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Immunomorphological Mechanisms of Tissue Damage in Dermatomycoses and Antiphospholipid Syndrome: Pathogenetic Parallels and Therapeutic Approaches

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Abstract The article examines the immunomorphological mechanisms of tissue damage in dermatomycoses and antiphospholipid syndrome (APS), identifies common pathogenetic parallels, and proposes approaches to optimize therapy. A comparative clinical, morphological, and immunohistochemical study was conducted involving 128 patients: military personnel with chronic dermatomycoses and pregnant women with APS. Both conditions demonstrated similar signs of inflammatory-endothelial destruction, including endothelial activation, ICAM-1 and VCAM-1 expression, CD68-positive cell infiltration, microthrombosis, and elevated serum levels of IL-1β, IL-6, and TNF-α. The study confirmed the existence of a universal mechanism of immunomorphological tissue injury inherent in both infectious-inflammatory and autoimmune processes. Pathogenetically oriented therapeutic approaches correcting endothelial dysfunction and inflammatory cascades are substantiated.

Keywords Dermatomycoses, Antiphospholipid syndrome, Immunomorphology, Endothelial activation, Cytokines, ICAM-1, VCAM-1, CD68

1. Introduction

In recent decades, there has been a growing scientific interest in studying the pathogenetic mechanisms of chronic inflammatory and autoimmune diseases associated with structural tissue alterations, microcirculatory disorders, and immune dysregulation. Among these, **dermatomycoses** and the **antiphospholipid syndrome (APS)** occupy a significant place. Despite their differing etiologies—infectious and autoimmune—they share several common morphofunctional and immunological features. Both diseases demonstrate typical forms of tissue injury mediated by disturbances in cellular immunity regulation, activation of inflammatory cytokines, endothelial dysfunction, and microthrombosis [14,17].

Modern concepts of the pathogenesis of APS and chronic mycoses increasingly approach the idea of **immunomorphological parallelism**, in which tissue damage results not only from the direct action of the pathogen or autoantibodies but also from a complex cascade of immune and hemostatic reactions. Clinically, manifestations such as trophic skin lesions in dermatomycoses and microangiopathy in APS share a common pathogenetic basis—an **inflammatory-thrombotic process** associated with cytokine-induced endothelial activation, immune complex deposition, and apoptosis of vascular wall cells [18,22].

Under conditions such as military service and pregnancy—both typical models of stress and hormonal load—these processes intensify, leading to destabilization of local immune homeostasis. Among military personnel, chronic dermatomycoses often develop due to prolonged exposure to adverse microbial factors, increased perspiration, microtrauma, and suppression of cellular immunity [2,7]. In pregnant women, APS induces pronounced endothelial disturbances resulting in placental insufficiency and recurrent pregnancy loss [1,12].

The morphological picture of both pathological states reveals similarities in mechanisms of tissue damage. In dermatomycoses, acanthosis, spongiosis, vacuolization of the basal layer, lymphocytic and macrophage infiltration, foci of fibrinoid necrosis, and thickening of vessel walls are commonly observed. In APS, histological examination demonstrates microthromboses, endothelial immunoglobulin deposits, subendothelial proliferation, and fibrinoid alterations in the walls of placental arterioles and capillaries [22,11]. Thus, both processes share a common morphological model — **immunovasculitis with a thrombo-inflammatory component**.

From an immunomorphogenetic perspective, a key element is endothelial activation under the influence of inflammatory

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mediators and autoantibodies. In APS, the main pathogenic factor is the presence of antibodies to phospholipids and β2-glycoprotein I, leading to vascular wall injury and platelet activation [15,13]. In dermatomycoses, similar effects are triggered by fungal antigens stimulating T-cell responses and production of proinflammatory cytokines (IL-1, IL-6, TNF-α), which in turn promote endothelial activation and local microthrombosis [6,8].

Recent studies have revealed that both diseases are characterized by comparable ultrastructural changes—endothelial cell destruction, basal membrane edema, accumulation of electron-dense material in the subendothelial space, increased expression of adhesion molecules (ICAM-1, VCAM-1), and loss of intercellular junctions [22,16]. These findings emphasize the role of the endothelium as a **universal target of immune injury**, common to both infectious-inflammatory and autoimmune diseases.

Clinically, this analogy has important implications. In dermatomycoses, therapeutic resistance and recurrent courses are often linked with immune dysfunction, including decreased T-cell cytotoxicity, Th1/Th2 imbalance, and activation of the phagocytic system [4,6]. In APS, analogous disturbances manifest as B-cell hyperactivation and autoantibody production against phospholipid-binding proteins, initiating a cascade of inflammatory-thrombotic responses [10,13]. Consequently, both pathologies can be considered as part of a **single immunopathological continuum** encompassing endothelial activation, inflammation, and microthrombosis.

A major challenge of modern medicine is the search for **universal therapeutic approaches** aimed not only at etiological elimination of pathogens or inhibition of autoantibodies but also at **correction of immunomorphological links of pathogenesis**. In dermatomycoses, this is achieved through systemic antimycotic therapy combined with immunomodulating agents (interferons, azoximers, probiotics) [3,8]. In APS, anticoagulant and antiplatelet therapy is directed at restoring endothelial function and preventing thrombosis [5,19]. However, the pathogenetic effectiveness of treatment largely depends on timely detection of immunomorphological changes that precede clinical manifestation.

The **relevance** of this study lies in the need to integrate morphological, immunological, and clinical data into a unified diagnostic and therapeutic framework for chronic inflammatory-thrombotic diseases. Investigating the immunomorphological mechanisms of tissue damage in dermatomycoses and APS enables the identification of common pathogenetic pathways and the development of targeted therapeutic strategies. For the first time, a comprehensive comparison of tissue alterations in infectious-inflammatory and autoimmune processes is proposed at the level of the microvascular network and cellular immune response.

The aim of the study is to identify common and specific immunomorphological mechanisms of tissue damage in dermatomycoses and antiphospholipid syndrome in order to define pathogenetic parallels and optimize therapeutic strategies.

Objectives of the study include: identifying morphological features of inflammatory-thrombotic processes in skin and placental tissues; determining the nature of endothelial and cellular immune alterations; evaluating the expression levels of immunohistochemical markers (ICAM-1, VCAM-1, CD31, CD68); and correlating immunomorphological data with clinical progression and therapeutic outcomes.

Scientific novelty lies in the interdisciplinary comparison of dermatological and obstetric-immunological models of tissue injury, which will help to propose new pathogenetically grounded methods for correcting inflammatory-thrombotic conditions.

2. Materials and Methods

This study was conducted as a comparative clinical, morphological, and immunohistochemical investigation of two groups of patients representing distinct nosological forms of chronic inflammatory-thrombotic processes — **dermatomycoses** and **antiphospholipid syndrome (APS)**. The research was carried out between 2020 and 2024 at the departments of dermatovenereology and pathomorphology of a medical university, as well as in clinical departments of obstetrics and gynecology.

A total of 128 patients participated in the study, divided into two main groups and one control group. The first group consisted of 68 **military personnel with chronic dermatomycoses**, who received treatment at specialized hospitals and outpatient clinics. The second group comprised 60 **pregnant women with APS**, hospitalized or monitored in obstetric units for placental insufficiency and recurrent miscarriage. A control group of 30 healthy volunteers without signs of autoimmune or infectious-inflammatory diseases of the skin or vasculature was also included. The mean age of patients in the first group was 27.4 ± 3.1 years, and in the second group 29.8 ± 4.5 years. All participants provided written informed consent, and the protocol was approved by the local ethics committee.

The inclusion criteria for dermatomycosis patients were the presence of clinically and mycologically confirmed fungal infections of the feet, legs, interdigital spaces, or trunk lasting more than six months, resistance to standard topical therapy, and the absence of systemic immunodeficiency or diabetes mellitus [2,7]. For APS, the selection was based on the Sydney diagnostic criteria (2006): the presence of clinical signs of thrombosis or obstetric complications (miscarriages, fetal growth restriction, preeclampsia) combined with laboratory evidence of antiphospholipid antibodies to cardiolipin or β2-glycoprotein I [15,13].

A multilevel approach combining clinical, laboratory, morphological, and immunohistochemical analyses was applied. Clinical examination involved assessing the intensity of inflammatory and vascular manifestations, disease duration, recurrence rate, and therapeutic efficacy. In dermatomycosis patients, the extent of skin lesions, infiltration, desquamation, fissures, and associated nail changes were recorded. In pregnant women with APS, the number of previous miscarriages,

gestational timing of complications, and signs of placental insufficiency were evaluated using ultrasound and Doppler imaging [1,12].

Morphological examination was performed on biopsy specimens obtained from the affected skin in dermatomycosis patients and from placental tissues of women with APS. The samples were fixed in 10% neutral formalin, dehydrated in graded alcohols, and embedded in paraffin. Sections of 4–5 μm thickness were stained with hematoxylin and eosin, Van Gieson, and Mallory's trichrome for the identification of collagen fibers. Structural changes in the epidermis, dermal vessels, and placental villi were analyzed, including the degree of dystrophy, necrosis, endothelial proliferation, and inflammatory infiltration [16,18].

For the immunohistochemical analysis, monoclonal antibodies to ICAM-1, VCAM-1, CD31, and CD68 were used to assess the expression of endothelial and cellular markers. Reactions were performed using the standard indirect immunoperoxidase technique with diaminobenzidine (DAB) as the chromogen. Microscopy was carried out with a Leica DM2500 system, and staining intensity was evaluated semi-quantitatively on a scale from 0 to 3. At least 30 tissue samples from each group were analyzed. Statistical analyses included the Mann–Whitney and Spearman tests, with $p < 0.05$ considered significant [22,3].

Immunological studies of peripheral blood were performed to determine levels of IgG and IgM antibodies to cardiolipin and β2-glycoprotein I, as well as circulating immune complexes. The cytokine profile (IL-1β, IL-6, TNF-α) was measured using enzyme-linked immunosorbent assay (ELISA). In patients with dermatomycoses, additional parameters were assessed, including neutrophil phagocytic activity and the level of secretory IgA [6,4].

For histometric evaluation, microvascular morphometry was performed using ImageJ software. Capillary diameter, basement membrane thickness, vascular density, and the percentage of endothelial damage were quantified. In APS, microthrombosis and hyalinosis in placental vessels were assessed, while in dermatomycoses, inflammatory infiltration density and epidermal lesion depth were analyzed [11,22].

Statistical analysis was carried out using the **SPSS 26.0** software package. Quantitative data were presented as mean (M), standard deviation (SD), and standard error (m). Correlations between cytokine levels, expression of immunohistochemical markers, and clinical parameters were determined using Spearman's coefficient. Statistical significance between groups was evaluated using Student's t-test ($p < 0.05$).

Through this comprehensive methodological approach, the study combined morphological, immunohistochemical, and clinical data to identify **universal patterns of tissue injury** in both infectious-inflammatory and autoimmune processes. The obtained findings served as a foundation for the subsequent analysis of pathogenetic parallels and the rationale for therapeutic strategies, presented in the following section, **Results and Discussion**.

3. Results and Discussion

The comprehensive analysis conducted in this study revealed fundamental similarities in the mechanisms of tissue damage occurring in infectious-inflammatory and autoimmune-thrombotic conditions. These findings justify considering **dermatomycoses** and **antiphospholipid syndrome (APS)** as two models along a single pathogenetic continuum — the inflammatory-endothelial injury pathway. Despite differing etiological factors, both diseases share a primary mechanism involving the disruption of endothelial and cellular homeostasis, activation of inflammatory mediators, and the development of microvascular dysfunction.

In dermatomycoses, the clinical picture was characterized by chronic inflammation manifested as erythema, lichenification, desquamation, fissures, and secondary bacterial complications. Morphologically, patients exhibited acanthosis, parakeratosis, focal spongiosis, vacuolization of basal keratinocytes, and membrane destruction. The dermal microvasculature showed capillary dilation, perivascular lymphocytic and macrophage infiltration, fibrin deposition, and plasma stasis, indicating the activation of a local thrombo-inflammatory mechanism [2,7]. Immunohistochemical analysis demonstrated increased expression of ICAM-1 and VCAM-1 on endothelial cells, confirming their activation under the influence of inflammatory cytokines. The same areas showed intense infiltration by CD68-positive macrophages, reflecting macrophage-mediated vascular wall destruction.

In APS, a distinct clinical pattern was observed, but the underlying morphogenetic processes were strikingly similar. Pregnant women with APS showed signs of chronic placental insufficiency, including intrauterine growth restriction, premature placental aging, fetal hypoxia, and microthromboses in the intervillous space. Morphological examination of placental villi revealed fibrinoid necrosis, vascular hyalinosis, stromal sclerosis, and immunoglobulin deposits along the vascular endothelium. Immunohistochemical staining revealed increased ICAM-1 and VCAM-1 expression, comparable to that seen in chronic dermatomycoses, thereby confirming shared mechanisms of endothelial activation [18,22].

A key immunomorphological observation in both groups was the consistent evidence of endothelial destruction. Both diseases exhibited swelling and desquamation of endothelial cells, thickening of the basement membrane, and the accumulation of electron-dense material in the subendothelial space — features indicating increased vascular permeability and local thrombogenicity. These changes correlated with elevated levels of circulating immune complexes and proinflammatory cytokines (IL-1β, IL-6, TNF-α) in blood serum, supporting the concept of systemic endothelial dysfunction in chronic inflammatory conditions [6,19].

Comparative evaluation demonstrated that the intensity of ICAM-1 and VCAM-1 expression in dermatomycosis patients was higher in the peripheral zones of inflammatory foci, whereas in APS it was diffusely distributed in the placental microvasculature. This difference reflects the

localized inflammatory nature of dermatomycoses and the systemic vascular inflammation characteristic of APS. Enhanced CD31 expression indicated endothelial proliferative activity, while the accumulation of CD68-positive cells suggested an active macrophage-histiocytic response aimed at clearing damaged cells and basement membrane components [22,3].

Immunological testing confirmed parallels in cellular immune regulation. Patients with dermatomycoses demonstrated reduced functional activity of T lymphocytes and a decreased CD4/CD8 ratio, indicating exhaustion of the effector immune response. In pregnant women with APS, hyperactivation of B cells was noted, accompanied by elevated levels of IgG antibodies to phospholipids and β2-glycoprotein I, leading to direct endothelial injury and platelet activation [15,13]. Both conditions thus exhibit a similar **inflammatory endotheliopathic syndrome**, differing only by the etiological trigger — fungal antigens in dermatomycoses and autoantibodies in APS.

Cytokine profiling further confirmed this similarity. Both patient groups exhibited elevated serum concentrations of IL-1β, IL-6, and TNF-α, with levels positively correlating with the severity of endothelial activation and microthrombosis. These data support the role of proinflammatory cytokines as mediators linking immune, vascular, and coagulation systems [4,6]. However, TNF-α and IL-6 levels were significantly higher in APS, reflecting the more systemic nature of the autoimmune vascular response compared to localized fungal inflammation.

Overall, the findings substantiate the hypothesis that chronic dermatomycoses and APS share a **universal mechanism of inflammatory-endothelial destruction**, morphologically manifesting as immunovasculitis and microthrombosis, and immunologically characterized by cytokine activation and cellular homeostatic imbalance. Endothelial cells serve as the principal target in both pathologies: in dermatomycoses, endothelial injury is driven by prolonged exposure to fungal antigens and toxins, whereas in APS it results from immune complex formation and antibody binding to phospholipid structures on cell membranes [19,18].

Therapeutic strategies for these disorders, despite their different etiologies, converge around shared goals — correction of endothelial and vascular dysfunction, and suppression of chronic inflammation. In dermatomycoses, the most effective regimens combined systemic antimycotics with immunomodulatory agents and probiotics to restore microbiota balance and local immunity [3,8]. In APS, treatment efficacy improved with the use of anticoagulants in combination with low-dose corticosteroids and antioxidants, contributing to stabilization of endothelial membranes and prevention of thrombosis [5,13]. Hence, modern pathogenetic therapy for both diseases should include not only etiological interventions but also restoration of the disrupted immunomorphological architecture of the affected tissues.

Taken together, the results demonstrate that **dermatomycoses and APS share distinct pathogenetic parallels** grounded in a unified tissue response pattern: endothelial activation, local thrombogenicity, and persistent inflammation. Immunohistochemical data confirm that ICAM-1 and VCAM-1 can be considered universal markers of inflammatory-thrombotic injury, while changes in CD31 and CD68 expression reflect ongoing morphogenetic remodeling of the vascular wall. This body of evidence supports the concept of a **universal immunomorphological mechanism of tissue damage**, manifesting across diverse inflammatory and autoimmune conditions.

4. Conclusions and Practical Recommendations

The conducted study demonstrated that dermatomycoses and antiphospholipid syndrome (APS), despite their different etiologies, share a common pathogenetic foundation based on inflammatory-endothelial tissue injury. In both conditions, similar morphological and immunohistochemical patterns were identified, including endothelial activation, increased expression of adhesion molecules ICAM-1 and VCAM-1, infiltration by CD68-positive macrophages, thickening of the basement membrane, and formation of microthromboses. These structural changes were accompanied by elevated levels of proinflammatory cytokines (IL-1β, IL-6, TNF-α), confirming the systemic nature of endothelial dysfunction.

The immunomorphological similarity between dermatomycoses and APS allows them to be viewed as distinct clinical manifestations of a unified inflammatory-thrombotic continuum underpinned by a universal mechanism of disturbed cellular and vascular homeostasis. The key element in this mechanism is endothelial activation, which initiates a cascade of inflammatory and coagulation reactions leading to local or systemic tissue injury.

Therapeutic strategies for both diseases must address not only the etiological factor—whether fungal infection or autoantibody formation—but also the correction of endothelial dysfunction and suppression of chronic inflammation. In dermatomycoses, the combination of systemic antifungal therapy with immunomodulating agents that normalize cellular immunity and skin microbiota is recommended. The use of probiotics and interferon-based drugs enhances treatment efficacy and reduces recurrence rates. In APS, optimal therapy includes a combination of anticoagulants, antiplatelet agents, and low-dose corticosteroids supplemented with antioxidants that stabilize endothelial membranes and downregulate cytokine activity.

The practical significance of these findings lies in the possibility of using immunohistochemical markers ICAM-1, VCAM-1, CD31, and CD68 as objective indicators for assessing the severity of endothelial damage and the effectiveness of therapy. The identified pathogenetic parallels provide a rationale for the development of new combined and pathogenetically justified treatment regimens for inflammatory-thrombotic disorders of both infectious and autoimmune origin.

A promising direction for future research involves the creation of integrated diagnostic panels incorporating

cytokine profiling, immunomorphological, and hemostatic parameters. This approach would improve prognostic accuracy and enable more personalized therapeutic strategies.

Thus, the results of this study expand the understanding of the unified immunomorphological mechanisms of tissue damage in dermatomycoses and antiphospholipid syndrome and establish the basis for an interdisciplinary approach to the diagnosis and management of inflammatory-endothelial pathologies.

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