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THE LINK BETWEEN PSORIASIS AND THE IMMUNOLOGICAL PATHOGENESIS OF ATHEROSCLEROSIS

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Abstract: Psoriasis and atherosclerosis are both chronic inflammatory diseases, morphologically manifested as "plaques", but the affected target organs are different. Pro Clinical epidemiological studies suggest that there is a correlation between psoriasis and atherosclerosis. Now, from the perspective of their immunological mechanisms and inflammatory pathways, we will analyze their immunological Do a literature review on the relationship between pathogenesis.
Keywords: Psoriasis; Atherosclerosis; Immunology; Pathogenesis

1 SIMILAR IMMUNE-MEDIATED INFLAMMATORY RESPONSES IN BOTH

Psoriasis is a common chronic relapsing skin disease with a prevalence of adult for 0.91%～8.5% [1]. It is caused by genetic factors and environmental factors Interaction of environmental factors, innate immunity and adaptive immunity autoimmune-mediated inflammatory skin disease, and this inflammatory reaction should be systematic of, resulting in skin and (or) mucosal damage damage, joint manifestations and a variety of comorbid diseases [2-4].
Coronary heart disease and cerebrovascular disease are the two most common fatal heart diseases. Vascular disease, the most important underlying pathological change is atherosclerosis change. The latter is a chronic disease involving large and medium-sized arteries that progresses slowly. Symptoms occur when it causes significant narrowing of the blood vessel lumen or thrombosis. Status [5]. Atherosclerosis was previously thought to be passive deposition of cholesterol processes in blood vessel walls; Currently believed to be innate immunity and adaptive Chronic inflammatory diseases in which immunity is involved [5-6].
Clinical epidemiological surveys have shown that patients with psoriasis are at increased risk of developing atherosclerotic vascular disease. Multiple studies have shown that patients with psoriasis have an increased risk of myocardial infarction [7-11] , and the frequency of stroke, peripheral vascular disease and other diseases also increases [9, 11-15]. A systematic review showed that patients with plaque psoriasis have an increased chance of developing subclinical atherosclerosis, which is mainly manifested by impaired endothelial function and increased arterial stiffness [16]. These studies suggest a link between psoriasis and atherosclerosis, but the cause remains unclear.
Psoriasis and atherosclerosis are both chronic inflammatory diseases. Morphologically, they all appear as " plaques ", but the affected target organs are different. right Whether psoriasis and atherosclerosis share a common genetic background problem, there is no unified conclusion in the current research [17-19].

1.1 Disease Initiation Stage

1.1.1 Many factors such as psoriasis trauma, infection, stress, drugs, and the external biological response modifier imiquimod can induce psoriasis

Gilliet et al [20] propose: Skin damage leads to cell death, Keratinocytes produce antimicrobial peptides (antimicrobial peptides, AMP) LL37. DNA / LL37 complex and LL37 / RNA complex objects pass through Toll- like receptor (Toll-like receptor, TLR) 9 and 7 Activate plasmacytoid dendritic cells (plasmacytoid dendritic cells, pDC), produces type I interferon (interferons, IFN) IFN- α and IFN -β, thereby activating myeloid dendritic cells (myeloid DCs, mDC); with this same When, LL37 / RNA The compound passes TLR8 activation mDC [21-22]. mDC promotes T cell activation, production Cytokines in inflammatory pathways in psoriasis. In addition, some cytokines heat shock protein (heat - shock proteins, HSP) can be directly activated live DC, even directly acting on T cell receptors to initiate psoriasis Immune activation [23].

1.1.2 atherosclerosis

When plasma is rich in cholesterol Very low-density lipoprotein and low-density lipoprotein (low - density lipo - protein, LDL) levels Lift high When, LDL will be deposited in the arteries Membrane [24]. LDL Apolipoprotein in B100 (ApoB100) and arterial Proteoglycans in the extracellular matrix of the inner membrane are bound by ionic bonds, Thereby initiating the development of atherosclerosis [25]. intima middle of LDL Converted to oxidized form after modifications such as oxidation, lipolysis, and proteolysis LDL (oxidized LDL, ox-LDL). ox-LDL and arterial bifurcation Turbulent flow can activate vascular endothelial cells, expressing Eselectin (E - selectin), vascular cell adhesion molecule 1 (vascul ar cell adhesion molecule 1, VCAM-1), cells between sticky attached point son 1 (intercellular cell adhesion molecule1, ICAM-1) and other adhesion molecules, which together with chemokines such as CCL2, CC L5, CXCL10 and CX3CL1 and others recruit monocytes, DCs and T cells etc. enter Membrane [5]. Macrophage colony-stimulating factor produced by endothelial cells promotes Differentiation of monocytes into macrophages. At the same time, macrophages upregulate pattern recognition receptor (pattern recognition recept or,

PRR) expression, including scavenger receptors (scavenger receptors, SR) and TLR. SR mediate uptake ox - LDL thus forming foam cells, producing Lipogenic streaks; And TLR mediate inflammatory response signal of Pathway [26].

1.2 Disease Maintenance Stage

1.2.1 Psoriasis

Mature within the dermis DC and inflammatory mDC secrete cytokines such as interleukins twenty three (interleukin-23, IL- 23) and IL-12, which activates T17 (Th17 and Tc17), T1 (Th1 and Tc1) and T22 (Th22 and Tc22) cells [2]. in T17 Cell activation is currently considered to play a dominant role in the pathogenesis of psoriasis. T17 cells produce IL -17, IL -21 and tumor necrosis factor (tumor Necrosis factor, TNF); T1 Cells produce IFN-γ and TNF; T22 cells produce IL-22 and TNF [2]. IL-17, IFN- γ, IL -22, TNF Cytokines such as keratinocytes can cause proliferation of keratinocytes and produce chemokines, cytokines and AMP [2]. The latter in turn feeds back into DCs, T cells, and neutrophils form a self- amplifying loop that allows skin inflammation to continue to develop. keratinocytes produce born of thin cells because son Bag include Inside Skin thin cells born long because sub (ECGF), vascular endothelial growth factor (VEGF), platelet-derived growth factor (PDGF), Transforming growth factor (TGF-β), IL-1, IL-6, IL -20, etc. ECGF, VEGF, PDGF Involved in the proliferation of blood vessels and fibers in psoriasis lesions, TGF-β, IL-1, IL-6, IL-20 May act on keratinocytes in an autocrine or paracrine manner, promoting Keratinocyte proliferation [2]. Throughout the maintenance phase of inflammation, activated Transcription factors are mainly involved in NF -κB, STAT1 and STAT3 [23].

1.2.2 Atherosclerotic macrophages and DCs and endothelial cells are abundantly expressed PRR

SR uptake After ox-LDL, intracellular cholesterol accumulation activates the inflammasome and secretes IL-1β [5]. ox-LDL Also available via TLR activates intracellular NF-κB, IRF, AP-1 and other transcription factors lead to pro-inflammation factor(IL-1, TNF, IL-12, IL-6), trend factor(MCP-1, RANTES, IP-10), eicosanoids (Leukotriene B4), Protease (collagenase, elastase, cathepsin), oxidases and costimulatory molecules (CD80, CD86, CD40) expression is upregulated [5]. These products further promote the aggregation and proliferation of various cells and lipid deposition in the arterial intima, leading to the gradual increase of atherosclerotic plaques. deposited in the intima ApoB100 is used as an antigen DCs are transported to the corresponding draining lymph nodes or spleen, and after uptake, they are expressed as antigenic peptides MHC -II Compound-like approach is presented to CD4 + T cell. T Cells differentiate into effectors after activation T and memory T cells re-enter the blood flow, and under the action of chemokines, adhere to the endothelium that highly expresses adhesion molecules and enter the atherosclerotic plaque, where they are absorbed by macrophages and macrophages in situ. DC Reactivate [5]. In the pathogenesis of atherosclerosis, Th 1 cells play a leading role, and Th2 and The role of Th17 immune response is still unclear [5]. in lymphoid organs B Cells are activating T Cells produced with the help of cells targeting LDL Antigenic epitope Antibodies [5]. In addition to LDL, other plaque antigens, such as β-2 glycoprotein I (β2GP I) and HSP Can be stimulated in situ or around the plaque T cells and B Cellular response, involved in the occurrence and development of atherosclerosis [27].

From immune cell activation to inflammation in psoriasis and atherosclerosis The process of symptom reaction formation can be summarized as:(1) Lymph node intraantigen extraction cell activation T cells secrete leukocyte function-related antigens 1 (leu - cocyte function-associated antig en-1, LFA-1); (2) activated T Cells migrate into blood vessels and adhere to the vascular endothelium (Macrophages are also involved in atherosclerosis); (3) LFA-1 and ICAM-1 (or CD20 and LFA-3) Mediates immune cell overflow; (4) activated T cells and DC interaction(In psoriasis there are Macrophages and keratinocytes are involved, and in atherosclerosis Macrophages and smooth muscle cells are involved); (5) reactivated T thin cells and macrophages secrete chemokines and cytokines, leading to inflammation reaction, forming psoriatic plaques and atherosclerotic plaques [28]. Similarities in the pathogenesis of the two include: In terms of innate immunity, it has TLR Mediated cytokine-driven inflammatory response; in adaptive free In terms of epidemics, not only do both Th1 cells are involved and may also exist Th17 cells and regulatory T cells (regulatory T cells, Tregs) Participate [5, 29-30].

In short, psoriasis and atherosclerosis have similar immune -mediated inflammatory responses, and the same cytokines, adhesins, costimulatory molecules, and immune cells in the inflammatory pathways of the two are not discussed here [31].

2 THE ROLE OF IMMUNE IMBALANCE CAUSED BY OBESITY IN THE PATHOGENESIS OF BOTH POSSIBLE EFFECTS

A large sample Meta- analysis shows: Compared with normal people, silver The prevalence and incidence of obesity in patients with schizophrenia are increased [32]. Number on hand It is suggested that there may be a two-way relationship between obesity and psoriasis [33-35].

Human adipose tissue contains adipocytes and immune cells (include macrophages and DC) etc., is the largest endocrine organ in the human body [36]. Can synthesize large amounts of adipocytokines (adipoc ytokine), including thin white (leptin), fat catenin (adi ponectin), against anti- white (resistin), visfatin (visfatin), Lipocalin-2, TNF-α, CX-CL5 et al [37]. At the same time, adipose tissue also belongs to the innate immune system. Adipocytokines and immune cells are more involved in inflammation-related insulin Resistance (insulin resistance, IR) [38].

This article summarizes the effects of four major adipocytokines on metabolism, Vascular and immune effects. Many of these effects are involved in the pathogenesis of psoriasis and atherosclerosis, and the overall effect of these changes may lead to immune imbalances that induce or exacerbate psoriasis and atherosclerosis.

3 SYSTEMIC INFLAMMATION IN PSORIASIS MAY PROMOTE ATHEROSCLEROSIS TRANSFORMATION OCCURS

Boehnkke etc [40] carry out "psoriatic march " " False Said that severe psoriasis is a chronic systemic inflammatory disease disease, the systemic inflammation associated with psoriasis may lead to IR, And then lead to endothelial dysfunction, ultimately leading to atherosclerosis occur.

Existing research has found that patients with psoriasis may indeed be in a state of chronic systemic inflammation [36-37, 39-40]. Indicators reflecting systemic inflammatory response in the blood of patients with psoriasis include: CRP, VEGF, indicators reflecting platelet activation such as P- selectin and adipocytokines were significantly increased [41-43]. In addition, the levels of many immune molecules in patients with moderate to severe psoriasis are increased in the peripheral blood, and the expression of corresponding genes in the skin lesions is enhanced, including IL-17,IL-1RA, TNF-α, CCL5,CCL2, CCL4 [2]. Some scholars apply KC - Tie2 The transgenic mouse model [44] demonstrated that persistent skin-specific inflammation promotes aortic root inflammation and thrombosis, and active treatment of skin inflammation may weaken the pro-inflammatory and pro-thrombotic pathways that lead to cardiovascular disease in psoriasis. Function [45].

Current research on the causes of inflammation IR Most of the studies are related to obesity Chronic low-grade inflammation is used as a model, and its specific mechanism is complex and has not yet been completely elucidate Ming [38]. ginseng Inflammation causes IR Cytokines include TNF-α, IL-1β, IL-6, leptin, adiponectin, resistin, monocyte chemotactic change protein 1 (monocyte chemoattractant protein-1, MCP-1), etc., involving JNK and IKKβ/ NF-κB etc. letter Number Pass Road [38, 46]. These cytokines activate JNK and IKK β/ NF -κB Signaling pathways that cause insulin receptor substrates 1 (insulin receptor substrate-1, IRS-1) or IRS-2 phosphorylation of serine kinase, thereby reducing PI3K and Akt activity, ultimately leading to IR [38, 46]. and, JNK and IKK β/ Activation of the NF -κB signaling pathway produces pro-inflammatory cells Cytokines, which then activate the signaling pathway to form a positive feedback loop, enlarge IR effect.

Research shows that NO Synergizes with prostacyclin to inhibit platelet aggregation, At the same time, the expression of adhesion molecules by endothelial cells is reduced, thereby reducing leukocytes. (Macrophages) Adherence to and penetration of the endothelium. NO Endothelial media can also be used Inhibits vascular smooth muscle cell proliferation and ox - LDL Form [47] , thus Prevent atherosclerosis.

IR sometimes accompanied by compensatory hyperinsulinemia, which can lead to Vascular endothelial cell synthesis NO decrease, while plasminogen activator inhibits preparation 1 (plasminogen activator inhibitor 1, the expression of PAI-1) is increased, and excess insulin binds to hepatocyte insulin receptors combined, by inhibiting serine kinase phosphorylation and mitogen-activated protein Kinase (mitogen-activated protein kinase, MAPK) activity, reducing high-density lipoprotein / Low-density lipoprotein ratio [48]. IR hour Endothelial cell apoptosis is accelerated, and regenerated epithelial cells replace apoptotic epithelial cells. epithelial cells, but this regenerated epithelium is dysfunctional and aging and cannot produce produce enough NO, thereby promoting atherosclerotic plaque formation The resulting inflammatory reaction is more likely to occur [47]. In addition, NO endothelial derived vasoconstrictor factor (especially endoperoxides and prostacyclins) and endothelin 1 production increases, they activate vascular smooth muscle cells to The body causes vasoconstriction, thereby enhancing endothelial dysfunction [47]. The combined effect of the above pathophysiological changes during IR promotes atherosclerosis transformation occurs.

In summary, from local inflammatory skin lesions Inflammatory factors such as TNF -α Can diffuse into blood circulation and cause systemic inflammatory response. systemic inflammation By-products of disease such as reactive oxygen species, dyslipidemia and other metabolic disorders depend on Depends on peripheral tissues such as liver and fat [49]. These media are independent or Complementarily act on endothelial cells, leading to endothelial dysfunction, manifesting for adhesion molecules (VCAM, ICAM) Increased expression, leukocyte extravasation and increased production of reactive oxygen species, NO Mediated smooth muscle relaxation and vasculature Decreased expansion function [49]. Eventually, endothelial dysfunction gradually evolves and progresses toward atherosclerosis.

In summary, the correlation between psoriasis and atherosclerosis may be It may be the result of the interaction of multiple factors. From the immunological pathogenesis See, psoriasis and atherosclerosis share similar immune-mediated inflammation Symptomatic reaction; Immune imbalance caused by obesity may be a common cause of both diseases. Tongtong; Systemic inflammation in psoriasis may promote atherosclerosis transformation occurs.

Many inflammatory diseases (Including rheumatoid arthritis, systemic erythema lupus, psoriasis, inflammatory bowel disease, etc.) [49] , but the exact mechanism leading to atherosclerosis varies in different inflammatory conditions. May vary among diseases. skin as a vibrant Immunoactive organ, skin lesions are easy to observe and measure, and specimens are easy to obtain. Therefore, psoriasis has become a research model for immune-mediated inflammatory diseases [50]. In the future, we will continue to deepen the research on the causes of psoriasis and atherosclerosis by combining immunology, molecular biology, genetics and other disciplines. input, may help find unique therapeutic targets for both inflammatory diseases. The understanding of disease opens a new chapter.

COMPETING INTERESTS

The authors have no relevant financial or non-financial interests to disclose.

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