Commentary

Juggling Art: Making Critical Clinical Decisions without Vital Laboratory Support in Autoimmune Rheumatic Patients in a Resource Poor Setting

Introduction
Laboratory testing is essential when assessing a patient with a suspected autoimmune rheumatic disease. The results can confirm the possible diagnosis, evaluate disease severity, its complications, and assist in determining the prognosis as well as monitor future disease activity of patients. Systemic autoimmune rheumatic conditions like Systemic lupus erythematous (SLE) or Rheumatoid arthritis (RA) can be difficult to diagnose as they mimic themselves and other medical conditions.

Diagnosis
There are well established criteria for the diagnosis of SLE[1] and RA.[2] Diagnosing an autoimmune condition can be challenging and it is reported that on average patients may take up to 4 years before diagnosis is made even in resource rich countries. In Ghana, average disease duration before diagnosis in SLE patients was reported by Dey et al to be about 53.6 weeks range <1 – 380 weeks.[3]

Superior diagnostic techniques are essential for early diagnosis. Given the myriad of symptoms which mimic other conditions, symptoms that overlap especially in the early stages, and the fact that many patients have more than one condition concurrently, the detection and use of autoantibodies is an essential element in making a timely and accurate diagnosis.

Table 1 Laboratory Tests for Classification, Diagnosis and Prognosis of Autoimmune Rheumatic

Rheumatoid Arthritis (RA)
Rheumatoid Factor (IgG) diagnoses RA; provides added specificity when used in combination with other RF or (cyclic citrullinated antibodies) CCP antibody assays
Anti CCP antibodies diagnoses RA and determines prognosis
ESR and CRP for determining disease activity
Sarcoidosis
Angiotensin Converting Enzyme (ACE) supports diagnosis of sarcoidosis
High serum Calcium supports diagnosis of sarcoidosis
Calcium, 24-Hour Urine with Creatinine support diagnosis of sarcoidosis and renal involvement
FBC (Full blood count includes Differential and Platelets) support diagnosis of sarcoidosis
Sjögren's Syndrome
ANA(Antinuclear antibody) screen
Rheumatoid factor
SS-A and SS-B antibodies.
Systemic Lupus Erythematosus
ANA screen
Other antibodies: Chromatin (nucleosomal), dsDNA,(double stranded Deoxyribonucleic acid) anti Sm(Smith) antibodies, ribosomal –p, Scl-70, RNP(ribonucleoprotein), SS-A, and SS-B antibodies
Complement components C3 and C4 and total complement (CH50).
Lupus Anticoagulant and Antiphospholipid
Beta-2-Glycoprotein I Antibodies (IgG, IgA, IgM)
Cardiolipin Antibodies (IgA, IgG, IgM)
Direct Antiglobulin Test (DAT) determines presence of autoimmune hemolytic anemia
Platelet Antibody, Direct (IgG) detects autoimmune thrombocytopenia
Ribosomal P Antibody diagnose neuropsychiatric SLE
RNP Antibody diagnose SLE or MCTD (mixed connective tissue disease)
White Blood Cell Count (WBC) determine presence of leucopenia
Kidney biopsy for diagnosis, staging of lupus nephritis and prognosis
anti-C1q antibodies predict development of kidney disease in SLE
Systemic Sclerosis
Centromere B Antibody diagnose limited cutaneous systemic sclerosis (CREST)
RNA Polymerase III Antibody, Scleroderma Antibody (Scl-70) diagnose systemic sclerosis
Systemic Vasculitis
ANCA (Anti-nuclear cytoplasmic antibody)screen with MPO(myeloperoxidase) and PR3(proteinase 3) differentiate types of systemic vasculitis
C-Reactive Protein (CRP) identify inflammatory or active conditions
Urinalysis and Creatinine assess renal function

47

Commentary

A timely diagnosis offers the prospect of early therapeutic action, which can often slow (e.g., erosion of joints in RA) or even halt disease progression (e.g., undifferentiated connective tissue disease or lupus). Early treatment of these conditions reduces long term damage and its attendant health care costs.[4]

The great advances made in autoantibody testing over the last two decades make it possible to use specific autoantibody markers to increase diagnostic precision in systemic autoimmune diseases. New diagnostic technologies enabling screening for multiple autoantibodies (Refer to Table 1) whose pattern make it possible to diagnose autoimmune diseases earlier and to intervene before serious end organ damage occurs.[5]

Prognosis

In patients with known or suspected systemic autoimmune disease, a panel of disease-specific markers is also useful in assessing prognosis. These disease markers make it possible to tell what possible complications may occur with the disease e.g. anti-C1q antibodies predict development of kidney disease in SLE(Refer to Table 1) and make for better monitoring and treatment tailored to the patient.[6] Biomarkers hold the promise of revolutionizing the management of autoimmune rheumatic conditions by enabling early diagnosis, rapid assessment and prediction of disease severity, personalized choice of therapy, and monitoring of response to therapy. The use of biomarkers for the early detection of autoimmune disease can result in safer and better treatments with fewer side effects for patients and the efficient use of drugs as they are tailored to the patient's unique immunologic and clinical features thus reducing side effects, saving cost and promoting the judicious use of healthcare resources.[7]

Need for improved timely laboratories

In Ghana and indeed most of sub-Saharan Africa, there is undue delay in obtaining serology test results because samples have to be sent outside the country to accredited laboratories in e.g. Germany and South Africa. On average it takes two (sometime three) weeks to obtain these vital antibody tests. This imposes delays in establishing a diagnosis, establishing critical organ involvement and differentiating between a flare-up and an infective process. This situation ultimately then affects the selection of appropriate therapeutic interventions.

These tests also come at huge costs. On average to complete a set of tests for a patient with, for example, SLE will cost about GHC 2000.00 (Two thousand Ghana cedis) or approximately USD 500.00 (Five hundred US dollars) in a country where the minimum wage is about two US dollars a day.

An audit of patient's clinic reviews show a high attrition rate after these tests are requested as patients feel the need to complete tests ordered before coming back for subsequent reviews leading to further delays in treatment.

To make the best of the situation, emphasis is placed on the clinical features of these conditions and clinical judgment when arriving at a diagnosis. This approach is helpful for the more standard presentations of the diseases, but when diagnosing patients with less distinctive features, most physicians get stuck with few differential diagnosis,. Indeed before investigations most referrals diagnose young females with small joint involvement as rheumatoid arthritis instead of SLE, as may be revealed later and to most trainees the foremost diagnosis for any one with joint pain is rheumatoid arthritis.

Renal biopsy is an important tool in the diagnosis of lupus nephritis, this is needed to identify the histological class, determine activity and chronicity indices, detect clinically important non-glomerular lesions, and exclude other diagnoses or comorbidities[8]. A renal biopsy is needed as a definitive diagnosis of lupus nephritis.

Histopathological analysis reports in Ghana takes up to three months to become available in some cases, though the technique of doing renal biopsies is readily available, mainly because the samples are sent to the United Kingdom for analysis. We therefore speculate on the patient's likely renal pathology and move on to take therapeutic decisions. This could result in patients who are stages 1, II or V lupus nephritis who don't need such intensive treatment being treated with drugs that have severe side effect profile. But for those with obviously severe renal disease taking this decision may not be such a risk and works in their favour.

In severe lupus nephritis cases , understanding the disease process together with some clinical and laboratory data is often enough to permit standard treatment despite the absence of a renal biopsy.[9] Monitoring schedules are stretched out to reduce the financial burden on patients (e.g. doing serum complements levels only when essential to distinguish a flare rather than as routine and adjusting liver function tests when on methotrexate to be done in two weeks from the start and thereafter at every visit instead of every month until stable)

If the purpose of the laboratory is to aid the clinician in patient management, then it is usually essential that the methods of detecting autoantibodies are specific, sensitive, reliable, reproducible and most importantly available on time.

Commentary

In our case, cheap and timely maybe more important than up-to-date. The laboratory has an essential role in the proper management of the autoimmune rheumatic patient, we are however a long way from efficient use of this and must carry on the juggling art of conjuring a diagnosis mainly with clinical criterion, and developing our own ways of monitoring and treating our high risk patients bearing in mind the constraints and hoping for the best in the future, all the while pushing for more heath infrastructure development.

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