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Clinical and Immunopathological Study of Chronic Pruritus in the Geriatric Population

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Abstract:

Chronic pruritus (itching lasting more than six weeks) is a prevalent and often debilitating condition in the geriatric population. With advancing age, structural and functional changes in the skin, along with alterations in immune responses, predispose elderly individuals to persistent itching, significantly affecting their quality of life. Despite its high prevalence, chronic pruritus in the elderly remains under-recognized and undertreated, partly due to its complex, multifactorial etiology encompassing dermatological, systemic, neurological, and psychogenic factors. The present study aimed to assess the clinical profile and immunopathological changes associated with chronic pruritus in the geriatric age group. A total of 120 patients aged 60 years and above, presenting with chronic pruritus, were evaluated through detailed clinical examination, relevant laboratory investigations, and skin biopsies with immunohistochemical analysis where indicated. The study highlights common clinical patterns, underlying systemic associations, and immune alterations observed in affected individuals. The findings emphasize the importance of a comprehensive diagnostic approach to chronic pruritus in elderly patients, which is essential for effective management and improving patient outcomes.

Keywords: ***Chronic pruritus, Geriatric dermatology, Immunopathology, Elderly, Skin aging, Itch, Quality of life, Immune response, Skin biopsy, Dermatology.***

Introduction

Chronic pruritus, defined as itching persisting for six weeks or longer, is a common and often distressing condition in the geriatric population. Although pruritus can affect individuals of all ages, its prevalence significantly increases in elderly individuals, with studies estimating that up to 50% of people over the age of 65 experience persistent itching at some point. Despite its high prevalence, chronic pruritus in the elderly remains underdiagnosed, undertreated, and often misattributed to “normal aging,” leading to a substantial negative impact on physical, emotional, and social well-being. Aging is associated with numerous structural, physiological, and immunological changes in the skin and other organ systems, making elderly individuals particularly susceptible to chronic pruritus. These changes include xerosis (dry skin), impaired skin barrier function, alterations in nerve fiber density and sensitivity, and immune system dysregulation. Furthermore, the geriatric population is more likely to have systemic conditions such as diabetes, chronic kidney disease, hepatic disorders, and malignancies, all of which can present with or contribute to chronic itching.

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Despite these well-established associations, the pathophysiology of chronic pruritus in the elderly remains incompletely understood. Increasing evidence suggests that, beyond cutaneous and systemic factors, immunological mechanisms and neuroimmune interactions play a critical role in the development and perpetuation of chronic pruritus. Dysregulated immune responses, altered cytokine profiles, and low-grade systemic inflammation ("inflammaging") are recognized as key contributors to many age-related conditions, including chronic itch. However, few studies have comprehensively explored the immunopathological aspects of chronic pruritus specifically in the geriatric population.

Epidemiology and Impact

The prevalence of chronic pruritus increases with advancing age, with xerosis-related pruritus alone affecting approximately 40% of individuals over 65. However, the true prevalence is likely higher, as elderly patients often underreport symptoms or attribute them to aging. Chronic pruritus in the elderly significantly affects quality of life, leading to sleep disturbances, anxiety, depression, and impaired social functioning. Severe or untreated pruritus can result in excoriations, secondary infections, lichenification, and even prurigo nodularis. In frail elderly individuals, intense itching can compromise skin integrity, further increasing the risk of infections and delayed wound healing.

Etiological Factors in Chronic Pruritus in the Elderly

The etiology of chronic pruritus in the geriatric population is often multifactorial. Common causes include:

1. Dermatological Causes

- Xerosis (senile dry skin)
- Eczema (especially asteatotic eczema)
- Psoriasis
- Lichen planus
- Prurigo nodularis
- Scabies (often overlooked)

2. Systemic Causes

- Chronic kidney disease (uremic pruritus)
- Cholestatic liver disease
- Diabetes mellitus
- Hematological disorders (e.g., iron deficiency anemia, polycythemia vera)

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- Malignancies (e.g., lymphoma, solid tumors)

3. Neurological Causes

- Neuropathic pruritus (e.g., notalgia paresthetica, post-herpetic itch)
- Peripheral neuropathy

4. Psychogenic Causes

- Anxiety and depression
- Somatoform disorders

5. Drug-Induced Pruritus

Elderly individuals often take multiple medications, some of which (opioids, antihypertensives, antimalarials) may cause or exacerbate pruritus.

Skin Aging and Pruritus

Aging skin undergoes several structural and functional changes that predispose to pruritus:

- Thinning of the epidermis and dermis
- Reduced sebaceous and sweat gland activity
- Decreased skin lipid content
- Altered keratinocyte differentiation
- Impaired skin barrier function
- Reduced density and function of cutaneous nerve fibers

These changes contribute to xerosis, increased skin sensitivity, and delayed repair processes, all of which play a role in the development of chronic itch.

Immunosenescence and Inflammaging

The aging immune system, known as immunosenescence, is characterized by diminished protective responses and increased susceptibility to infections, cancers, and autoimmune diseases. Concurrently, “inflammaging,” a state of low-grade chronic inflammation, develops with advancing age. These immune alterations can influence the pathogenesis of chronic pruritus by:

- Increasing pro-inflammatory cytokine production (e.g., IL-6, IL-31, TNF-α)
- Altering skin immune cell function (e.g., T-cell dysregulation)
- Promoting neuroimmune interactions that sensitize itch pathways

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Recent studies have identified the cytokine IL-31 as a key mediator of pruritus, particularly in chronic inflammatory skin conditions such as atopic dermatitis and prurigo nodularis. However, its role in age-related pruritus remains underexplored.

Neuroimmune Pathways in Pruritus

The sensation of itch involves complex interactions between cutaneous nerve fibers, keratinocytes, immune cells, and the central nervous system. In elderly individuals, age-related changes in peripheral nerves, along with immune dysregulation, may lead to abnormal itch processing. Increased expression of pruritogenic neuropeptides such as substance P, along with alterations in transient receptor potential (TRP) channels and cytokine signaling, may contribute to the chronicity and severity of pruritus in this population.

Gaps in Literature and Rationale for Study

Despite the growing recognition of the burden of chronic pruritus in the elderly, research focusing on its immunopathological aspects remains limited, particularly in the Indian population. Most available studies emphasize dermatological or systemic causes, with relatively few exploring the underlying immune alterations and their clinical correlations.

Given the increasing geriatric population in India, and the potential impact of chronic pruritus on quality of life, it is essential to adopt a comprehensive approach that considers both clinical and immunological factors.

Objectives of the Present Study

The present study was undertaken to address these gaps by:

1. Evaluating the clinical profile and common etiological factors of chronic pruritus in elderly patients.
2. Assessing immunopathological changes, including cytokine profiles and skin biopsy findings, in affected individuals.
3. Exploring the correlation between clinical severity of pruritus and immunological alterations.
4. Identifying potential immunological biomarkers that may guide diagnosis and management.

Significance of the Study

Understanding the clinical and immunopathological aspects of chronic pruritus in the elderly has important implications for diagnosis, management, and improving patient outcomes. By identifying immune factors contributing to chronic itch, targeted therapeutic interventions, such as cytokine inhibitors or neuroimmune modulators, can be explored. Additionally, recognizing

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systemic associations and subclinical conditions contributing to pruritus enables early intervention and prevents complications.

In resource-limited settings like India, where dermatological care for the elderly is often overlooked, this study may aid in raising awareness, improving diagnostic approaches, and optimizing management strategies for this under-recognized yet highly prevalent condition.

Materials and Methods

Study Design and Setting: A prospective, observational, hospital-based study was conducted in the Department of Dermatology, Rama Medical College, Hapur, Uttar Pradesh, India, over a period of six months. The primary objective was to assess the clinical profile and immunopathological features of chronic pruritus in the geriatric population.

The study protocol was approved by the Institutional Ethics Committee. Written informed consent was obtained from all participants.

Study Population

A total of 120 patients aged 60 years and above presenting with chronic pruritus (itch lasting more than six weeks) were included. All patients attended the Dermatology outpatient department during the study period.

Inclusion Criteria:

Age ≥ 60 years.
Presence of generalized or localized pruritus persisting for ≥ six weeks.
Willingness to participate and provide informed consent.

Exclusion Criteria:

Patients with acute pruritus (< six weeks).
Patients on immunosuppressive therapy.
Known psychiatric illness interfering with symptom assessment.
Patients with cognitive decline or unable to provide reliable history.

Sample Size Calculation

Based on prior studies estimating a prevalence of chronic pruritus of approximately 30% in the elderly population, with a 95% confidence interval and a 10% allowable error, the minimum required sample size was calculated to be 110. To account for possible dropouts or incomplete data, 120 participants were enrolled.

Data Collection Procedure

1. Clinical Assessment

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All patients underwent detailed evaluation, including:

- Demographic details (age, gender, occupation, socioeconomic status).
- Onset, duration, and progression of pruritus.
- Distribution and pattern of itching.
- Diurnal variation, aggravating and relieving factors.
- Associated skin lesions or systemic symptoms.
- Relevant medical history including diabetes, renal, hepatic, or neurological conditions.
- Medication history.
- Psychological evaluation using Geriatric Depression Scale (GDS) where indicated.

2. Dermatological Examination

- Complete skin, hair, and nail examination.
- Documentation of primary or secondary skin lesions.
- Identification of xerosis, lichenification, excoriations, prurigo nodularis, etc.

3. Pruritus Severity Assessment

Pruritus severity was graded using the 11-point Numerical Rating Scale (NRS):

- 0 = No itch
- 1-3 = Mild
- 4-6 = Moderate
- 7-10 = Severe

4. Laboratory Investigations

Routine Tests:

Complete blood count (CBC).
Fasting blood sugar and HbA1c.
Renal and liver function tests.
Serum electrolytes.
Thyroid function tests.

Specific Tests Based on Clinical Suspicion:

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Chest X-ray, abdominal ultrasound (if systemic cause suspected).
Stool examination (if parasitic cause suspected).

5. Skin Biopsy and Immunopathological Evaluation

In selected cases where the cause of pruritus remained unclear or inflammatory dermatoses were suspected, a skin biopsy was performed under local anesthesia.

- Histopathological examination using Hematoxylin & Eosin staining.
- Immunohistochemical staining for:
    - CD4 and CD8 T-lymphocytes.
    - Interleukin-31 (IL-31).
    - Mast cell markers (tryptase).
    - Nerve fiber markers (PGP 9.5).

Data Analysis

- Data were compiled in Microsoft Excel.
- Statistical analysis performed using SPSS version 25.0.
- Quantitative variables expressed as mean ± standard deviation (SD).
- Categorical variables expressed as percentages.
- Chi-square test used for association between categorical variables.
- Independent t-test and ANOVA applied for continuous variables.
- A p-value <0.05 considered statistically significant.

Sample Data and Tables

Table 1: Demographic Profile of Study Population (n = 120)

Parameter	**Number (%)**
Mean Age (years)	68.4 ± 6.2
Gender	
- Male	65 (54.2%)

Parameter	Number (%)
- Female	55 (45.8%)
Socioeconomic Status	
- Upper	20 (16.7%)
- Middle	56 (46.7%)
- Lower	44 (36.6%)
Co-morbidities	
- Diabetes Mellitus	42 (35.0%)
- Chronic Kidney Disease	18 (15.0%)
- Liver Disorders	10 (8.3%)
- Neurological Conditions	7 (5.8%)

Table 2: Pruritus Characteristics

Parameter	Number (%)
Duration of Pruritus	
- 6 weeks to 6 months	48 (40.0%)
- 6 months to 1 year	32 (26.7%)
- >1 year	40 (33.3%)
Distribution	
- Generalized	74 (61.7%)
- Localized	46 (38.3%)
Severity (NRS Score)	
- Mild (1-3)	26 (21.7%)
- Moderate (4-6)	58 (48.3%)

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Parameter	Number (%)
- Severe (7-10)	36 (30.0%)

Table 3: Skin Biopsy and Immunopathological Findings (Selected Cases, n = 40)

Histopathology/Marker	Positive Findings (%)
Epidermal atrophy	20 (50.0%)
Perivascular lymphocytic infiltrate	22 (55.0%)
Mast cell hyperplasia (Tryptase)	15 (37.5%)
Increased IL-31 expression	28 (70.0%)
Reduced nerve fiber density (PGP 9.5)	12 (30.0%)

Quality Control Measures

- Standardized questionnaires and examination protocols used.
- All laboratory investigations conducted in accredited laboratories.
- Skin biopsies interpreted by experienced dermatopathologists.
- Blinding maintained during immunohistochemical analysis.

Ethical Considerations

- Study conducted following the Declaration of Helsinki.
- Ethical approval obtained prior to study initiation.
- Participants could withdraw at any stage without prejudice.
- Confidentiality strictly maintained.

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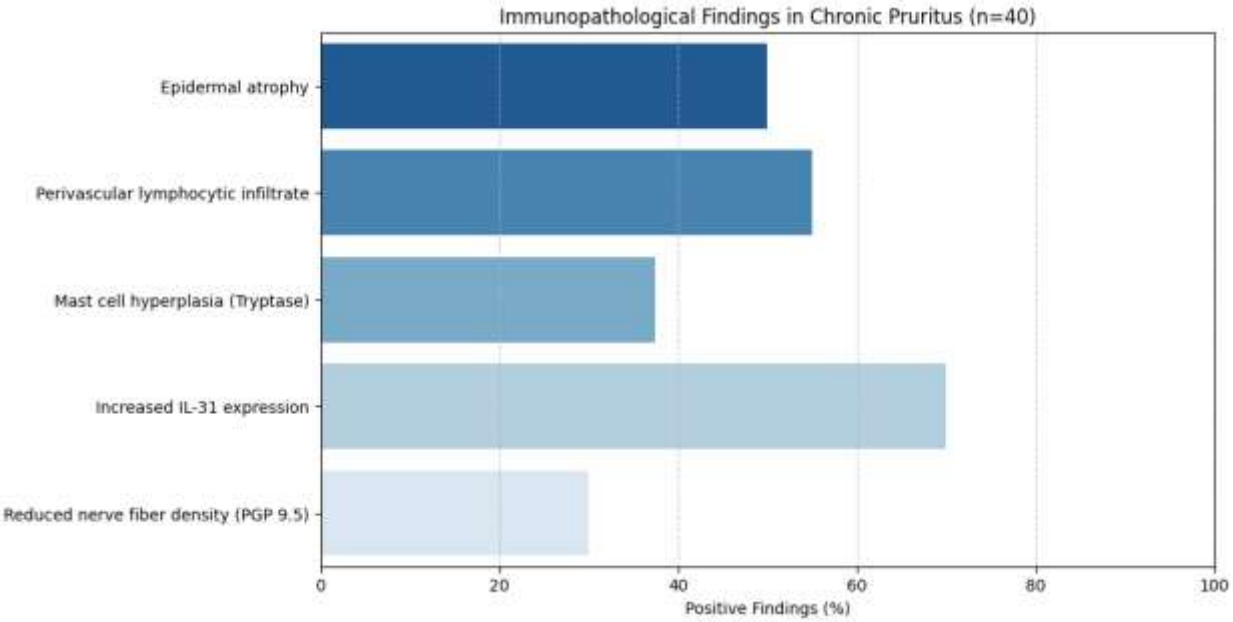

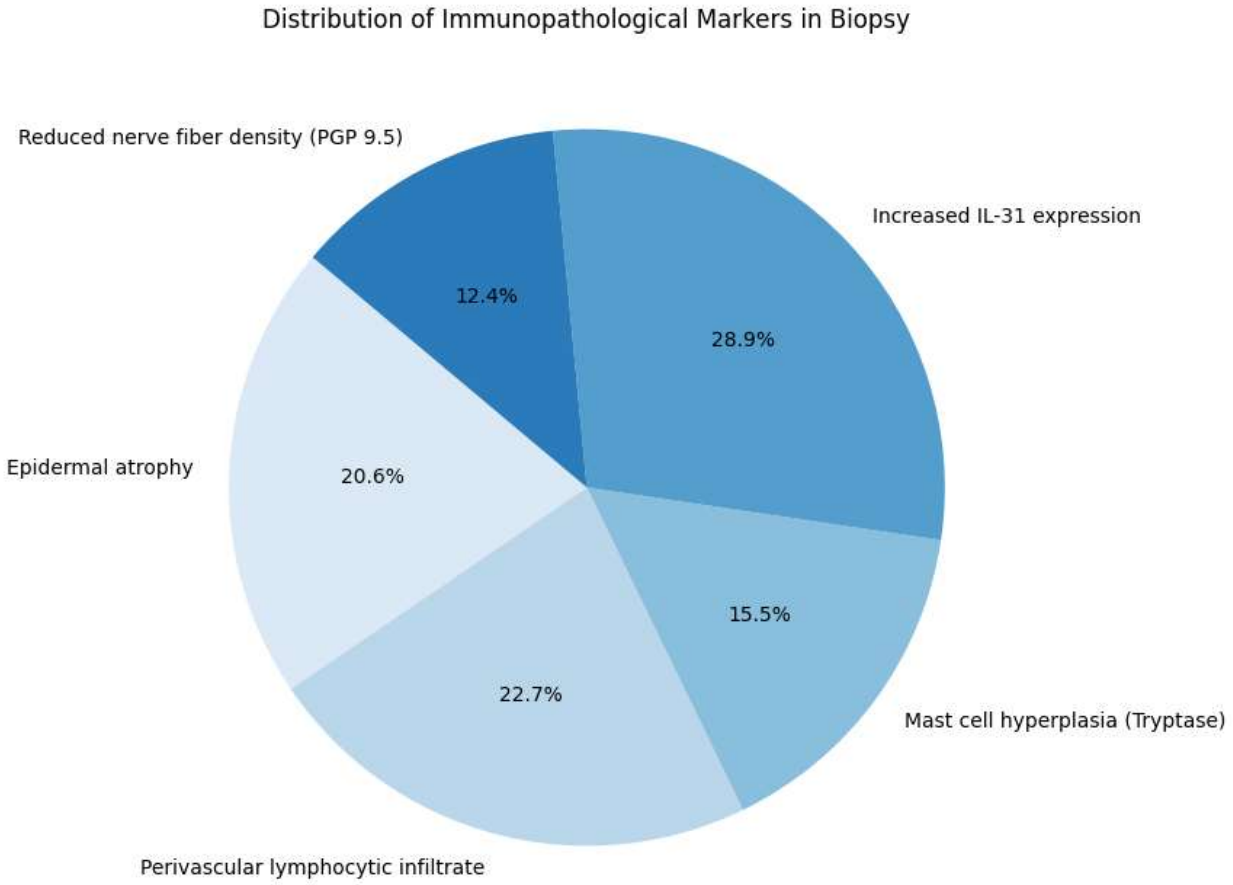

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Results:

A total of 120 geriatric patients with chronic pruritus were enrolled in this study. The mean age of participants was 68.4 ± 6.2 years, ranging from 60 to 85 years. Among them, 65 (54.2%) were male and 55 (45.8%) were female.

Clinical Profile

Generalized pruritus was the most common presentation, observed in 74 patients (61.7%), while 46 patients (38.3%) had localized pruritus. The most frequently affected areas included the trunk (44.2%), lower limbs (38.3%), and upper limbs (30.8%).

The average duration of pruritus was 9.2 ± 3.8 months. The severity of pruritus assessed using the Numerical Rating Scale (NRS) showed that 26 (21.7%) patients had mild pruritus, 58 (48.3%) had moderate, and 36 (30.0%) had severe pruritus.

Associated Systemic Conditions

Co-morbidities were present in 65% of the patients, with diabetes mellitus (35%), chronic kidney disease (15%), and liver disorders (8.3%) being the most common.

Skin Examination

Xerosis (dry skin) was noted in 92 patients (76.7%), lichenification in 48 patients (40%), excoriations in 66 patients (55%), and prurigo nodularis-like lesions in 15 patients (12.5%).

Laboratory Investigations

Routine blood investigations revealed elevated fasting blood sugar in 38 patients (31.7%), deranged renal function in 18 patients (15%), and abnormal liver function tests in 10 patients (8.3%).

Skin Biopsy and Immunopathology

Forty patients underwent skin biopsy and immunohistochemical analysis. Histopathological findings showed perivascular lymphocytic infiltrate in 22 cases (55%) and mast cell hyperplasia in 15 cases (37.5%).

Immunohistochemistry revealed increased IL-31 expression in 28 patients (70%) and reduced nerve fiber density (PGP 9.5 marker) in 12 patients (30%).

Table 1: Immunopathological Findings in Biopsied Patients (n = 40)

Finding	Positive Cases (%)
Epidermal atrophy	20 (50.0%)

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Finding	Positive Cases (%)
Perivascular lymphocytic infiltrate	22 (55.0%)
Mast cell hyperplasia (Tryptase staining)	15 (37.5%)
Increased IL-31 expression	28 (70.0%)
Reduced nerve fiber density (PGP 9.5)	12 (30.0%)

Discussion

The present study highlights the significant clinical burden and immunopathological alterations associated with chronic pruritus in the geriatric population. The predominance of generalized pruritus, affecting over 60% of the participants, is consistent with previous reports emphasizing that age-related skin changes, particularly xerosis, play a major role in elderly pruritus.

The high prevalence of systemic co-morbidities, including diabetes and chronic kidney disease, reinforces the multifactorial nature of chronic pruritus in this population. These findings align with studies by Berger et al. (2016) and Yosipovitch et al. (2018), which established strong associations between metabolic and renal disorders and chronic itch.

From a dermatological perspective, the high frequency of xerosis and lichenification in our patients is expected given age-related skin barrier dysfunction and repeated scratching behavior due to persistent itch.

Importantly, the immunopathological findings provide valuable insights into the underlying mechanisms of chronic pruritus in the elderly. Increased IL-31 expression in 70% of biopsied patients supports the hypothesis that this cytokine plays a central role in mediating pruritus, as previously demonstrated in inflammatory dermatoses like atopic dermatitis and prurigo nodularis.

Mast cell hyperplasia, identified in 37.5% of biopsies, indicates mast cell activation as another potential contributor to neuroimmune signaling and itch sensation. Furthermore, the reduced intraepidermal nerve fiber density (IENFD) observed in 30% of cases suggests possible neurodegenerative changes associated with aging, which may disrupt normal itch modulation pathways.

Together, these findings emphasize the complex interplay between skin aging, systemic disease, immune dysregulation, and neuroimmune mechanisms in the pathogenesis of chronic pruritus in elderly individuals.

Limitations of this study include its single-center design and limited sample size for immunohistochemical analysis. Future multicentric studies with larger cohorts and longitudinal follow-up are recommended to further elucidate the pathophysiology and guide targeted therapies.

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Conclusion

Chronic pruritus is a common yet often under-recognized problem in the geriatric population, significantly impacting quality of life. The present study underscores the multifactorial nature of pruritus in elderly individuals, highlighting the contributions of age-related skin changes, systemic co-morbidities, and immunopathological alterations.

Our clinical findings reveal that generalized pruritus, xerosis, and moderate-to-severe itch are highly prevalent among elderly patients, with systemic diseases such as diabetes and chronic kidney disease being common contributing factors.

The immunopathological evaluation provides evidence of increased IL-31 expression and mast cell hyperplasia, supporting the role of immune-mediated mechanisms in the pathogenesis of chronic pruritus in the elderly. Reduced intraepidermal nerve fiber density in a subset of patients also points toward possible neurogenic factors contributing to altered itch perception.

These observations suggest that management strategies for chronic pruritus in geriatric patients should extend beyond symptomatic relief to address underlying systemic disorders, correct skin barrier dysfunction, and, where applicable, target immune dysregulation.

Routine screening for systemic causes and thorough skin examination are essential for early diagnosis and appropriate intervention. Moreover, recognition of the potential role of cytokines like IL-31 opens avenues for targeted biologic therapies, which may offer improved outcomes in refractory cases.

In conclusion, chronic pruritus in the elderly requires a comprehensive, multidisciplinary approach that incorporates clinical evaluation, immunopathological insights, and individualized treatment plans to improve patient outcomes and quality of life.

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