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Short Article

Recurrent inflammation in otorhinolaryngology as a manifestation of autoimmune diseases

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Abstract

Background. Recurrent inflammation of the ear, nose, sinuses, and throat may be the first manifestation of autoimmune diseases. Common symptoms such as chronic otitis media, recurrent sinusitis, hoarseness, or nasal pain often do not cause concern but may be symptoms of diseases such as granulomatosis with polyangiitis (GPA), rheumatoid arthritis (RA), and Sjogren's syndrome (SS). Early recognition of the relationship between ENT symptoms and the autoimmune process allows for faster implementation of treatment directed at the underlying disease, significantly improving prognosis and reducing the risk of permanent multi-organ complications.

Aim. The aim of this article is to present the relationship between recurrent inflammation in the head and neck region and autoimmune diseases. Symptoms in the nose, throat, or mouth may be the first noticeable sign of a systemic disease, making it crucial to consider these conditions, especially in cases that are resistant to standard therapy.

Material and methods. This article consists of a review of 27 publications selected based on the size of the study groups and the current state of knowledge.

Results. Autoimmune and otolaryngological diseases are closely linked, and their coexistence can lead to exacerbation of symptoms and a decline in patients' quality of life.

Conclusions. Early detection of these correlations and appropriate multidisciplinary treatment, including collaboration between otolaryngologists, rheumatologists, dermatologists, and family physicians, is crucial for the effective treatment of these conditions.

Key words: recurrent sinusitis, recurrent otitis media, rheumatoid arthritis, Sjögren's syndrome

Introduction

Recurrent inflammation in otolaryngology is a common health problem worldwide. It stems from various etiologies, including infections, allergies, anatomical abnormalities, comorbidities, and environmental factors. This phenomenon is not only burdensome for patients but can also lead to chronic health problems that require long-term treatment and monitoring. At the same time, we are observing an increase in the incidence of autoimmune diseases worldwide. Symptoms such as dry mouth and throat, recurrent pharyngitis and laryngitis, hoarseness, recurrent sinusitis, and nosebleeds are very common and often cause little concern, yet they may be the only noticeable manifestation of autoimmune diseases. In such cases, proper diagnosis and treatment of the underlying disease are crucial, as this allows for the control of inflammation and the prevention of recurrence.

Recurrent sinusitis (CRS)

Chronic and recurrent sinusitis (CRS) is a significant health problem for people of all ages worldwide. In a meta-analysis by Hye Kyu Min and co-authors, covering over 237 million people from 20 countries, the incidence of CRS was on average 8.71%, while the incidence of CRS with nasal polyps was approximately 0.65% [1]. Symptoms may include recurrent facial pain, nasal congestion, impaired sense of smell and taste, and chronic cough. In some patients, co-occurrence with rheumatological diseases is observed, which may point to an autoimmune basis for both conditions. This is confirmed by an analysis of 9 studies involving 86,081 patients with CRS. The results show an association of CRS with an increased risk of: rheumatoid arthritis (RA) (OR = 1.70), systemic lupus erythematosus (SLE) (OR = 1.61), and ankylosing spondylitis (AS) (OR = 1.48). It is worth emphasizing that such a strong association was not observed in patients with acute sinusitis. This suggests that CRS may be a marker or coexisting risk factor for rheumatological diseases, which should be considered in the diagnostic process. [2]

Another study included 14,867 individuals with CRS and 14,867 controls. It showed that the co-occurrence of RA in individuals with CRS was 6.51 per 1,000 person-years, and the adjusted hazard ratio (HR) for developing RA in the CRS group was 1.41. This study

demonstrated that CRS is associated with an increased risk of later developing RA, with the highest risk occurring within the first 4 years after CRS diagnosis. [3]
Yanjing Liang and co-authors used Mendelian randomization (MR) analysis to analyze the association of autoimmune diseases with CRS. Inflammatory mediators such as IL-10, CXCL10, and CD6 were analyzed. They demonstrated that these mediators constitute a common substrate for autoimmune diseases such as multiple sclerosis (MS), rheumatoid arthritis (RA), celiac disease (CD), type 1 diabetes, hypothyroidism, and CRS. [4]
Additionally, the analysis by Junhao Tu and co-authors showed that asthma (PP.H4 = 0.99) shares the same genetic variant (IL-33 rs3939286) as CRS. Isolation of this gene variant confirmed a causal relationship between CRS and allergic and autoimmune diseases (such as AN, asthma, atopic dermatitis, and psoriasis). [5]
Another study identified CRS as a risk factor for interstitial lung disease (ILD) in Sjogren's syndrome (SS). After group matching, both cohorts (SS+CRS vs. SS without CRS) included 3,047 patients. After 5 years, the incidence of ILD development was observed to be 2.56% in patients with CRS vs. 1.66% in patients without CRS; after 10 years: 3.01% vs. 1.96%. The risk of ILD was significantly higher in patients with SS and CRS (relative risk ~1.53–1.57).[6]

Recurrent Otitis Media

Recurrent otitis media, especially otitis media, is a significant clinical problem for both adults and children. Its chronic nature is associated not only with bothersome symptoms such as pain, ear discharge, or hearing impairment, but also, in children, with long-term consequences for normal development. Epidemiologically, chronic otitis media remains a significant global health burden. A review of 29 studies showed a global prevalence of approximately 3.8% of the population, representing nearly 297 million people, the majority of whom (approximately 85%) live in low- and middle-income countries. [23]
Laura Baldizán Velasco and Carmelo Morales-Angulo described 48 cases of patients with IgG4-related disease (IgG4-RD) who presented with otological symptoms. The clinical picture of the patients resembled chronic or recurrent otitis media and was accompanied by hearing impairment. In approximately 67% of cases, ear involvement was the first symptom of systemic disease. [9]
Another review summarizes the ear symptoms associated with ANCA-associated vasculitis (AAV) and addresses the issue of Otitis Media with ANCA-Associated Vasculitis (OMAAV).

The publication describes that OMAAV can present as chronic or recurrent otitis media, often refractory to standard therapy. This provides a new perspective on the diagnosis and treatment of leukorefractory forms of otitis media [10].

Of 610 patients with antineutrophil cytoplasmic antibody (AAV)-associated vasculitis, 6 (0.8%) presented with ear involvement alone as the initial symptom. Symptoms included otitis media, mixed or sensorineural hearing loss, and vertigo. After initiating immunosuppressive therapy, some recovered middle ear function. This demonstrates that GPA may, in some cases, initially manifest only through ear symptoms, forcing us to expand the diagnostic workup to include autoimmune diseases in cases refractory to standard treatment. [11]

Another example of a connective tissue disease with otological symptoms is relapsing polychondritis (RP). This article describes the case of a patient suffering from recurrent otitis externa and hearing loss. After 6 months of high-dose prednisone therapy, the patient achieved remission of the auricular inflammation; however, the hearing loss remained. [7]

Another study analyzed the cases of 40 patients with small-vessel vasculitis (SV). In this analysis, 77.5% of patients with systemic vasculitis reported ear symptoms (including hearing loss, ear fullness, tinnitus, and ear pain). This indicates that vasculitis has a significant impact on the hearing system, and ear symptoms may be a common and underestimated manifestation of rheumatological diseases. [8]

Recurrent Aphthous Stomatitis (RAS)

Recurrent oral ulcers, known as recurrent aphthous stomatitis (RAS), are one of the most common diseases of the oral mucosa. Their exact etiology remains unclear. Genetic, immunological, environmental, and microbiological factors likely play a role [24]. In the general population, the prevalence of RAS typically ranges from 5% to 25%. [25]

A meta-analysis of 113 studies analyzed 53,307 patients with SLE. Thirty-one percent of patients had oral mucosal lesions, and 30% had oral ulcers. [12]

A retrospective study described 155 patients with primary Sjögren's syndrome (pSS). Nineteen patients (12.3%) had oral lesions of autoimmune etiology (OLAIE). [13]

In a study of 4,637 patients diagnosed with RAS and the same number of matched controls without aphthous ulcers, patients with RAS had a significantly increased risk of developing

autoimmune diseases during the follow-up period, including Behçet's disease, SLE, Ankylosing spondylitis (AS), as well as thyroid disease and rheumatoid arthritis (RA).
[14]
Exfoliative gingivitis (GS) is a clinical term meaning "scaly gums" and is associated with various oral symptoms. A total of 34 patients (38.63%) were diagnosed with subepithelial autoimmune diseases (SADs), and 54 (61.36%) were diagnosed with intraepithelial autoimmune diseases (IADs). [15]
A prospective study compared 73 patients with RA vs. 73 healthy controls. Patients with RA had greater periodontal pocket depth, greater attachment loss, increased bacterial plaque, and decreased salivary flow. [16]

Recurrent Laryngitis

Recurrent laryngitis poses a significant clinical challenge in otolaryngology. Although isolated episodes of acute laryngitis are common and usually self-limiting, some patients experience frequent recurrences or persistent inflammation, which can impact quality of life, voice, and breathing comfort. Factors responsible for the symptoms include viral infections, laryngopharyngeal reflux (LPR), inflammatory factors, and immunological disorders. In a cohort study of newly diagnosed cases of chronic laryngitis, the most common symptoms were dysphonia (53%), throat pain or discomfort (45%), globus (40%), cough (33%), and excessive throat clearing (28%). [26]
A study of 47 patients with RA and 40 controls showed that 72.4% of RA patients had laryngoscopy findings, and 12.8% had dysphonia. [17]
Zi Wei Liu and co-authors analyzed 109 patients with autoimmune diseases (including RA and connective tissue diseases) and 41 controls. Patients with autoimmune diseases reported vocal symptoms more frequently than control patients (measured using the VHI-10) [18]. Another study included 31 patients (14 with SLE, 17 with RA) with vocal cord pathology and 93 control patients (42 with SLE, 51 with RA). Among patients with vocal cord lesions, the most common were paralysis (12 patients) and tumors (14 patients) [19]. Another study examined 27 patients with rheumatic diseases (12 with SLE, 11 with systemic sclerosis, 3 with mixed connective tissue disease – MCTD) using videolaryngostroboscopy. The results showed that 5 patients had a "bamboo node" on the vocal folds, and 92.3% of patients had signs of gastroesophageal reflux on endoscopy [20].

Recurrent Sialadenitis

Recurrent sialadenitis, particularly of the parotid or submandibular glands, poses a clinical challenge due to its complex etiology and impact on quality of life. Although sialadenitis can be acute and self-limiting, some patients experience frequent recurrent episodes of inflammation, which may be related to anatomical obstructions (e.g., stones, ductal stenosis), autoimmune conditions (e.g., Sjögren's syndrome), or infections. The most common manifestation of recurrent sialadenitis is pain and swelling of the salivary gland, often worsening with salivary stimulation, such as during meals. [27]

A case report illustrating autoimmune etiology in sialadenitis is a 48-year-old woman with recurrent purulent sialadenitis. After 17 years of troublesome symptoms, she was diagnosed with Sjögren's syndrome. This suggests that rheumatological conditions should always be considered in the differential diagnosis of recurrent purulent parotitis, as these symptoms can appear many years before the diagnosis of the underlying condition.[21]

In a study of 77 patients with various rheumatic diseases (such as spondylarthropathies, ankylosing spondylitis, rheumatoid arthritis, MCTD) and 77 controls, 39% (30/77) of the patients had secondary Sjögren's syndrome.[22]

Discussion

Autoimmune and otolaryngological diseases are closely linked, and their coexistence can lead to exacerbation of symptoms and a decline in patients' quality of life. Early detection of these correlations and appropriate multidisciplinary treatment, including collaboration between otolaryngologists, rheumatologists, dermatologists, and family physicians is crucial for the effective treatment of these conditions.

Conclusions

Early detection of these correlations and appropriate multidisciplinary treatment, including collaboration between otolaryngologists, rheumatologists, dermatologists, and family physicians, is crucial for the effective treatment of these conditions.

Disclosure

Author's contribution:

Conceptualization: Joanna Madoń, Marta Czechowicz, Patryk Gadziński
Methodology: Joanna Madoń, Marta Czechowicz, Patryk Gadziński
Formal analysis: Joanna Madoń, Marta Czechowicz, Patryk Gadziński
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Writing - rough preparation: Joanna Madoń, Marta Czechowicz, Patryk Gadziński
Writing - review and editing: Joanna Madoń, Marta Czechowicz, Patryk Gadziński
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