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BLOOD MARKERS FOR RHEUMATOID ARTHRITIS-Review of Literatures.

Pathology

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ABSTRACT

Rheumatoid arthritis (RA) is a common autoimmune disease estimated to affect roughly 1% of the global population.
Rheumatoid arthritis (RA) is a chronic autoimmune disease that affects about 1.5% of the population. It is driven by multiple pathophysiological factors and manifests with high heterogeneity both among and within patients along the disease course. Rheumatoid arthritis causes significant loss in work productivity, with up to one-third of those diagnosed unable to work within two years of the onset of RA. Traditional methods of diagnosing RA rely both on a physical examination and on blood markers that differentiate RA from other autoimmune connective tissue diseases. , The diagnosis of RA is established primarily on clinical criteria and serologic findings. Hist

KEYWORDS:

Rheumatoid Arthritis, auto-immune disease.

INTRODUCTION

THE Common Blood markers used to diagnose rheumatoid arthritis Includes ESR,C-RP,

Rheumatoid Factor (RF), .Anti-cyclic citrullinated peptide antibody (anti-CCP), Protein biomarker 14-3-3eta.

While low-grade elevation of these markers is non-specific, marked elevation of CRP and ESR is generally associated with significant illness. ESR of greater than 100mm/hour should prompt investigation for infection, malignancy and autoimmunity depending on the clinical circumstances.

DISCUSSION-

1.Erythrocyte sedimentation rate (ESR)
The ESR measures general inflammation, and is not specific for RA. It measures the rate at which red cells settle in one hour. The higher the value, the higher the level of inflammation.

2. C-Reactive protein (CRP)
CRP was first described in 1930 as a component in the sera of patients with lobar pneumonia that could precipitate the polysaccharide from "fraction C" of pneumococcus.

CRP lacks the required specificity to be used in isolation as a diagnostic test for any condition
. CRP is stable in serum or plasma and can be measured by relatively simple and inexpensive analytical methods such as enzyme-linked immunosorbent assay (ELISA), turbidimetry and nephelometry.

Conditions where CRP is routinely measured for Assessment of disease activity of autoimmune/ autoinflammatory conditions includes Rheumatoid arthritis ,Juvenile idiopathic arthritis, Seronegative arthritis, Ankylosing spondylitis, Reactive arthritis ,Psoriatic arthritis

This blood test also measures the presence and level of inflammation in the body. It, too, is not specific for RA. CRP is a protein produced by the liver that becomes elevated with inflammation.

CRP of greater than 200mg/L is typically seen in the setting of bacterial infection/sepsis,

3)ANA (Antinuclear antibody)
Antinuclear antibody (ANA) testing involves the use of indirect immunofluorescence to detect antibodies that bind to various nuclear antigens. Most laboratories employ a HEp-2 cell line (a line of human epithelial cells) as the substrate for this test. The sensitivity of ANA tests can differ when other animal-based substrates are used.
ANAs are reported as titers, and higher values (greater than 1:320) are more likely to represent true-positive results.

4)RHEUMATOid Factor (RF)
The rheumatoid factor is an auto-antibody directed against the Fc portion of immunoglobulin found in the blood of about 80 %of people with rheumatoid arthritis. This is the most common blood test used in diagnosing RA. However, up to 30 %of those with RA won't have a positive RF, and it may not be present early in the course of the disease. Other diseases also may show elevated RF levels.

Rheumatoid factor is a type of antibody found in an estimated 80% of rheumatoid arthritis patients. It's an antibody that attacks healthy tissue and leads to joint inflammation potentially resulting in the development of rheumatoid arthritis symptoms.

Rheumatoid factor (RF), which is an antibody specific for the Fc portion of human IgG, has been considered a marker for RA. RF is, in fact, one of the diagnostic criteria for RA that was established by the American College of Rheumatology.(1)

5).Anti-cyclic citrullinated peptide antibody (anti-CCP)
Anti–cyclic citrullinated peptide (anti-CCP) antibodies have been recognized as a highly sensitive marker for rheumatoid arthritis (RA), Citrulline antibody is an immune protein (antibody) that binds to a nonstandard amino acid (citrulline) that is formed by removing amino groups from the natural amino acid, arginine.

Citrullinated proteins have recently been described as specific antigens of rheumatoid antibodies (4). Citrullination is a protein degradation mechanism in which a peptidylarginine is deimided to peptidylcitrulline by peptidylarginine deiminase enzymes Anti-CCP is thought to be present in anywhere between 60% and 80% of rheumatoid arthritis patients. Often the anti-CCP antibody will be found in patients' blood anywhere from 5 to 10 years before they ever exhibit symptoms of rheumatoid arthritis A Mayo prospective clinical evaluation of the CCP antibody test showed a diagnostic sensitivity for RA of 78% with fewer than 5% false positive results in healthy controls (see Cautions). CCP antibodies have also been reported in approximately 40% of seronegative RA patients, and, like rheumatoid factor (RF), a positive CCP antibody result indicates an increased likelihood of erosive disease in patients with RA.

<20.0 U (negative)
20.0-39.9 U (weak positive)
40.0-59.9 U (positive)
> or =60.0 U (strong positive)

It has been shown that anti-CCP antibody is highly specific for RA (98%) with similar sensitivity to RF (68%- 80%) It has been published that its presence in early disease was a marker of a more aggressive disease and highly predictive of more severe radiological damage (31, 32).

This is a newer blood marker that has begun to be widely used to diagnose RA, especially in combination with RF. CCP antibodies are rarely seen in patients who don't have RA, and so this test was incorporated into the American College of Rheumatology's revised 2010 criteria for diagnosis of RA.

For serological measurements, higher weighting is ascribed to patients

who have higher titers of both anticitrullinated protein antibodies (ACPA) and rheumatoid factor (RF)

6). Protein biomarker 14-3-3eta
In 2007, Kilani, et al demonstrated by Western blot analysis that a novel soluble biomarker, 14-3-3η, was present at significantly higher levels in the synovial fluid and serum of patients with arthritis compared to healthy individuals and that serum levels correlated strongly with the matrix metalloproteinases (MMP) MMP-1 and MMP-310. (5)

Serum 14-3-3η is a constituent of exosomes, and following extracellular release has been shown to participate in a positive feedback interactive loop with TNF in promoting inflammation(6)

Serum 14-3-3η is a novel joint-derived proinflammatory mediator implicated in the pathogenesis of rheumatoid arthritis (RA).

Serum 14-3-3η is a novel RA mechanistic marker that is highly specific, associated with worse disease, and complements current markers, enabling a more accurate diagnosis of RA.

Soluble 14-3-3η acts through signaling cascades such as the extracellular signal-regulated kinase and p38 pathway to upregulate proinflammatory cytokines, including interleukin 1β (IL-1β), IL-6, tumor necrosis factor-α (TNF-α), and factors that are involved in joint degradation such as MMP-9 and receptor activator of nuclear factor-κB ligand (RANKL)(6).

Quest Diagnostics introduced a new blood test for RA based on a protein biomarker known as 14-3-3. This test outperformed both RF and anti-CCP blood tests in identifying early cases of RA.

Elevated blood levels of the 14-3-3eta biomarker outperformed conventional RF or CCP antibody testing in a recent study of early RA, being positive in 60-82% of patients diagnosed with RA compared to RF alone (32-82%) or CCP antibody alone (44-82%). The combination of all three markers further increased sensitivity to 72-100%. In addition, co-morbid conditions, such as type 1 diabetes, osteoporosis and gout, do not abnormally raise blood levels of 14-3-3eta Potential new biomarkers for diagnosis of rheumatoid arthritis A study conducted by Swedish researchers compared donated blood samples before onset of RA symptoms (pre-patient) and after onset with matched control subjects. The plasma levels of 30 cytokines and other markers were measured. Cytokines are a group of proteins that can promote or reduce inflammation. Researchers concluded that those people who later developed RA had "significantly increased levels of several cytokines, cytokine-related factors and chemokines representing the adaptive immune system (Th1, Th2, and Treg cell-related factors)." This study and others like it may help point the way toward development of additional RA-specific blood tests and ultimately, drug therapies based on novel biomarkers.

REFERANCES

1). Banal F, Dougados M, Combescure C, Gossec L: Sensitivity and specificity of the American College of Rheumatology 1987 criteria for the diagnosis of rheumatoid arthritis according to disease duration: a systemic literature review and meta-analysis. Ann Rheum Dis 2009 July;68:1184-1191
2) Walter P. Maksymowych, Stanley J. Naides etal, Serum 14-3-3ç is a Novel Marker that Complements Current Serological Measurements to Enhance Detection of Patients with Rheumatoid Arthritis
3) Quest Diagnostics
4). VAN VENROOIJ WJ, PRUIJN GJ: Citrullination: a small change for a protein with great consequences for rheumatoid arthritis. Arthritis Res 2000; 2: 249-51
5). Kilani RT, Maksymowych WP, Aitken A, Boire G, St-Pierre Y, Li Y, et al. Detection of high levels of 2 specific isoforms of 14-3-3 proteins in synovial fluid from patients with joint inflammation. J Rheumatol 2007;34:1650–7. 11. Chavez-Munoz C, Kilani RT, Ghahary A. Profile of
6). Maksymowych WP, van der Heijde DM, Allaart CF, Landewé R, Boire G, Tak PP, et al. 14-3-3eta is a novel mediator associated with the pathogenesis of rheumatoid arthritis and joint damage. Arthritis Res Ther 2014;16:R99.