Early diagnosis of systemic lupus erythematosus in primary care by family doctors

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Abstract:

The goal of this article is to describe effective evidence-based diagnosis and clinical presentation of SLE with a focus on the role of the primary care physician. We searched for articles published up to end of 2017 in the following five electronic databases: PubMed, Science Direct, Embase, Web of Science, and Scopus, for both English and non-English language articles with the following keywords: “systemic lupus erythematosus”, “diagnosis”, “management”, “primary care”, “family medicine. SLE is an autoimmune inflammatory disorder that most often influences females of childbearing age, specifically African Americans. A medical diagnosis is made by verifying the existence of at least 4 of 11 criteria suggested by the ACR. A normal patient may have arthritis, a malar or discoid rash, and might test positive for ANA and anti-Smith or anti-dsDNA antibodies. One of the most common complication of vital organ participation is nephritis. Virtually all patients need to take HCQ and most will certainly need corticosteroids. The dosage of the last should be kept as low as feasible. Immunosuppressive medications are regularly given too, especially for vital body organ illness. With better management, patients with lupus are living longer yet are at increased risk of disease and treatment-related complications, including infection, cardiovascular disease, and osteoporosis. These issues ought to be monitored and managed in the primary care setting.

Introduction:

Systemic lupus erythematosus (SLE) affects numerous organ systems and is connected with the production of a variety of autoantibodies [1]. Although genetic, environmental, and hormone impacts have all been shown to play a duty, the specific etiology of SLE remains unidentified. It is much a lot more usual in ladies than in men, with female-to-male proportions approximated to be in between 8:1 and 13:1 [2]. The management of systemic lupus erythematosus (SLE) offers a special challenge to primary care doctors. The clinical manifestations of this "great imitator" are extremely variable, and diagnosis needs medical judgment, an ideal degree of uncertainty, and sensible research laboratory testing. Patients with SLE can have acute condition flare-ups that require intensive therapy to avoid deadly difficulties, and their management frequently calls for that multiple experts be involved. The medications used usually have narrow restorative indices, with many negative results. Although SLE is a complex illness, it can be detected and handled to a huge degree in a primary care setting with suitable professional care and involvement. Early diagnosis and treatment is beneficial for patients past short-term symptomatic improvement, in regards to decreasing the risk of condition flares, although therapy efficacy have to be balanced against medicine poisonings. Inadequate therapy is regular before a medical diagnosis is made, throughout periods when a patient is lost to follow-up or is noncompliant, or in the early phases of a scientific flare when symptoms could be marginal [1]. Likewise, due to the fact that patients with lupus endure longer as an outcome of better therapy choices they are at a boosted risk of chronic diseases, consisting of hypertension, hyperlipidemia, and heart disease, which require the surveillance and preventive care that is well understood to primary care physicians. The objective

of this short article is to describe reliable evidence-based medical diagnosis and management of SLE with a concentrate on the duty of the primary care doctor.

The goal of this article is to describe effective evidence-based diagnosis and clinical presentation of SLE with a focus on the role of the primary care physician.

Methodology:

We searched for articles published up to end of 2017 in the following five electronic databases: PubMed, Science Direct, Embase, Web of Science, and Scopus, for both English and non-English language articles with the following keywords: “systemic lupus erythematosus”, “diagnosis”, “management”, “primary care”, “family medicine. Study designs that were included were randomized controlled trials, case-control studies, cohort studies, prospective and retrospective uncontrolled studies, cross-sectional studies, and review studies. Case reports and case series were excluded. We searched bibliographies for all retrieved and relevant publications to identify other studies.

Discussion:

· CLINICAL PRESENTATION

Early diagnosis and treatment of SLE could prevent illness flares along with possibly permanent damage to significant body organs such as the kidneys, lungs, heart, or nerves [3].Although there are numerous irregular providing syndromes that might lead to substantial hold-ups in medical diagnosis, the majority of patients present with even more easily recognizable illness patterns

including joint pain and swelling, facial rash and/or photosensitivity, pleuritic or pericardial chest pain, Raynaud phenomenon and relentless exhaustion, and fever or weight reduction. Around 60% or even more of the patients have skin and/or joint indications at discussion [4], [5].It is emphasized that the diagnostic criteria for arthritis in SLE include not just joint pain however some proof of joint inflammation such as tenderness, discomfort on variety of motion, or swelling, commonly of the hands. The common malar rash of SLE could be easily confused with other facial rashes such as rosacea and seborrheic dermatitis. Possibly practical however not analysis functions of the malar rash of SLE include lack of burning, itching, tingling, or other discomfort; the rash of lupus usually saves the nasolabial folds, a difference defined in the American College of Rheumatology (ACR) criteria for SLE [6], [7].A substantial minority of patients existing with pleurisy or pericarditis [4], [8].

Table 1. Clinical Findings in SLE

Arthritis
Cutaneous manifestations Photosensitivity Butterfly rash Discoid lesions Subacute cutaneous lupus
Alopecia Raynaud's phenomenon
Oral ulcers
Serositis
Nephritis
Neurologic disease

· ACR DIAGNOSTIC CRITERIA

Early medical diagnosis and treatment of SLE can protect against disease flares in addition to potentially irreparable damages to significant organs such as the kidneys, lungs, heart, or nerve system [3].Although there are many irregular presenting disorders that may cause considerable hold-ups in medical diagnosis, the majority of patients existing with more quickly well-known

condition patterns including joint discomfort and swelling, facial rash and/or photosensitivity, pleuritic or pericardial upper body pain, Raynaud phenomenon and consistent fatigue, and fever or weight reduction. About 60% or more of the patients have skin and/or joint symptoms at presentation [4], [5].It is stressed that the analysis requirements for arthritis in SLE consist of not just joint discomfort however some proof of joint inflammation such as inflammation, pain on series of activity, or swelling, usually of the hands. The typical malar rash of SLE can be quickly confused with various other facial rashes such as rosacea and seborrheic dermatitis. Potentially handy however not analysis features of the malar breakout of SLE include lack of burning, itching, prickling, or various other discomfort; the rash of lupus commonly spares the nasolabial folds, a distinction specified in the American College of Rheumatology (ACR) standards for SLE [6], [7].A significant minority of patients present with pleurisy or pericarditis [4], [8].

Box 1.ACR diagnostic criteria for SLE [13].

The diagnosis of SLE requires the presence of 4 or more of the following 11 criteria, serially or simultaneously, during any period of observation.

Clinical Criteria

1. Malar rash: fixed erythema, flat or elevated, over the malar eminences, often tending to spare the nasolabial folds
2. Discoid rash: erythematous, elevated spots with adherent keratotic scaling and follicular plugging; potentially atrophic scarring in older lesions
3. Photosensitivity: rash as a result of uncommon reaction to sunlight, as identified by patient history or doctor monitoring
4. Oral ulcers: oral or nasopharyngeal ulcer, usually painless, observed by doctor
5. Arthritis: nonerosive arthritis including 2 or even more peripheral joints, identified by swelling, inflammation, or effusion
6. Serositis: pleuritis, by encouraging background of pleuritic discomfort, rub heard by medical professional, or proof of pleural effusion; or pericarditis documented by electrocardiography, rub heard by medical professional, or evidence of pericardial effusion
7. Renal disorder: relentless proteinuria, much less compared to 500 mg/24 h (0.5 g/d) or less than 31 if quantitation is not carried out; or cellular casts (may be red cell, hemoglobin, granular, tubular, or combined mobile casts).
8. Neurologic disorder: seizures or psychosis occurring in the absence of upseting medications or known metabolic derangement (eg, uremia, ketoacidosis, electrolyte inequality).
9. Hematologic disorder: hemolytic anemia with reticulocytosis; or leukopenia, less compared to 4000/mm3 (4.0 109/ L) on 2 or more occasions; or lymphopenia, less compared to 1500/mm3 (1.5 109/ L) on 2 or even more events; or thrombocytopenia, much less than 100 103/ mm3 (100 109/ L) in the absence of angering medicines.

Immunologic Criteria.
10. Immunologic disorder: anti-dsDNA in irregular titer; or presence of antibody to Sm nuclear antigen (anti-Sm); or favorable searching for of antiphospholipid antibody based upon an uncommon serum level of IgG or IgM anticardiolipin antibodies, a favorable examination outcome for lupus anticoagulant making use of a standard approach, or a false-positive serologic test result for syphilis that is understood to be favorable for at the very least 6 months and is confirmed by an adverse outcome in Treponema pallidum immobilization or fluorescent treponemal antibody absorption test.
11. ANA: an abnormal ANA titer by immunofluorescence or comparable assay at any type of time and in the absence of drugs understood to be connected with drug-induced lupus.

· LABORATORY AND OTHER DIAGNOSTIC TESTING

Patients with clinical symptoms strongly suggesting SLE, such as arthritis or rash, may also have asymptomatic manifestations that can only be identified on judicious laboratory testing. In particular, early lupus nephritis or chronic hematologic disease (anemia, leukopenia, thrombocytopenia) is frequently asymptomatic. Although undirected laboratory evaluation is not recommended, if SLE is suspected, an initial evaluation including complete blood count (CBC) with differential, urinalysis (preferably including microscopic analysis), and measurement of serum creatinine level is reasonable. Other studies that should be considered are summarized in Table 2.

· ANA AND OTHER ANTIBODY TESTING

Patients with clinical symptoms highly suggesting SLE, such as arthritis or rash, could also have asymptomatic symptoms that could just be determined on judicious laboratory testing. In particular, very early lupus nephritis or chronic hematologic illness (anemia, leukopenia, thrombocytopenia) is often asymptomatic. Although undirected laboratory analysis is not recommended, if SLE is presumed, a preliminary examination including total blood count (CBC) with differential, urinalysis (ideally including tiny evaluation), and measurement of serum creatinine level is sensible. Various other studies that need to be thought about are summarized in Table 2.

The ANA test is very sensitive for SLE yet, depending upon how it is done and translated, could have poor uniqueness. A positive ANA test outcome can take place in many various other disease states along with in a lot of healthy and balanced people [10] In primary care practice, an excellent majority of favorable ANA examination results could be false positives, and stand for either no illness at all or (much less frequently) an inflammatory problem besides SLE.

In this light, ANA testing need to be executed in patients in whom SLE is suspected on other clinical and/or laboratory grounds such as those listed above. An unfavorable fluorescent ANA (FANA) test result essentially eliminate SLE [6].The infrequent patient with an unfavorable result for ANA by FANA usually has a positive outcome for SSA antibody [11].If lupus is clinically thought, getting an SSA antibody as well as an FANA might speed up the diagnosis. The most beneficial clinical information can be acquired by buying an ANA by FANA with a titer instead of screening with an enzyme-linked immunosorbent assay examination for ANA. Studies recommend that the last test does not have sensitivity and uniqueness, [12] and that it offers neither a titer neither an ANA pattern to clarify the patient's disorder and guide additional testing.

If an FANA is bought, lupus is extremely unlikely if the ANA titer on a standard substrate has a titer of less compared to 1:160. The duty of ANA testing is addressed even more in an additional short article in this concern. If ANA is favorable in a patient with compatible clinical functions, the most useful added examinations are anti-dsDNA, anti-Smith, and serum complement degrees. Anti-dsDNA and anti-Smith antibodies are very certain for lupus, and enhanced anti-dsDNA and lowered complement degrees could show energetic lupus or an approaching exacerbation of disease. Phospholipid antibodies, consisting of lupus anticoagulant testing and anticardiolipin antibodies, should also be gotten. If raised, they assist validate a diagnosis of lupus, [7] and show

an enhanced danger of venous and arterial thromboembolic illness in addition to feasible pregnancy complications.

Table 2. Further diagnostic testing for major organ involvement in early SLE

Presenting Symptom or Finding	Suggested Diagnostic Test
Unexplained chest pain	Echocardiogram for possible pericarditis or pericardial effusion
Unexplained dyspnea or chronic cough	Chest radiograph, possible chest computed tomography, echocardiogram
Anemia	Reticulocyte count, RBC smear microscopy, Coombs test
Unexplained, significant proteinuria, hematuria, or RBC casts	Quantify urinary protein (urine albumin:creatinine ratio), consider biopsy to confirm lupus nephritis

· Differential Diagnosis

Because the manifestations of SLE are so diverse, several diverse conditions are in the differential diagnosis (see Table 3).' The trouble is made extra confusing by the lengthy checklist of conditions that have been related to a positive ANA. In enhancement, there is frequently overlap between numerous rheumatic diseases such as an overlap between SLE and scleroderma or SLE and polymyositis. Since arthritis is one of the most typical manifestation of SLE, the condition that may be most often puzzled with SLE is rheumatoid arthritis. Patients with SLE may provide with a clinical photo that is controlled by arthritis; a cautious background and health examination in these situations could disclose other ideas of SLE and ought to lead the examiner to acquire serologies for SLE.

Infections could also imitate SLE, including viral infections (especially transmittable mononucleosis and sometimes human immunodeficiency infection) and chronic microbial infections such as subacute bacterial endocarditis. Since of nonspecific immune activation, it is not uncommon for patients with various infections to have a favorable ANA. Since immunosuppressive medicines are frequently used in SLE, it is incredibly vital to rule out the

possibility of any type of chronic infection prior to making a diagnosis of SLE. In scientific practice, soft tissue discomfort syndromes such as fibromyalgia prevail, and sometimes patients could together have a favorable ANA. A mindful clinical examination in these situations will generally cannot expose any kind of systemic condition or various other features regular of SLE.

Lastly, a cautious drug history should constantly be taken in order to exclude the possibility of druginduced lupus. Medications that have been most frequently linked in medication induced lupus consist of procainamide, hydralazine, chlorpromazine, methyldopa, and isoniazid. This syndrome is defined by arthritis and pleuropericarditis. Similar to SLE, most patients with drug-induced lupus have positive ANAs. Higher than 66% of patients with medicine induced lupus will certainly have antihistone antibodies. Nevertheless, antihistone antibodies may also be located in about 25% of patients with SLE. The major distinctions in between drug-induced lupus and SLE are that in drug-induced lupus, patients normally do not have kidney or CNS condition and do not have antidouble stuck DNA or anti-Smith antibodies. Additionally, druginduced lupus is uncommon in African-Americans, and there is no sex partiality.' The treatment of drug-induced lupus is just to terminate the annoying drug. In patients who develop a favorable ANA on a specific medicine yet have no indications or symptoms of drug-induced lupus, it is not necessary to discontinue the presumed medicine.

Table 3. Differential Diagnosis of SLE

Other rheumatic conditions Rheumatoid arthritis Fibromyalgia Lyme disease Vasculitis Cryoglobulinemia Rheumatic fever Still’s disease
Hematologic malignancies
Thrombotic thrombocytopenia purpura

Glomerulonephritis
Chronic infections Subacute bacterial endocarditis Viral infections (including human immunodeficiency virus) Secondary syphilis
Sarcoidosis
Multiple sclerosis
Whipple's disease
Chronic fatigue syndrome
Depression

Conclusion:

SLE is an autoimmune inflammatory disorder that most often influences females of childbearing age, specifically African Americans. A medical diagnosis is made by verifying the existence of at least 4 of 11 criteria suggested by the ACR. A normal patient may have arthritis, a malar or discoid rash, and might test positive for ANA and anti-Smith or anti-dsDNA antibodies. One of the most common complication of vital organ participation is nephritis. Virtually all patients need to take HCQ and most will certainly need corticosteroids. The dosage of the last should be kept as low as feasible. Immunosuppressive medications are regularly given too, especially for vital body organ illness. With better management, patients with lupus are living longer yet are at increased risk of disease and treatment-related complications, including infection, cardiovascular disease, and osteoporosis. These issues ought to be monitored and managed in the primary care setting.

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