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ORIGINAL ARTICLE

Distinct characteristics of nasal polyps with and without eosinophilia[☆]

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KEYWORDS

Nasal polyps;
Th2 cells;
Th17 cells

Abstract

Introduction: Eosinophilic and noneosinophilic NPs are different subtypes of NPs and require different treatment methods.

Objectives: To compare the histologic characteristics, mRNA and protein expression between Nasal Polyps (NPs) with and without eosinophilia.

Methods: NPs tissues were obtained from eighty-six NPs patients during surgery. Eosinophilic and noneosinophilic NPs were distinguished according to immunochemical results of the specimen. The histological, mRNA and protein expression features were compared between the two groups.

Results: In eosinophilic NPs, we observed a significantly higher GATA-3, IL-5, IL-4, IL-13 mRNA and protein expression. In noneosinophilic NPs, IL-17, IL-23 and RORc mRNA and protein expression were increased. Immunohistochemistry tests showed, more mast cells and less neutrophils in eosinophilic NPs compared with noneosinophilic NPs. Eosinophilic NPs patient presented more severe symptom scores when compared to noneosinophilic NPs.

Conclusion: We demonstrate for the first time that Th2 is the predominant reaction in eosinophilic NPs while Th17 is the predominant reaction in noneosinophilic NPs. Our study may provide new treatment strategy for RSC.

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PALAVRAS-CHAVE

Pólipos nasais;
Células Th2;
Células Th17

Diferenças nas características de pólipos nasais com e sem eosinofilia

Resumo

Introdução: Pólipos nasais (PNs) eosinofílicos e não eosinofílicos são diferentes subtipos de PNs e requerem diferentes métodos de tratamento.

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Objetivos: Comparar as características histológicas e a expressão de mRNAs e proteínas entre PNs com e sem eosinofilia.

Método: Amostras de PNs foram obtidos de 86 pacientes durante a cirurgia. PNs eosinofílicos e não eosinofílicos foram diferenciados segundo os resultados imunoistoquímicos de cada amostra. As características histológicas e de expressão de mRNAs e de proteínas foram comparadas entre os dois grupos.

Resultados: Em PNs eosinofílicos, observamos uma expressão significativamente maior dos mRNAs e proteínas GATA-3, IL-5, IL-4 e IL-13. Nos PNs não eosinofílicos, aumentou a expressão dos mRNAs e proteínas IL-17, IL-23 e RORc. Nos testes imunoistoquímicos, observamos maior número de mastócitos e menor número de neutrófilos nos PNs eosinofílicos, em comparação com PNs não eosinofílicos. Os pacientes com PNs eosinofílicos obtiveram escores de sintomas mais graves vs. PNs não eosinofílicos.

Conclusão: Demonstramos, pela primeira vez, uma reação Th2 predominante em PNs eosinofílicos e uma reação Th17 predominante em PNs não eosinofílicos. Nosso estudo pode proporcionar novas estratégias terapêuticas para a rinossinusite crônica.

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Introduction

Chronic rhinosinusitis (CRS) is characterized by persistent inflammation of nasal and paranasal mucosa, and is divided into two types according to the absence or presence of nasal polyps (NPs): CRS without NPs and CRS with NPs (CRSwNP).¹ Histological features of NP include inflammation of Th2 cells accompanied by infiltration with eosinophils, thickening of basement membrane, and hyperplasia of the epithelium.²⁻⁵ In Western populations, eosinophil infiltration is found in most NPs and considered as a major pathological marker of NPs.^{6,7} However, more and more studies on Chinese NPs showed that many NPs patients in China presented as non-eosinophilic inflammation.⁸ For example, several studies have shown that a considerable proportion of Chinese NPs were neutrophil dominate, but the detailed difference between eosinophilic and non-eosinophilic NPs is still unknown.⁹

Similar studies on asthma have demonstrated that eosinophilic asthma is pharmacologically responsive to glucocorticoid, but non-eosinophilic asthma may be resistant to glucocorticoid.^{10,11} In a recent study on the response of NPs patients to oral corticosteroid therapy conducted by Wen, they found eosinophilic NPs patients were more sensitive to corticosteroid compared with non-eosinophilic NP patients.¹² Besides, eosinophilic NPs had a higher tendency of recurrence after surgery. All these studies demonstrated that eosinophilic and non-eosinophilic NPs may be different subtypes of NPs and needed different treatment methods.

This study aimed to investigate the expression of key transcription factors and cytokines for Th1/Th2/Th17 cells between eosinophilic and non-eosinophilic NPs and provide new information on CRSwNP.

Methods

Patients

Eighty-six patients with NPs were enrolled consecutively in this study. The diagnosis was mainly based on pathological

examination. According to previous methods,¹³ eosinophilic and non-eosinophilic NPs were categorized based on immunochemical results by the presence of either <5 or ≥5 eosinophils/high powered fields (HPF), respectively. The baseline data were collected and Lund-Kennedy and Lund-Mackey score were obtained to evaluate the severity of NPs. None of the subjects used oral or nasal corticosteroids during four weeks before surgery. Details of all subjects are summarized in Table 1. This study was approved by the local ethics committee (No. 20130106) and informed consent was obtained.

Every specimen was cut into two portions. One portion was stored at -80°C for mRNA and protein analysis. The other portion was used for IHC staining.

Symptom scores

At the clinical visit, the patients gave an overall assessment of their rhinitis symptoms. The symptoms of nasal blockage, nasal itching, sneezing, and rhinorrhea were rated on a 4-point scale, where 0 = no symptoms, 1 = mild, 2 = moderate, and 3 = severe. Total symptom scores ranged from 0 to 12 and represented the sum of the scores for nasal blockage, nasal itching, sneezing, and rhinorrhea.

Immunohistochemical staining

For immunohistochemistry, the sections underwent dewaxing, dehydration, and then were placed in 0.3% H₂O₂ for 20 minutes at room temperature to reduce nonspecific background staining. After antigen retrieval by 10 mM citrate buffer for 15 minutes, antihuman monoclonal antibodies for MBP (eosinophils, 1:100, Santa Cruz), anti-HNE (neutrophils, 1:200, Dako) and anti-tryptase (mast cells, 1:100, Santa Cruz) were incubated overnight at 4°C for immunohistochemical staining, respectively. The sections were washed with PBS and incubated with secondary antibody (Gene Tech – Shanghai, China) at room temperature for one hour on the next day.

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