Addressing the Ongoing Challenges of Systemic Lupus Erythematosus

As founder and Clinical Director of the new Lupus Center and the Director of Rheumatology Clinical Research at NewYork-Presbyterian/Columbia University Medical Center, Anca D. Askanase, MD, MPH, is well aware that a comprehensive understanding of lupus continues to elude the rheumatology community.

“We’re still in the infancy stage with lupus,” says Dr. Askanase, an internationally renowned clinician, diagnostician, and researcher with more than 15 years specializing in lupus. “We need to come up with some unifying diagnoses, outcome measures, and treatment algorithms that work for the whole disease.”

Among the challenges, notes Dr. Askanase, are that lupus can range from mild to life threatening and it happens in stages. “It’s an accumulation over time of immune system abnormalities that leads to tissue inflammation, pathology, and the signs and symptoms of lupus,” says Dr. Askanase. “Many patients may be experiencing some symptoms long before they seek a doctor’s opinion. I think the diagnosis is harder when things slowly add up, where it’s a process that occurs over a period of years.”

It is an opinion widely shared. “Historically, we’ve been using classification and diagnosis criteria for...” (continued on page 2)

Systemic Lupus Erythematosus: Understanding and Managing Renal Involvement

Twice a year on a Friday, Kyriakos A. Kirou, MD, DSc, Clinical Co-Director of the Mary Kirkland Center for Lupus Care and Director of the Lupus Nephritis Program at Hospital for Special Surgery, and other HSS rheumatologists are joined by nephrologists and a renal pathologist from... (continued on page 3)

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– Dr. Anca D. Askanase
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“Obviously, there are many pressing questions surrounding this disease that need to be more accurately and rapidly answered,” says Dr. Askanase. “Those answers may ultimately emerge from large-scale international collaborations, such as the SLICC, which are pooling cohorts of lupus patients to create a comprehensive database. There is strength in numbers. Having a very large database of patients will help us to answer some of the very important questions. These include actual risk for malignancy or central nervous involvement, long-term sequela of lupus, and whether we are able to make an impact on mortality and morbidity over time.”

For More Information
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Reference Articles


In addition to many other complications of lupus – including cardiovascular, pulmonary, musculoskeletal, gastrointestinal, and neuro-psychiatric – lupus nephritis is a prominent feature of the disease. “Approximately half of lupus patients develop lupus nephritis, usually early in the course of SLE,” says Dr. Kirou, “and approximately 10 to 20 percent of those will progress to dialysis or transplantation.

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Clinical Presentation of Lupus Nephritis

- Proteinuria
- Microscopic hematuria
- Edema
- Hypertension
- Rising serum Cr level
- Nephrotic syndrome

“When the kidney is affected, a very common finding is swelling of the feet,” explains Dr. Kirou. “Blood pressure can be high, which can cause headaches. And in a minority of patients, the urine becomes dark signifying the presence of blood, or foamy because protein is present. These are all clues for the rheumatologist to consider that the patient may have nephritis.”

Dr. Kirou notes that as the disease becomes more active, the patient may have a high ANA titer and a positive anti-double-stranded DNA test. “The levels of complement proteins C3 and C4 are often low, especially in lupus nephritis, reflecting the activation of the immune system,” explains Dr. Kirou. “Below 90 mg/dl for C3 and below 16 mg/dl for the C4 are considered low, but the lower they become, the more likely they are to be indicative of severe disease.”

While symptom presentation and laboratory tests can indicate a diagnosis of lupus nephritis, Dr. Kirou notes that renal ultrasound may be recommended to first rule out other causes of kidney disease. A kidney biopsy is then typically performed on all patients with clinical evidence of previously untreated active lupus nephritis.

“The biopsy will allow us to determine the degree of activity, the degree of inflammation in the kidney, and the degree of scarring,” says Dr. Kirou. “If a lot of scarring is present but not much disease activity, then we generally do not recommend immunosuppresant medications since there’s little or no room for improvement. These patients will likely go on to need hemodialysis or kidney transplant. Patients who are active on the biopsy will need aggressive therapy. The biopsy also helps us decide what therapy to administer. Our renal pathologist, Dr. Surya Seshan, reads the biopsies of all of our patients and helps us arrive at the right diagnosis and then the right treatment approach for each patient.”

Classifying and Treating Lupus Nephritis

A kidney biopsy also enables the lupus nephritis to be classified according to the International Society of Nephrology/Renal Pathology Society 2003 Classification of Lupus Nephritis and evaluated in terms of its activity and chronicity. The biopsy can also help exclude other causes for the renal disease such as acute tubular necrosis due to medications or hypovolemia.

“Class I represents very minor involvement of the kidneys and is not significant clinically. Class II also indicates a very mild degree of disease, with some inflammation present but not enough to trigger therapy,” explains Dr. Kirou. “The disease becomes more serious with Class III and Class IV, representing the proliferation of cells within the kidney or other cells coming from blood in the kidney, which will eventually cause trouble with scarring and kidney function.”

Class V may exist by itself or in association with Classes III and IV and is different than those. “With Class V, lupus nephritis is a membranous disease,” says Dr. Kirou. “So now the problem is in the basement membrane where the glomerular capillaries – small blood vessels where blood filtration to form the urine takes place – are attached. This Class V lupus nephritis, or membranous nephritis, can be mild or more severe depending on the amount of protein leaking into the urine. Classes III, IV, and V often require aggressive treatment. Most doctors will use steroids or similar compounds because they work quickly. The treatment may begin with a high dosage administered intravenously for one to three days just to get a head start on attacking the inflammation. This would be followed by an oral regimen of about 40 to 60 mg of prednisone per day.
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classically either cyclophosphamide or mycophenolate mofetil. After we achieve some control, hopefully the disease will respond and we will start to see reduced swelling and a decrease in proteinuria and blood in the urine, as well as an improvement in blood pressure. When we reach that stage, we want to maintain it because if we don’t, the disease will come back. It’s a relapsing disease. So we will want to give a maintenance therapy for at least two years or so.”

Looking Ahead
Dr. Kirou recommends that in the immediate future “physicians should be more sensitized to treating lupus nephritis very aggressively and very early on. “Time is kidney,” says Dr. Kirou. “It’s important to act quickly and effectively, especially to prevent scarring, which is irreversible. The more attacks there are on the kidney, the more likely the patient will need dialysis.”

The work of Dr. Kirou and his colleagues at HSS and NewYork-Presbyterian extends to collaborations with rheumatologists and nephrologists with an interest in lupus nephritis across the country and around the world through organizations such as the Lupus Nephritis Trials Network. The mission of this international organization of clinicians and scientists is to foster collaborations that include clinical trials designed to prevent chronic kidney disease and end-stage renal failure in patients with lupus; develop guidelines for assessing and treating patients with lupus nephritis; and pursue investigations on a wide variety of therapeutic agents, treatment methodologies, and biomarkers of disease.

Dr. Kirou is also an investigator in the ALLURE study, a Phase III randomized, double-blind, placebo controlled study to evaluate the efficacy and safety of abatacept or placebo in combination with mycophenolate mofetil and corticosteroids in subjects with active Class III or IV lupus nephritis. The study is expected to enroll approximately 400 patients in 120 sites worldwide.

Reference Articles


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