moderate or high doses of glucocorticoids[10 11]. Pre-emptive use of antibiotics is not recommended, nevertheless a low index of suspicion to diagnose an infection – including possible Pneumocystis pneumonia[12] – and commence antibiotics promptly is warranted in high-risk groups including elderly or neutropenic patients, those with comorbidities (e.g. diabetes) or who are receiving glucocorticoids.

Osteoporosis and fragility fractures are potentially avoidable and readily treated comorbidities in patients with SLE.[13 14] Factors impacting adversely on bone mass density, particularly chronic use of glucocorticoids, should be corrected.[15] Osteoprotective and/or anti-osteoporotic interventions should be similar to those in the general population or patients with other chronic inflammatory disorders, yet caution is recommended in cases of kidney disease and reduced glomerular filtration rate. To this end, SLE patients should also be screened for vitamin D insufficiency, which should be corrected considering its presumed multifaceted effects on the disease.[16]

Learning objectives

- Describe primary prevention strategies for SLE comorbidities including cardiovascular disease, infection and osteoporosis
- Explain screening and treatment options for key comorbid diseases in patients with SLE

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Hot Topic Lecture

01 APS IN SLE PATIENTS: BEST TREATMENT PRACTICE

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Recently, recommendations for the management of antiphospholipid syndrome (APS) in adults were published by the European League Against Rheumatism based on evidence from a systematic literature review and expert opinion.[1] The antiphospholipid antibody (aPL) type, the presence of multiple (double or triple) *versus* single aPL type, their titre (moderate-high titre *versus* low titre) and the persistence of aPL positivity in repeated measurements are defined as the ' aPL profile'. The aPL profile is an important factor determining the risk of thrombotic and obstetric events, and consequently the intensity of treatment. The presence of aPL in asymptomatic individuals or patients with systemic lupus erythematosus (SLE) does not confirm the diagnosis of APS but can be associated with increased risk of thrombosis or pregnancy morbidity, depending on aPL characteristics and coexistence of other risk factors.[2] Low dose aspirin (LDA) is recommended for asymptomatic aPL carriers, patients with SLE without prior thrombotic or obstetric APS, and non-pregnant women with a history of obstetric APS only, all with high- risk aPL profile. Immunosuppressive drugs plus steroids do not protect against recurrent thrombosis in APS. Patients with APS and first unprovoked venous thrombosis should receive long-term treatment with vitamin k antagonists (VKA) with a target international normalized ratio (INR) of 2.0–3.0. In patients with APS, with first arterial thrombosis, treatment with VKA with INR 2.0–3.0 or 3.0–4.0 is recommended, considering the individual's bleeding/thrombosis risk. In all cases treatment should be continued even if the patient becomes aPL negative. Direct oral anticoagulants (DOACs) could be considered in APS patients with venous thrombosis who are not able to achieve a target INR despite good adherence to VKA or those in whom VKA is contraindicated (e.g. allergy or intolerance to VKA).[3] Rivaroxaban should not be used in patients with APS with triple aPL positivity.[4] Based on the current evidence, the use of DOACs in patients with APS and arterial events is not recommended due to the high risk of recurrent thrombosis. For patients with recurrent arterial or venous thrombosis despite adequate treatment, addition of LDA, increase of INR target to 3.0–4.0 or switch to low molecular weight heparin may be considered. Other potential strategies for refractory APS cases include rituximab and hematopoietic stem cell transplantation. Thrombocytopenia is not rare in APS and is mostly mild, not requiring intervention. Bleeding is uncommon in these patients and it is important not to stop VKA therapy because low platelet counts do not protect against thrombosis. Careful monitoring is advocated for mild-moderate thrombocytopenia, and corticosteroids are recommended for severe cases. In women with prior obstetric APS, combination treatment with LDA and prophylactic dosage heparin during pregnancy is recommended. In patients with recurrent pregnancy complications, increased heparin to therapeutic dose, addition of hydroxychloroquine or addition of low dose prednisolone in the first trimester may be considered. Use of intravenous immunoglobulin might be considered in highly selected cases.

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