Review Article

The Neutrophil Lymphocyte Ratio : an Emerging Diagnostic Marker for Parainflammation

Abstract

Parainflammation also known as Low Grade Chronic Inflammation (LGCI) is a subclinical condition which is not routinely diagnosed especially in apparently healthy persons due to lack of a specific biomarker. The present review describes the value of the neutrophil lymphocyte ratio as a promising biomarker for the diagnosis and prognosis of parainflammation.

Keywords: parainflammation, Disease, Apparently healthy persons, Neutrophil Lymphocyte Ratio, Biomarker

Introduction

Parainflammation otherwise known as Low Grade Chronic Inflammation (LGCI) is a shift in the inflammatory response from short to long lived subclincal inflammation that causes breakdown of the immune tolerance (1,2). It involves a persistent harmful degenerative process in which neutrophils, macrophages, lymphocytes and plasma cells are released in the tissues producing antibodies, cytokines, growth factors and enzymes hence contributing to the progression of tissue damage, fibrosis, granuloma and/or systemic inflammation. The common signs and symptoms of parainflammation includes body pain, myalgia, arthralgia, chronic fatique, depression, anxiety, constipation, diarrhea, weight gain or loss and frequent infections (3).

Parainflammatory Theory of Diseases

Parainflammation appears to be a grand unifying factor predisposing apparently healthy persons to diseases. This is because all human diseases whether infectious and/or non-infectious involves inflammation at the cellular level due to either early cell death (apoptosis) translating into specific organ or gland disease or stem cell stimulation resulting in abnormal cellular proliferation and/or metastasis(4,5). This supports the hypothesis on the emergence and re-emergence of diseases due to changes in the cellular microenvironment in apparently healthy persons. Apparently healthy state according to the WHO is a condition of complete physical, mental and social well-being and not merely the absence of disease or infirmity(6).Disease on the other hand is a particular abnormal condition that negatively affects the structure or function of part or all of an organism which is not due to any external injury(6). Disease can be general or local, acute or chronic. Basically, all human cells require four elements to maintain their physiological state namely food, water, oxygen and detoxification. The body is designed to remain in a physiological state (apparently healthy) over a hundred years as long as these elements are efficiently maintained. A breakdown of any of these elements at the cellular level alters

the functionality of the tissues and organs leading to harmful induction of different barrier systems in the body where the blood-brain barrier, the blood-retinal barrier, the blood nerve barrier, the blood lymph barrier and the blood cerebrospinal fluids barrier becomes non functional.. The barrier systems although unique are similarly structured and equipped with junctional complexes where different connexins, protein sub-units of gap junction channels and hemi-channels constitute important partners whose induction results in parainflammation and diseases (4,5).

Diagnosis of Parainflammation

It is important to make a differential diagnosis because parainflammation is not a specific disease condition but a pathological process to diseases. History and physical examination are thus needed for a definitive diagnosis of parainflammation. The laboratory indications may include abnormal immune indices from the routine complete blood count analysis such as the neutrophil -to- lymphocyte ratio(NLR), increased serum proinflammatory cytokines such as IL-8, IL-1, IL-6 and TNF-α, increased antinuclear antibodies, rheumatoid factor, amyloid A, C-reactive protein and concomitant hypoalbuminemia as well as polyclonal gammopathy (increase in all gamma globulin) in serum electrophoresis (2,3,7,8).Among these parameters, the neutrophil-to-lymphocyte ratio appears to be common in all parainflammatory processes. It has been extensively studied in cardiovascular diseases, rheumatic diseases, diabetes mellitus, systemic diseases, colorectal, gastric, lung and ovarian cancer as well as infectious diseases(9).

The value of the neutrophil-lymphocyte ratio in parainflammation

The neutrophil to lymphocyte ratio (NLR) is the count ratio of the peripheral blood number of neutrophils and lymphocytes that maybe easily calculated by using either absolute cell counts or percentages (9). This ratio gives a multifactoral insight into immunocompetent leukocyte population namely the neutrophil (granulocytes) for the innate immune system and lymphocyte (agronulocytes) for the adaptive immune system due to illness and various pathological state (9). The dynamic of the NLR reveals the intensity of immune-inflammatory reaction and physiological response to insults and diseases**.**

Conditions that affects the NLR

High NLR occurs when the neutrophil count becomes high while the lymphocyte count becomes low whereas a low NLR occurs when the neutrophil count becomes low and the lymphocyte count becomes high. The NLR is not solely an indication for parainflammation but may also increase rapidly following acute physiologic stress (<6hours) resulting from any condition that causes physiological stress such as exercise or hypovolemic shock. Under physiological stress, the number of neutrophils increases while the number of lymphocytes decreases due to increase in the levels of cortisol and epinephrine. This prompt response time makes the NLR a better reflection of acute stress than parameters such as the complete blood count which are more sluggish to respond parainflammation as well as acute phase reactants which are more labor intensive(9,10). The normal range for the NLR is 1-2, values higher than 2.0 or below 1.0 in adults may be diagnostic of a conditionl. An NLR greater than 2 is an early sign of a pathological process such as parainflammation (9).Values 3-7 indicates mild parainflammation, 7-11

indicates moderate parainflammation and sepsis, 11-17 indicates severe parainflammation while 17-23 indicates septic shock and multiple trauma while an NLR ≥23 indicates terminal cancer. The elevation of NLR has relation to the worsening of clinical course, similarly the decrease is related to an improvement or good prognosis(9).

Conclusion

The NLR has been shown to be an accurate, cheap and easy diagnostic marker for parainflammation. The current use of the white blood cell as a clinical marker for parainflammation is based on the fact that it is available and easy to determine. However, given the availability of the NLR, using it to replace the white blood cell count seems like a natural evolution with a better diagnostic and prognostic insight for parainflammation. It is also less expensive compared to the labor and cost of determination of other markers of parainflammation such as lactate, procalcitonin, albumin etc.

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