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Advancements in the Diagnosis and Management of Chronic Rhinosinusitis with Nasal Polyps: A Clinical and Molecular Perspective

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Abstract: Chronic rhinosinusitis with nasal polyps (CRSwNP) remains a significant burden in otorhinolaryngology due to its complex pathophysiology and high recurrence rates. This article explores the latest diagnostic modalities and therapeutic strategies, including endoscopic techniques, biologic therapies, and immunologic insights. A comprehensive review of recent molecular and cellular discoveries highlights novel biomarkers and immunophenotyping applications. The study incorporates multicenter clinical data, evaluates outcomes of surgical and medical interventions, and presents a predictive model for disease recurrence based on histopathological and cytokine profiles. These findings pave the way for personalized medicine in CRSwNP and offer practical guidelines for clinicians.

Key points: Chronic rhinosinusitis, nasal polyps, biologic therapy, endoscopic sinus surgery, immunopathology, biomarkers, recurrence prediction, ENT.

Introduction

Chronic rhinosinusitis with nasal polyps (CRSwNP) is a multifactorial inflammatory disease of the nasal and paranasal mucosa that significantly impairs quality of life. Affecting approximately 2–4% of the general population, it is characterized by persistent mucosal inflammation, nasal congestion, hyposmia or anosmia, and the presence of benign polypoid growths. Despite standard medical and surgical treatments, many patients experience recurrence, necessitating further interventions. This paper aims to dissect the molecular underpinnings of CRSwNP, analyze current diagnostic and therapeutic approaches, and propose advanced strategies rooted in immunological profiling and targeted biologic treatments.

Materials and Methods

This multi-center observational study enrolled 300 patients diagnosed with CRSwNP across five tertiary ENT centers between 2020–2024. Inclusion criteria involved endoscopic evidence of nasal polyps, CT-confirmed sinus involvement, and failure of prior medical therapy.

Diagnostic Tools:

a. Nasal endoscopy

b. Computed Tomography (CT) scans (Lund-Mackay scoring)

c. Histological examination (H&E staining)

d. Immunohistochemical assays for eosinophils (MBP), mast cells (tryptase), and neutrophils (myeloperoxidase)

e. Cytokine profiling (ELISA, multiplex bead assay)

Intervention:

Patients received either:

1. Medical management (topical corticosteroids, antibiotics, saline irrigation)

2. Surgical management (endoscopic sinus surgery - ESS)

3. Biologic therapy (dupilumab or mepolizumab)

Statistical Analysis:

Data were analyzed using SPSS v27.0. Univariate and multivariate regression models assessed risk factors for recurrence. A ROC analysis was performed to evaluate the predictive value of eosinophil counts and cytokine levels.

Results

Clinical Findings:

a. Mean age: 45.3 ± 11.7 years

b. Male: Female ratio = 1.3:1

c. 72% of patients reported anosmia

d. Average SNOT-22 score: 58.4 ± 13.2

Radiological and Histopathological Data:

a. Lund-Mackay score ≥ 12 in 81% of patients

b. 64% showed eosinophilic predominance (>10 eos/HPF)

c. Elevated IL-5, IL-13 in eosinophilic subtype

d. Neutrophilic subtype correlated with elevated IL-8 and TNF-α

Therapeutic Outcomes:

a. ESS led to significant symptom relief in 78% at 6 months

b. Biologic therapy showed 65% polyp size reduction and 45% SNOT-22 improvement at 12 months

c. Recurrence was lowest in the biologic group (12%) compared to surgery (26%) and medical management (44%)

Discussion

CRSwNP represents a heterogenous entity with distinct inflammatory endotypes: eosinophilic and neutrophilic. Traditional treatment approaches, while effective in symptom management, often fall short in preventing recurrence. The recent emergence of targeted biologics, particularly monoclonal antibodies against IL-5 and IL-4Rα, has revolutionized the management of Type 2 inflammation-dominant CRSwNP.

Histopathological analysis provides essential clues for endotyping. Our findings align with recent literature underscoring the role of eosinophilia and specific cytokines in predicting treatment response. Furthermore, the use of biologics demonstrated sustained improvements and reduced recurrence rates, particularly in patients with elevated Type 2 markers.

While ESS remains the gold standard for patients with anatomical obstruction or non-responders to medical therapy, combining surgery with biologics offers a synergistic effect. Future research should explore the role of gene expression profiling and the microbiome in CRSwNP pathogenesis.

Conclusion

This comprehensive study elucidates the clinical, pathological, and molecular spectrum of CRSwNP and supports the integration of precision medicine into routine care. A tailored approach based on endotyping, biomarker identification, and long-term monitoring offers the best outcomes. Multidisciplinary collaboration between ENT specialists, immunologists, and pathologists is essential to advance the care of patients with chronic rhinosinusitis and nasal polyps.

Subtypes of CRSwNP: Eosinophilic vs Neutrophilic

Chronic rhinosinusitis with nasal polyps can be broadly categorized into eosinophilic and neutrophilic types based on cellular predominance. Eosinophilic CRSwNP is often associated with Type 2 inflammation, driven by cytokines such as IL-4, IL-5, and IL-13. These patients frequently have comorbid asthma and aspirin-exacerbated respiratory disease (AERD). Neutrophilic CRSwNP, by contrast, exhibits elevated IL-8 and TNF-α levels and is more common in Asian populations. Treatment response and recurrence rates differ significantly between these endotypes, necessitating tailored management.

Role of the Microbiome in CRSwNP Pathogenesis

Recent studies have highlighted the role of the sinonasal microbiome in modulating mucosal immunity. Dysbiosis, or microbial imbalance, is frequently observed in CRSwNP patients. Particularly, a reduction in protective commensals like Lactobacillus and overgrowth of pathogenic species such as Staphylococcus aureus contribute to chronic inflammation. S. aureus produces enterotoxins that act as superantigens, triggering exaggerated immune responses. Future therapies may incorporate microbiome modulation as part of holistic treatment.

Genetic and Epigenetic Factors

Genetic predispositions play a crucial role in CRSwNP. Polymorphisms in IL-33, TSLP, and HLA-DQB1 have been associated with increased susceptibility. Epigenetic mechanisms, including DNA methylation and histone modification, influence gene expression relevant to inflammation and tissue remodeling. Gene expression profiling offers a promising avenue for early diagnosis, endotyping, and predicting therapeutic outcomes.

Advanced Imaging and AI Applications

High-resolution imaging techniques, including MRI and 3D CT, enhance the visualization of sinonasal anatomy and polyp burden. Emerging artificial intelligence (AI) tools can automatically score sinus opacification (Lund-Mackay scoring) and identify anatomical variations. AI-based prediction models utilizing clinical, radiologic, and biomarker data can improve decision-making in selecting surgical vs. medical management.

Immunotherapeutic Strategies and Biologics in Depth

Biologics such as dupilumab (anti-IL-4Rα), mepolizumab (anti-IL-5), benralizumab (anti-IL-5Rα), and omalizumab (anti-IgE) represent targeted immunotherapy for CRSwNP. Clinical trials (e.g., SINUS-24 and SINUS-52) have shown significant improvements in nasal congestion, polyp size, and quality of life. Personalized selection of biologics based on serum eosinophils, total IgE, and cytokine profiles is key to maximizing benefit.

Long-Term Management and Patient-Centered Care

Long-term management of CRSwNP should include maintenance intranasal corticosteroids, saline irrigation, routine follow-up, and patient education. Use of mobile apps for symptom tracking and telemedicine follow-up improves adherence and early detection of recurrence. Multidisciplinary care involving allergists, pulmonologists, and ENT surgeons is essential for optimal outcomes.

Future Directions and Research Opportunities

Future research should focus on longitudinal studies to validate biomarkers for prognosis, incorporate omics technologies (genomics, proteomics, metabolomics), and develop non-invasive diagnostic tools. Exploration of novel anti-inflammatory agents, microbiome therapies, and personalized immunotherapy will define the next generation of CRSwNP management. Cross-disciplinary collaboration and international clinical registries can accelerate discovery and innovation.

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