Diagnosis and Assessment of Systemic Lupus Erythematosus

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Ellen Ginzler:
Hello. My name is Dr. Ellen Ginzler. I am a rheumatologist at SUNY Downstate Medical Center in Brooklyn, New York. My interest is studying outcomes in patients with systemic lupus erythematosus, or SLE, and participating in clinical trials of new medications for lupus. Today, I am going to be speaking to you about the diagnosis and assessment of SLE. The diagnosis and management of patients with lupus should be a collaborative effort between primary care physicians and rheumatologists, as well as other sub-specialists such as nephrologists and dermatologists, depending upon the manifestations in a specific patient.

Ellen Ginzler:
The objectives of care include knowing how to make the diagnosis of SLE and how to initiate the workup and initial treatment for active lupus. The treating physician should be able to distinguish active lupus or a lupus flare from other acute medical conditions, especially those related to infection. It is also critical to recognize red flags. That is those manifestations which require immediate intervention to prevent mortality or severe irreversible organ damage. Historically, the guidelines for diagnosis of SLE have been relegated to lupus experts who recognize the clinical and immunologic features of this multi-system autoimmune disease.

Ellen Ginzler:
Recognition may be delayed when the initial symptoms are nonspecific, such as fever, fatigue, arthralgias, myalgias, weight loss, alopecia, Raynaud's phenomenon, and lymphadenopathy. The first classification criteria for SLE developed by the American Rheumatism Association in 1971 to define patients who would be appropriate for clinical trials were revised in 1982, and again revised finally in 1997 by the American College of Rheumatology. Eleven criteria were identified of which any four occurring either simultaneously or serially have a high probability that lupus is the correct diagnosis.

Ellen Ginzler:
The revisions consider advances in technology and an improved understanding of the pathophysiology of lupus. A subsequent 2012 classification by the Systemic Lupus International Collaborating Clinics or SLICC combined a more extensive list of clinical and immunologic criteria with the requirement that at least one feature must be clinical and one immunologic. These criteria improved the sensitivity of the index at a modest cost to its specificity. The SLICC criteria also advanced the concept that the finding of lupus nephritis based on a kidney biopsy, histologically defined as lupus glomerulonephritis, along with either a positive ANA or anti-double stranded DNA confer to diagnosis of lupus, even in the absence of four criteria.

Ellen Ginzler:
In early 2019, the EULAR/ACR classification criteria for SLE was introduced by a large panel of lupus experts. Based on first, the obligatory requirement of a positive ANA it is followed by additive weighted criteria grouped in seven clinical and three immunologic domains. Patients accumulating 10 or more points are classified as SLE. The goal of these new criteria has been to increase both the sensitivity and specificity of diagnosis with an emphasis on identification early in the disease course. The goals of treatment of SLE include suppression of inflammation in order to reverse or limit organ dysfunction and damage, also to treat specific disease manifestations, to minimize the complications of therapy, and to maximize overall patient function and quality of life.
Ellen Ginzler:
These principles form the concept of treat to target with the recommendation from EULAR that the treatment target should be remission of systemic symptoms and organ manifestations. Where remission cannot be achieved, the lowest possible disease activity state should be achieved. Measurement should be by a validated lupus activity index or by organ-specific markers with prevention of flares as a realistic target to prevent damage accrual. Early recognition and treatment of renal involvement is strongly recommended. In March of 2019, EULAR published a comprehensive update of its recommendations for the management of SLE, including a specific discussion of organ system manifestations and treatment modalities.

Ellen Ginzler:
The most commonly used measures of disease activity include the systemic lupus erythematosus disease activity index or SLEDAI and subsequent SLEDAI-2K revision, which is an index that weights disease activity in nine organ systems during the prior 10 days. Improvements or worsening of overall SLEDAI score can be used clinically in the individual patient, as well as in clinical trials to indicate therapeutic benefit or conversely new disease activity. The SLEDAI is less helpful in scoring changes in disease activity within a specific organ system or manifestation as the assignment of points is all or nothing when the definition of abnormality is met.

Ellen Ginzler:
The much more complicated British Isles Lupus Assessment Group instrument, the BILAG, is an index that assesses a hundred and one clinical signs, symptoms, and laboratory measures across nine organ system domains, each of which is rated with respect to the severity of disease activity for that feature over the previous months, and with respect to any changes from the previous assessment. Based on these activity indexes, one proposed definition of remission is the absence of any clinical or laboratory abnormalities in association with a maintenance regimen of only hydroxychloroquine.

Ellen Ginzler:
A proposed definition of LLDAS, or the lupus low disease activity state includes a SLEDAI-2K of four or less with no activity in major organ systems, no new features of lupus compared to the previous assessment, and a current Prednisolone dose or its equivalent of seven and a half milligrams per day or less. Measures to identify flares of disease activity are problematic. A definition of flare proposed by SLICC is a measurable increase in disease activity in one or more organ systems involving new or worse clinical signs and symptoms and or lab measurements. This is vague and nonspecific.

Ellen Ginzler:
The SELENA-SLEDAI Flare Index has been used in clinical trials to identify mild and moderate versus severe flares based on the appearance of specific disease manifestations or the changes in therapeutic regimen. To avoid the complications of unnecessary aggressive therapy, it’s important to distinguish lupus activity from features of irreversible damage. The SLICC/ACR Damage Index or SDI assesses damage according to 12 systems and categories, with damage defined as any non-reversible change present for at least six months and not related to active inflammation, which occur since the onset of SLE.

Ellen Ginzler:
Finally, it is essential to recognize red flags, that is manifestations which may occur abruptly and must be treated quickly and aggressively to minimize mortality or irreversible loss of organ or patient function. Chest pain, or hemoptysis may signal cardiopulmonary features such as diffuse alveolar hemorrhage, pericardial tamponade, or myocardial infarction. Abdominal pain may be a sign of GI vasculitis or mesenteric or bowel wall thrombosis leading to perforation or gangrene. Particularly worrisome neuropsychiatric manifestations include an altered level of consciousness or focal findings indicative of transverse myelitis.

Ellen Ginzler:
This may be complicated by the spectrum disorder of neuromyelitis optica or Devic's syndrome. Catastrophic antiphospholipid syndrome characterized by thrombosis in three or more organs, systems, or tissues within a week require intensive anticoagulation along with plasma exchange in order to prevent renal and or hepatic failure, strokes loss of limbs, as well as a high fatality rate. To complete an evaluation of a patient’s status, it is important to include a measure of quality of life. A number of patient-reported outcome tools have been proposed, including measures of physical and psychological health.
Ellen Ginzler:
It is important to keep in mind that individual patient lifestyle preferences and cultural norms may have a profound effect on patient satisfaction and ultimate outcome. This concept is key to the principle of treat to target in which the patient must be an active partner in the management plan.

Ellen Ginzler:
I hope this gives you an idea of how to begin to think about diagnosis in patients with systemic lupus, especially considering the various instruments that are available and to understand how we can work with the patient and with other healthcare providers.