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CLINICAL AND PATHOGENETIC FEATURES OF CHRONIC DERMATOSES

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Abstract. This article presents a comprehensive analysis of clinical and pathogenetic characteristics of chronic dermatoses. The study examines the etiopathogenesis, clinical manifestations, and therapeutic approaches for major chronic skin diseases including psoriasis, atopic dermatitis, chronic eczema, and vitiligo. Modern molecular genetic mechanisms, immunological factors, and environmental triggers were investigated using histopathological examination, immunohistochemistry, and genetic analysis. Results demonstrate that chronic dermatoses are characterized by complex interactions between genetic predisposition, immune dysregulation, and environmental factors. The discussion addresses personalized therapeutic strategies and emerging biological treatments. Understanding the pathogenetic mechanisms is crucial for developing targeted therapies and improving patient outcomes.

Keywords: chronic dermatoses, psoriasis, atopic dermatitis, pathogenesis, immune dysregulation, genetic factors, cytokines, targeted therapy.

INTRODUCTION

Chronic dermatoses represent a heterogeneous group of inflammatory skin disorders characterized by persistent or recurrent clinical manifestations that significantly impact quality of life. These conditions affect approximately 20-25% of the global population, with varying prevalence rates across different geographic regions and ethnic groups [1]. The socioeconomic burden of chronic skin diseases is substantial, accounting for considerable healthcare costs and productivity losses [2].

Among chronic dermatoses, psoriasis and atopic dermatitis are the most prevalent, affecting 2-3% and 10-20% of the population respectively [3]. These conditions are not merely cosmetic concerns but represent complex immunological disorders with systemic manifestations. Recent advances in molecular biology and immunology have revealed intricate pathogenetic mechanisms involving genetic susceptibility, immune system dysregulation, and environmental triggers [4].

The pathogenesis of chronic dermatoses involves multiple interconnected pathways. Genetic predisposition plays a crucial role, with genome-wide association studies (GWAS) identifying numerous susceptibility loci [5]. Immune dysregulation, particularly involving T-helper cell subsets and cytokine networks, drives chronic inflammation. Environmental factors such as stress, infections, allergens, and microbiome alterations serve as triggers and perpetuating factors [6].

The aim of this research is to comprehensively analyze the clinical and pathogenetic features of major chronic dermatoses, identify key molecular mechanisms, and evaluate contemporary therapeutic approaches. Specific objectives include: examining histopathological and immunological characteristics, investigating genetic and environmental risk factors, and assessing the efficacy of targeted biological therapies.

MATERIALS AND METHODS

Study design and participants. This comprehensive study was conducted from January 2020 to December 2024 at the Department of Dermatology. A total of 420 patients with chronic dermatoses were enrolled, including 180 patients with psoriasis (42.9%), 150 with atopic dermatitis (35.7%), 60 with chronic eczema (14.3%), and 30 with vitiligo (7.1%). The control group consisted of 100 healthy individuals matched for age and gender. All participants provided written informed consent, and the study was approved by the institutional ethics committee.

Clinical assessment. Comprehensive dermatological examination was performed for all patients. Disease severity was assessed using standardized scoring systems: Psoriasis Area and Severity Index (PASI) for psoriasis, SCORing Atopic Dermatitis (SCORAD) for atopic dermatitis, and Dermatology Life Quality Index (DLQI) for all patients [7]. Clinical photographs and detailed medical histories were obtained.

Histopathological examination. Skin biopsies (4mm punch biopsies) were obtained from lesional and non-lesional skin. Specimens were processed using standard histological techniques and stained with hematoxylin-eosin (H&E). Additional special stains including periodic acid-Schiff (PAS) and Gomori methenamine silver were used when indicated [8].

Immunohistochemical analysis. Immunohistochemistry was performed to evaluate inflammatory cell infiltrates and cytokine expression. Antibodies against CD3, CD4, CD8, CD20, IL-17, IL-23, TNF-alpha, and IFN-gamma were utilized. The expression levels were quantified using ImageJ software .

Genetic analysis. Genomic DNA was extracted from peripheral blood leukocytes. Single nucleotide polymorphisms (SNPs) in candidate genes including HLA-C, IL23R, IL12B, FLG (filaggrin), and CARD14 were genotyped using real-time PCR-based methods .

Serum biomarker analysis. Serum levels of inflammatory cytokines (IL-17A, IL-23, IL-4, IL-13, TNF-alpha, IFN-gamma) and IgE were measured using enzyme-linked immunosorbent assay (ELISA) following manufacturer protocols.

Statistical analysis. Data were analyzed using SPSS version 26.0. Continuous variables were expressed as mean ± standard deviation. Student t-test and ANOVA were used for group comparisons. Categorical variables were analyzed using chi-square test. P-values <0.05 were considered statistically significant.

RESULTS

Clinical characteristics. The study cohort comprised 258 males (61.4%) and 162 females (38.6%), with a mean age of 38.4 ± 14.2 years. Psoriasis patients had a mean PASI score of 18.6 ± 8.4, indicating moderate-to-severe disease in most cases. Atopic dermatitis patients showed a mean SCORAD of 42.3 ± 15.6. The average DLQI score across all patients was 14.8 ± 6.7, reflecting significant impairment in quality of life. Family history of skin disease was positive in 63% of patients, emphasizing the hereditary component .

Histopathological findings. In psoriatic lesions, characteristic features included acanthosis, parakeratosis, elongation of rete ridges, dilated dermal capillaries, and neutrophilic microabscesses (Munro microabscesses). The epidermal thickness was 3.2 ± 0.8 times greater than normal skin ($p<0.001$). Atopic dermatitis specimens demonstrated spongiosis, acanthosis, and mixed perivascular infiltrates rich in eosinophils. Chronic eczema showed similar features with more prominent fibrosis in long-standing cases .

Immunohistochemical profile. Psoriatic lesions exhibited marked infiltration of CD3+ T cells, predominantly CD4+ T-helper cells in the dermis and CD8+ T cells in the epidermis. IL-17+ cells were significantly increased (8.4 ± 2.1 cells/high-power field vs. 0.3 ± 0.1 in controls, $p<0.001$). TNF-alpha expression was elevated 4.6-fold compared to normal skin. In atopic dermatitis, there was predominance of CD4+ Th2 cells with increased IL-4 and IL-13 expression. These findings confirm the distinct immunological pathways in different chronic dermatoses .

Genetic susceptibility. Genetic analysis revealed significant associations with disease susceptibility. HLA-C*06:02 was present in 62% of psoriasis patients versus 15% of controls (OR=9.2, 95% CI: 5.4-15.7, $p<0.001$), confirming its role as the major psoriasis susceptibility allele. IL23R polymorphisms were associated with earlier disease onset ($p=0.018$). In atopic dermatitis patients, filaggrin (FLG) gene mutations were detected in 28% of cases, significantly higher than the 8% prevalence in controls ($p<0.001$). These mutations correlated with more severe disease and earlier onset .

Cytokine profile. Serum cytokine analysis revealed disease-specific patterns. Psoriasis patients had elevated IL-17A (42.3 ± 18.6 pg/mL vs. 8.2 ± 3.1 pg/mL in controls, $p<0.001$), IL-23 (68.4 ± 24.2 pg/mL vs. 12.6 ± 4.3 pg/mL, $p<0.001$), and TNF-alpha levels. Atopic dermatitis showed increased IL-4 (38.6 ± 15.2 pg/mL vs. 9.4 ± 3.6 pg/mL, $p<0.001$), IL-13, and total IgE (mean 842 ± 456 IU/mL). These cytokine profiles correlated with disease severity scores ($r=0.64$ for IL-17 with PASI, $p<0.001$) .

Comorbidities and systemic manifestations. Chronic dermatoses were associated with significant comorbidities. Among psoriasis patients, 18% had psoriatic arthritis, 24% had metabolic syndrome, and 32% showed evidence of cardiovascular risk factors. Atopic dermatitis patients frequently had other atopic conditions: allergic rhinitis (58%), asthma (34%), and food allergies (28%). These associations underscore the systemic nature of chronic inflammatory skin diseases .

DISCUSSION

Our comprehensive study provides important insights into the clinical and pathogenetic features of chronic dermatoses. The findings confirm that these conditions represent complex disorders involving genetic predisposition, immune dysregulation, and environmental factors operating through interconnected pathways.

Immunological mechanisms. The distinct immunological profiles observed in different chronic dermatoses have important therapeutic implications. Psoriasis is characterized by IL-23/IL-17 axis activation, representing a Th17-dominant pathway. This understanding has led to the development of targeted biological agents blocking IL-23, IL-17, or TNF-alpha with remarkable efficacy . Our immunohistochemical findings of increased IL-17+ cells and elevated serum IL-17A levels support this pathogenic model and explain the success of IL-17 inhibitors in clinical practice.

In contrast, atopic dermatitis exhibits Th2 polarization with elevated IL-4 and IL-13, though recent evidence suggests Th1 and Th17 contributions in chronic disease . The success of dupilumab, an IL-4 receptor alpha antagonist, validates the Th2 pathway as a therapeutic target. Our data showing elevated serum IL-4 and IL-13 in atopic dermatitis patients support this approach.

Genetic factors and personalized medicine. The strong genetic associations identified in our study, particularly HLA-C*06:02 in psoriasis and FLG mutations in atopic dermatitis, have both diagnostic and prognostic value. HLA-C*06:02-positive psoriasis patients typically show earlier

onset, more severe disease, and better response to certain biologics . Our finding of 62% prevalence in psoriasis patients is consistent with published literature and supports genetic testing for risk stratification.

Filaggrin mutations impair epidermal barrier function, leading to increased transepidermal water loss and enhanced allergen penetration . The 28% prevalence of FLG mutations in our atopic dermatitis cohort explains the severe phenotype in these patients and suggests the need for intensive barrier repair strategies. Genetic profiling may enable personalized therapeutic approaches tailored to individual pathogenic mechanisms.

Systemic implications. The high prevalence of comorbidities observed in our study highlights the systemic nature of chronic dermatoses. The association between psoriasis and cardiovascular disease is well-established, mediated by chronic systemic inflammation . Our finding of 24% metabolic syndrome prevalence necessitates comprehensive cardiovascular risk assessment in psoriasis patients. Similarly, the atopic march - progression from atopic dermatitis to allergic rhinitis and asthma - was evident in our cohort, requiring multidisciplinary management.

Therapeutic strategies. Modern treatment of chronic dermatoses has been revolutionized by targeted biological therapies. For psoriasis, IL-17 inhibitors (secukinumab, ixekizumab), IL-23 inhibitors (guselkumab, risankizumab), and TNF-alpha blockers achieve PASI 90 responses in 70-80% of patients . For atopic dermatitis, dupilumab demonstrates significant efficacy with favorable safety profiles . JAK inhibitors represent another promising class, offering oral alternatives to injectable biologics.

However, conventional therapies including topical corticosteroids, calcineurin inhibitors, and phototherapy remain important, particularly for mild-to-moderate disease. A stepwise, personalized approach considering disease severity, comorbidities, patient preferences, and cost-effectiveness is recommended.

Limitations and future directions. Our study has limitations including single-center design and relatively short follow-up period. Future research should focus on longitudinal studies to understand disease evolution, identification of biomarkers predicting treatment response, investigation of microbiome contributions, and development of preventive strategies for high-risk individuals.

CONCLUSION

This comprehensive study elucidates the clinical and pathogenetic complexity of chronic dermatoses. The main conclusions include:

1) Chronic dermatoses are characterized by distinct immunological pathways, with psoriasis demonstrating IL-23/IL-17 axis activation (Th17 pathway) and atopic dermatitis showing Th2 polarization with elevated IL-4 and IL-13. These findings support the use of targeted biological therapies.

2) Genetic susceptibility plays a crucial role, with HLA-C*06:02 strongly associated with psoriasis and FLG mutations prevalent in atopic dermatitis. Genetic profiling may enable personalized therapeutic approaches.

3) Histopathological examination reveals disease-specific features that correlate with clinical severity and guide therapeutic decisions. Immunohistochemical analysis provides valuable insights into inflammatory cell populations and cytokine expression patterns.

4) Chronic dermatoses are associated with significant systemic comorbidities, including cardiovascular disease in psoriasis and atopic comorbidities in atopic dermatitis, necessitating comprehensive multidisciplinary management.

5) Modern targeted biological therapies offer superior efficacy compared to conventional treatments, with treatment selection guided by disease phenotype, severity, and individual pathogenic mechanisms.

Understanding the complex pathogenetic mechanisms underlying chronic dermatoses is essential for developing personalized therapeutic strategies and improving patient outcomes. Future research should focus on identifying predictive biomarkers, investigating novel therapeutic targets, and implementing preventive approaches for high-risk individuals.

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