

difficulties and was admitted at the Emergency Room. At physical examination, dysarthria and paresis of left upper limb was confirmed. Blood pressure was 160/95 mm Hg.

Discussion Point

- Recognising and treating focal cerebral involvement in SLE

Learning Objectives

- Recognise and describe clinical, laboratory and imaging features, which help assess focal cerebral involvement in patients with SLE.
- Explain the principles and strategies for the management of cerebral manifestations in SLE.
- Demonstrate clinical awareness of potential severe cerebral complications in SLE

Case 2: A woman with recurrent myelitis and SLE

Thomas Huizinga

A woman was diagnosed with systemic lupus erythematosus (SLE) at the age of 28 years old based on arthritis, skin erythema, mouth ulcers, sunlight hypersensitivity, ANF +, anti dsDNA + and anticardiolipin antibodies. At the age of 34 she developed papillitis of both eyes with vision loss. Her MRI revealed no abnormalities and she was treated with methylprednisone 500 mg for 5 days. At the age of 35 she developed a recurrence, no neuritis bulbaris was observed and SLE was thought to be the most likely cause so she was treated with cyclophosphamide 750 mg/kg for 6 months and prednisone 60 mg for 4 weeks and then 10 mg/kg lowering every 4 weeks. After 6 months she had completely improved. At the age of 37 she gradually developed, over a number of weeks, problems urinating and sensory disturbances left thigh and right leg, physical exam revealed hypesthesia in her left leg, and feelings of a different temperature in legs compared to arms.

MRI revealed transverse myelitis at C6-Th2, compatible with SLE and she was retreated with cyclophosphamide and prednisone (figure 1). Subsequently, she did quite well for a number of years under subsequent treatment with azathioprine and cyclosporin for joint and skin involvement. At the age of 52 she developed hypesthesia of the thorax and MRI revealed a myelitis over a long span Th2-Th10 while receiving cyclosporin. A laboratory test for aquaporin 4 antibodies was negative. Combination treatment with prednisone and rituximab followed by belimumab was given, to which she responded quite well. After 2 years she developed less strength in both legs, sensibility disturbance in both legs and specifically C9 and Th7 dermatome, new miction problems and inability to defecate. MRI revealed new lesions at TH4-TH8 while a sharp reduction of previous lesions was observed; aquaporin antibodies tested positive. Based on the recurrence, rituximab maintenance therapy was given every half year. In 2020 she started to suffer from recurrent infections and her IgG levels were 5.6 mg/ml after which intravenous IgG suppletion was started and the infectious problems disappeared.

Discussion Point

- Diagnosis, management and recurrence of myelitis in SLE

Learning Objectives

- Describe the clinical presentation of myelitis and its recurrence
- Explain treatment options of myelitis
- Discuss the role of aquaporin-4 antibodies in myelitis

Workshop

22 REPRODUCTIVE HEALTH IN SLE

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Case 1: 23 year-old-female seeking contraception

Lisa Sammaritano

A 23-year-old woman with systemic lupus erythematosus (SLE) who recently relocated wishes to establish rheumatology care. She was diagnosed with SLE aged 14 years with idiopathic thrombocytopenic purpura; she was treated with high dose steroid with good response and tapered off steroid within 6 months. She was well until age 20 when she presented with malar rash, inflammatory arthritis of PIPs, MCPs and knees, fatigue, and petechia following a vacation in the Caribbean. She was diagnosed with SLE with positive ANA and double stranded DNA. Her hemoglobin was 6.0 gm/dl with positive Coombs and low haptoglobin, her platelet count was 12,000. C3 and C4 were low. She was treated with intravenous 'pulse' methylprednisolone followed by high dose prednisone, azathioprine and hydroxychloroquine with good response.

She currently feels well without complaints other than mild morning stiffness in her hands and occasional malar rash. Current medications are azathioprine 125 mg daily, hydroxychloroquine 300 mg daily, and prednisone 5 mg daily. Physical exam at the visit is unremarkable and routine labs including urinalysis are normal. She has been using barrier contraception (condoms) but asks about other options. She is very worried that any hormone therapy will cause her lupus to flare again. How do you assess her, and what do you recommend?

a. Serologies show negative anti-dsDNA, normal C3C4, and negative antiphospholipid antibodies (aPL) including lupus anticoagulant (LAC), anticardiolipin (aCL) and anti-beta 2 Glycoprotein I (ab2GPI).

b. Serologies show negative anti-dsDNA, normal C3C4, and positive LAC, positive aCL IgG 68 and positive ab2GPI IgG 45

Discussion Point

- The best way to assess patients with SLE for safe and effective contraception, in the setting of negative and positive aPL

Case 2: 33-year-old seeking assisted reproductive technology

A 33-year-old woman with SLE presents for routine follow-up. You have followed her since her diagnosis at age 27 years when she presented with oral ulcers, photosensitive rash, arthritis, pleuritis, positive ANA and positive dsDNA antibody. She started hydroxychloroquine with control of her symptoms after a brief steroid taper. At age 31 she developed nephritis, Class IV and V on renal biopsy. She was treated with intravenous 'pulse' methylprednisolone, rituximab (two doses of 1 gm each) and mycophenolate 2000 mg daily. She continues on the mycophenolate 2000 mg daily, enalapril 20 mg daily and prednisone 5 mg daily. Her serum creatinine has been 1.2 mg/dl, and her dsDNA antibody is low positive with mildly low C3 and normal C4 (markedly improved from her initial

onset of nephritis). The urine protein/creatinine ratio is 1100 mg/gm, down from 3700 mg at onset of nephritis and stable over the last year. She is not in a relationship now but wants to preserve her ability to have biological children in the future and she is very concerned that she will develop recurrent nephritis. She has decided she would like to freeze her eggs and asks your opinion.

a. aPL (LAC, aCL, ab2GPI) are all negative

b. aPL are 'triple positive', with high levels of LAC, aCL and ab2GPI

Discussion Point

- The best way to assess and guide a patient with SLE who is planning oocyte cryopreservation, in the setting of negative and positive aPL

Learning Objectives

- Explain the importance of safe and effective contraception for women with SLE at risk for unintended pregnancy and be able to assess patients and recommend the best options for them
- Describe the risks of ovarian stimulation for patients with SLE, with and without aPL, and suggest and discuss specific management options with the reproductive endocrinologist

Case 3: 36-year-old female seeking pregnancy counselling

Rebecca Fischer-Betz

Maggy is a 36-year-old female office assistant with 8-year history of systemic lupus erythematosus (SLE). Past manifestations of SLE included polyarthritis, pleuritis, positive ANA and dsDNA antibodies and low complement. She had been initially treated with corticosteroids and hydroxychloroquine. Two years ago she had a flare with polyarthritis and treatment with methotrexate was added. Currently she is feeling well. She asks about the possibility of a pregnancy. Her menstruation is regular and has had no previous pregnancies.

Laboratory tests revealed Hb 12,8 g/dl; Plt 233 K/ μ l; leucocytes 3.800/ μ l; Anti-dsDNA 122 (< 80 IU/ml), complement is normal. She is presently taking methotrexate 12.5 mg sc/week and hydroxychloroquine 200 mg/day.

Discussion Points

- Performing pregnancy counselling in women with SLE
- Treatment options available prior to conception and during pregnancy

Case 4: 29-year-old female with lupus nephritis

Rebecca Fischer-Betz

Sara is a 29-year old female from Sri Lanka living with her husband in Germany for five years. She was diagnosed with SLE about one year ago based on the presence of fever, fatigue, leukopenia, positive antinuclear antibodies, positive anti-dsDNA and low complement. In addition, she had proteinuria (>5 g/24 hours) and abnormalities of urinary sediment. A renal biopsy showed Class IV proliferative lupus nephritis. She was initially treated with prednisolone and cyclophosphamide (Euro Lupus protocol) followed by mycophenolate mofetil. She had an early abortion 3 years ago (unplanned pregnancy). Her menstruation cycle has been irregular since she stopped taking an estrogen-containing pill after diagnosis. She worries about infertility. She currently reports joint pain and fatigue, she sleeps a lot. Her physical examination is unremarkable, no arthritis, no edema, blood pressure 125/85 mmHg. Laboratory tests reveal Hb 10,8 (12–16 g/dl) g/dl, creatinine 1,1 (<0,9) mg/dl, urinalysis 40 RBC, Pr/Cr 2,1 g/g, anti-dsDNA 433 (<80 IU/ml), complement C3 66 (90–180

mg/dl), C4 <6 (10–40 mg/dl). Antiphospholipid-antibodies are negative. She is presently taking prednisone 10 mg, mycophenolate mofetil 2 g/day, ramipril 5 mg/day and furosemide 20 mg. Her older brother is also suffering from lupus nephritis. He has stopped immunosuppressive treatment several months ago and is doing well.

Discussion Point

- When and how to plan pregnancy in a patient with lupus nephritis

Learning Objectives

- Demonstrate knowledge of the influence of SLE on pregnancy and vice versa
- Describe main predictors of pregnancy complications in women with SLE
- Describe currently accepted management of SLE prior to conception and during pregnancy
- Explain the importance of pregnancy counselling in SLE patients

Hot topics: the role of complement in SLE

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COMPLEMENT IN SLE

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The complement system and systemic lupus erythematosus (SLE) have been intertwined for nearly 70 years. Complement consumption secondary to increased turnover was an early salient observation. Autoantibodies to nuclear materials forming immune complexes were likely mediating tissue damage. A second and fascinating observation was that a complete deficiency of C1q, C4 or C2 predisposed to SLE. These two key findings have been the heart of lupus-related complement research over the next 50 years.

Complement as a biomarker A major more recent goal here has been to explore complement's activating fragments; namely, fluid phase split products and cell-bound complement activation products (CB-CAPS). The hope here was to provide more sensitive and specific biomarkers to monitor disease activity. A thorough review of these data was recently published.¹ While both split products and CB-CAPS show promise, there remain issues in demonstrating clinical superiority to standard serum C4 and C3. Limitations that commonly arise relate to the complex methodology, availability and interpretation.

Complement in etiopathogenesis The underlying hypothesis has been that complement is required for the proper handling of nuclear debris and thereby prevent an inappropriate autoimmune response. This arena remains a work in progress, but several informative studies have recently been published:^{2–5} In my comments, I will highlight several issues: A) the deficiency story; B) C3b instructing how the opsonic material is processed; C) Evidence that the C4A gene regulates autoreactive B cells in murine lupus; D) C4A gene as a major player in sex-biased vulnerability in SLE; and E) Discovery of an intracellular complement system.

Complement therapeutics Rare genetic variants in complement regulators have been identified in aHUS and C3G and successfully treated with anti-C5 mAbs. This therapeutic development