Role of Pentraxin 3 in Lupus Nephritis

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Abstract

Systemic lupus erythematosus is a complex, multisystem autoimmune disease characterized by production of high-titer autoantibodies directed against ubiquitously expressed self-antigens. The roles of pentraxins 3, dysregulated apoptosis and deficient clearance of apoptotic material in SLE have attracted much attention.

Aim of the Work: To find a role of pentraxin 3 in lupus erythematosus activity.

Patients and Methods: Our study was conducted on 40 female SLE nephritis patients aged (18-40y) with activity. Disease activity was determined by the SLE disease activity index (SLEDAI). All the patients were under ttt with non steroidal therapy and they did not receive immuno suppressive therapy, and 20 healthy female age matched subjects served as control. All were collected from in patient Kasr El Aini Hospital. All were subjected to full clinical evaluation, CBC, 24h urinary protein, renal biopsy for SLE nephritis staging, ANA, anti ds DNA, ESR, and serum level of pentraxin 3.

Results: It was found that serum level of pentraxin is significantly lower in patients than control p-value 0.0001. We also found that pentraxin was -vely correlated with ESR (p<0.05), but not correlated with 24h urinary albumin p-value >0.05.

Conclusion: Pentraxin 3 deficiency may have a role in SLE renal activity.

Key Words: SLE — Pentraxin 3.

Introduction

ALTHOUGH it is well known that hereditary as well as environmental factors are of aetiological importance in systemic lupus erythematosus (SLE), and despite a large body of information, the disease remains an enigma and continues to frustrate scientists, clinicians and patients.

Deviant cytokine patterns and hormonal factors and abnormal T cell and B cell function with a wide range of autoantibodies and immune complexes (ICs) have all been implicated in the aetio-pathogenesis of SLE recently, the pentraxins are a group of highly conserved proteins including the short pentraxins, C-reactive protein and serum amyloid P, and the long pentraxin family member, pentraxin 3, all of which are involved in innate immunity and in acute-phase responses. In addition to their role in innate immunity and inflammation, each of these proteins participates in the removal of damaged and apoptotic cells. Deficiency of pentraxins 3, dysregulated apoptosis leads to deficient clearance of apoptotic material in SLE have attracted much attention.
Pentraxin serum level was measured using ELISA kit supplied by quantakine R&D system USA.

**Results**

We found that pentraxin 3 is statistically significantly lower in lupus patients (1.98 ± 0.641 nmol/L) than control (7.36 ± 7.3 nmol/L), p-value 0.0001. There was a ve correlation between pentraxin in active lupus patients and ESR level r = -0.56, p-value 0.05. We also found no correlation between pentraxin and urinary albumin in patients with active lupus nephritis (r 0.196, p-value 0.513). Also there was no correlation to the stage of nephritis.

**Discussion**

Systemic lupus erythematosus (SLE) involves polyclonal autoimmunity against multiple nuclear autoantigens and presents clinically in a broad spectrum of manifestations ranging from mild fever, skin rashes, and arthralgia to severe inflammation of kidney, lungs, or brain. It has become evident that SLE is not a single disease with a uniform trigger but rather a syndrome that can develop from many different causes. The pathogenesis of SLE is largely based on variable combinations of genetic variants that promote loss of tolerance or tissue inflammation [1-4] e.g. some gene affect apoptosis, opsonization of dying cells, phagocytosis or the digestion of self-DNA which increase the exposure of nuclear particles to the immune system. Another set of risk genes enhance the immune recognition of self nucleic acids by toll-like receptors (tlr) in dendritic cells which increases the production of type I interferon, and eventually the expansion of autoreactive lymphocytes. A third class of genetic lupus risk factors affects tissue inflammation [5].

Pentraxin 3, C-reactive protein (CRP) and serum amyloid p (SAP), are acute phase proteins that are strongly induced in hepatocytes in response to IL-6 [6].

Pentraxin 3 (ptx3) has multiple roles in innate immunity. For example, ptx3 regulates C 1 q binding to pathogens and dead cells and regulates their uptake by phagocytes. It also inhibits p-selectin-mediated recruitment of leukocytes. Both of these mechanisms are known to be involved in autoimmunity and autoimmune tissue injury [7].

Our results showed a highly significant low ptx3 level in patients with lupus nephritis than control group (p=0.0001), and as the main function of ptx3 is to promote clearance of apoptotic cells by the phagocytic system and opsonization, so its deficiency will impair their clearance and invite auto-immune reaction, and this goes with Bottazz et al., who found that pentraxin has multiple regulatory roles on innate immunity. It modulates opsonization including dead cell clearance, complement activation, and leukocyte recruitment, all processes that affect autoimmunity and autoimmune tissue injury [8]. Ptx was reported to regulate the C1q-mediated phagocytosis of apoptotic cells in vitro [6]. As impaired clearance of apoptotic cells is a well established pathomechanism of SLE [8].

We found no correlation between pentraxin 3 and 24 hour urinary albumin excretion in lupus nephritis.
nephritis, pentraxin 3 was lower in patients with stage 2,3 than in other patients but this was not statistically significant (p<0.05) and this goes with Benedetla [9], who found that ptx3-positive cells were detected in the interstitium of nephropathies showing inflammatory interstitial injury. In vitro, cultured human mesangial cells synthesized ptx3 when stimulated with TNF-α and exhibited specific binding for recombinant ptx3. Moreover, stimulation with exogenous ptx3 promoted mesangial cell contraction and synthesis of the proinflammatory lipid mediator platelet-activating factor. This provides evidence that mesangial cells may both produce and be a target for ptx3. The detection of this long pentraxin in the renal tissue of patients with glomerulonephritis with mesangial proliferation and absence of of ptx3 staining in grades 4 and 5, suggests its potential role in the modulation of glomerular and tubular injury.

But there was –ve correlation with ESR which may indicate the role of pentraxin in lupus nephritis activity as found by Deban et al. [10] who stated that a contribution of ptx to SLE is speculative to date. Ptx might promote SLE via modulating the clearance of apoptotic cells or by driving complement-mediated tissue pathology.

Ptx3 deficiency impaired removal of apoptotic material could lead to the release of nuclear structures, possibly also modified during apoptosis. The release of (modified) nuclear structures could then induce an immune response to these autoantigens leading to the production of autoantibodies. Chromatin, a complex of proteins and double-stranded (ds) DNA, is an autoantigen that is clustered in apoptotic blebs. Autoantibodies against chromatin (including anti-dsDNA, anti-histone and nucleosome-specific antibodies) are a hallmark of SLE. Moreover, the formation of anti-chromatin / chromatin complexes can lead to the binding of these complexes to basement membranes, including the glomerular basement membrane (gbm). Here, the positively charged histone tails of chromatin bind to negatively charged molecules in the gbm, such as heparin sulphate proteoglycans [10].

Conclusion:

We conclude that pentraxin 3 deficiency may have a role in the pathogenesis of lupus nephritis.

References