Abstracts

Friday 6th September 2024

Opening session (HYBRID): enigma variations

01 LUPUS AND HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS

Jessica Manson. *University College Hospital, London, UK*

10.1136/lupus-2024-la.1

Hemophagocytic lymphohistiocytosis (HLH) is a well-recognised complication of systemic lupus erythematosus (SLE). In one small case series, HLH was noted in approximately 5% of patients with lupus.[1] Differentiating lupus flare from HLH can be challenging, since both can cause fever and cytopenia. A recent review of published literature included studies that combined information about a total of 249 patients with lupus and HLH.[2] HLH episodes were described concomitant with first lupus presentation, at the time of subsequent lupus flare and associated with a secondary triggering infection. Other recognized HLH drivers in people with SLE include drugs, malignancy and pregnancy. Mortality is quoted to be up to 19%.[2]

Epidemiological studies show that the number of people diagnosed with HLH of all causes has increased significantly over the last 20 years.[3] This rise is likely multifactorial in origin, in part due to increased recognition and in part due to complications of newer therapies including chimeric antigen receptor (CAR)-T cell therapy, and novel infections such as COVID-19. The risk of HLH in patients with lupus treated with CAR-T cell therapy is not yet known.

In recent years there has been the development of international guidelines for the identification, diagnosis and initial management of HLH.[4 5] These guidelines describe a framework to approach any patient unwell with HLH, which include the work-up and rapid diagnosis of lupus as a possible HLH driver. There is a clear focus on the need for cross-speciality working, which is associated with improved outcomes.

Managing the patient with HLH complicating lupus involves managing the lupus, any additional trigger, and controlling the secondary HLH related hyperinflammation. This will sometimes require using multiple immunosuppressive therapies in parallel. From the HLH perspective, this may include anakinra, intravenous immunoglobulin, ciclosporin, and in the most unwell patients, etoposide. Prospective trials of managing HLH in patients with SLE are lacking.

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Learning Objectives

At the end of this presentation participants will be able to:

- Describe the approach to a patient who presents with HLH and unknown drivers
- Describe which patients with lupus are most at risk of HLH and explain how to recognise the condition early
- Discuss how a patient with lupus and HLH should be treated
- Describe the role of cross-speciality working for all patients with HLH

02 LUPUS AND CANCER

Sasha Bernatsky. *McGill University, Montreal, Canada*

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Malignancy risk in systemic lupus erythematosus (SLE) is about 15% higher than the general age-and-sex-matched population. Hematologic cancers, especially B-cell lymphomas, are about three-fold increased in SLE, while breast, uterine, ovarian, and prostate cancer are associated with lower risk.[1 2]

Increased susceptibility to both SLE and malignancy could result from genetic variations that drive molecular mechanisms, including increased expression of APRIL, higher levels of interleukins (IL-6 and IL-10), and polymorphism of tumour necrosis factor pathways (e.g. TNF α-induced protein 3), or DNA repair.[1 3 4] Specific human leukocyte antigen alleles (e.g. HLA-DR2 and HLA-DR3) are linked to both SLE and lymphoma.[5]

Cyclophosphamide may be a risk factor for hematological and non-melanoma skin cancers in SLE, but this explains only a small proportion of cancers in SLE.[6] Antimalarial drugs are likely associated with lower risk of breast and skin cancers in SLE.[7] Regarding newer therapies, one study of tacrolimus showed no increased cancer risk in SLE.[8] Secondary hematologic malignancies, in non-lupus lymphoma patients treated with cellular therapies, highlights the need to further study these new agents as lupus therapeutics.[6 9]

Smoking correlates with increased lung cancer risk, and lung fibrosis may also be a risk factor.[7] Patients with SLE are at increased risk of developing the squamous intraepithelial lesions that precede cervical cancer development, as well as other malignancies strongly associated with human papilloma virus, including vulvar and anal carcinoma.[1]

At present, promotion of preventive measures such as smoking cessation and regular cancer screening programmes (particularly for cervical dysplasia) in SLE are common-sense interventions. Cervical dysplasia screening could also bring to attention rare vulvar and vaginal cancers.[10] European Alliance of Associations for Rheumatology (EULAR) guidelines recommend annual Papanicolaou smear tests in heavily immunosuppressed patients (e.g. cyclophosphamide).[11] Individuals exposed to cyclophosphamide should undergo lifelong annual urine cytology, with prompt investigation of abnormal cytology, to rule out bladder cancer. Otherwise, patients with SLE should follow cancer screening according to local general population guidelines.

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Learning Objectives

At the end of this presentation participants will be able to:

- Determine what cancers people with SLE may be at higher (or lower) risk of
- Identify SLE treatments that may pose higher risk for specific cancers
- Explain smoking as a cancer risk factor for SLE patients

03 LUPUS AND INFECTIONS

Bregtje Lemkes. *Amsterdam University Medical Center, The Netherlands*

10.1136/lupus-2024-la.3

Immune dysregulation in systemic lupus erythematosus (SLE) results in the autoimmune manifestations of SLE, but also leads to an impaired immune response to pathogens and vulnerability to infections in SLE patients. These patients exhibit a complex immune dysfunction, characterized by both impaired cellular and humoral immunity alongside defects in innate immunity. This occurs even in the absence of immunosuppressive therapy, highlighting the intrinsic nature of the immune dysregulation. Consequently, infection-related complications remain a significant cause of morbidity and mortality in SLE.[1]

The respiratory tract, urinary tract, skin and soft tissue are among the most common sites of infection in SLE patients, frequently caused by an increased susceptibility to common pathogens such as *Streptococcus pneumonia*, *Escherichia coli* and *Staphylococcus aureus*. However, these patients are also at an increased risk of Herpes zoster, Mycobacterium tuberculosis and even opportunistic pathogens such as *Pneumocystis jirovecii* and *Cryptococcus neoformans* or Cytomegalovirus disease.[2]

The risk of these infections in SLE patients is also greatly impacted using immunosuppressive medication.[3] Depending on the mechanism of immune suppression, susceptibility to infections with different pathogens will increase. Prolonged use of corticosteroids, for instance, is associated with mycobacterial disease and risk of *Pneumocystis jirovecii* pneumonia. Anti-CD20 therapy (rituximab), however, increases the risk of hepatitis B reactivation, viral infections and common pathogens causing respiratory infections.[4]

Knowledge of which pathogens to expect, in the often severely immunocompromised SLE patient, is essential in guiding diagnostics in case of acute inflammatory disease, especially because it can be difficult to distinguish between an infection and SLE flare. Moreover, it must guide infection prevention strategies. Recent data show a hopeful reduction in the proportion of mortality contributed to infectious diseases in an Italian cohort of SLE patients, indicating an overall better management of the infectious disease risk in the SLE patient.[5]

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Learning Objectives

At the end of this presentation participants will be able to:

- Explain how immune dysregulation in SLE leads to both autoimmune manifestations and increased susceptibility to infections
- Identify common infection sites and typical pathogens in patients with SLE, even in the absence of immunosuppressive therapy
- Describe how different immunosuppressive medications used in SLE treatment can further increase susceptibility to specific pathogens
- Discuss the challenges in diagnosing infections in SLE patients and the importance of considering both infection prevention and early diagnosis