti-dsDNA: 55 UI, normal C3:0.81 g/l

Arterial blood gas analysis demonstrated severe hypoxemia (PO2: 40 mmHg; PCO2 20 mmHg)

Chest CT scan displayed diffuse bilateral opacities. A diagnosis of Acute Respiratory Distress syndrome was done and the patient was refereed to Intensive care unit.

Discussion Point

- Management of a severe infection of pulmonary origin in SLE