The possible role of fungi in the pathogenesis of nasal polyposis and the role of antifungal agents in its management

Thesis

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Contents

Abbreviations

AE : anterior ethmoid.

AFS : allergic fungal sinusitis.

Asp flav : Aspergillus flavus.

Asp fum : Aspergillus fumigatus.

Asp nig : Aspergillus niger.

Cand : Candida albicans.

CF : cystic fibrosis

CT **:** Computed tomography.

Dem : Dematiaceous fungi.

Disc : nasal discharge.

EFRS : Eosinophilic fungal rhinosinusitis

EMRS : Eosinophilic mucin rhino sinusitis

Fr : frontal sinus.

GM-CSF : Granulocyte-macrophage colony-stimulating factor

Head. : headache.

HSD : hypertrophic sinus disease.

ICAM-1 : Intercellular adhesion molecule-1.

IgE : immunoglobulin E.

IL : Interleukin.

Irr. : nasal irritation.

LFA-1	: Lymphocyte function associated antigen-1.
Mx	: maxillary sinus.
NAFRS	: Non-allergic fungal rhinosinusitis
NC	: nasal cavity.
NSAID	: non steroid anti inflammatory drugs.
Obs.	: nasal obstruction.
OD	: a dose once daily.
Olf	: olfactory disturbance.
Oper. find	: operative finding.
P E	: posterior ethmoid.
PO	: oral medicine.
Prev. oper.	: previous operation.
QID	: a dose four times daily.
RAST	: Radio-allergo-sorbent test.
Recur.	: recurrence.
SAEs	: Staphylococcus aureus enterotoxins.
Sp.	: sphenoid sinus.
TNF-a	: Tumor necrosis factor-alpha.
VLA-4	: Integrins A4.
VCAM-1	: Vascular cell adhesion molecule-1.

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INTRODUCTION

Nasal polyposis is an inflammatory condition of unknown etiology. It results from chronic inflammation of the nasal and sinus mucous membranes which causes reactive hyperplasia that results in the formation of polyps. The precise mechanism of polyp formation is incompletely understood. Despite the great progress that had been made in the rhinology, it can be stated that neither the causal nor the formal pathogenesis of nasal polyposis has been clarified ***(Larsen et al., 1992)***.

Although historically many have believed polyps to be a manifestation of allergy, in part because of the histological prominence of eosinophils, epidemiologic evidence for this is lacking. The incidence of allergy is not higher in patients with nasal polyps than in the population as a whole ***(Lane and Kennedy, 2003)***, nor do polyp patients have elevated rates of positive allergy skin tests ***(Drake et al., 1984).***

Some authors now believed that all nasal polyposis are due to infection with fungus on the account that fungus was isolated in most cases, this may need a more accurate proof as fungus is present commensally in many parts of the body ***(Lotfy and Wahab, 2001)***.

Most of the patients who are presenting with nasal polypi, whether unilateral or bilateral turn out to have an

underlying fungal sinusitis ***(Handoussa, 2002)***. Allergic fungal rhinosinusitis is the most common form of fungal sinus disease and nasal polyposis is one of its five criteria of diagnosis ***(Lane and Kennedy, 2003).***

In a study made on 19 patients who had chronic rhinosinusitis with polyposis, 21 % were diagnosed as allergic fungal sinusitis ***(Abdel Rahman et al., 2001).***

Allergic fungal rhinosinusitis is not caused by the abnormal presence of fungus in the nose but rather an abnormal response to non pathogenic fungi that exist in the environment ***(Lane and Kennedy, 2003).***

Allergic fungal sinusitis has been clinicopathologically defined as non-invasive form of fungal infection. The underlying mucous membrane is intact. Erosion of the bone of the laminae papyracea, base of skull and posterior septum are often absent, and expansion of the involved sinus into the orbit or intracranial cavity is observed ***(Handoussa, 2002 and Madani and Shokohi, 2002).***

Some authors consider that allergic fungal sinusitis, when diagnosed is absolute indication for surgery because it is not responsive to medical management without concomitant surgery ***(Quraishi and Ramadan, 1997)***. The reason for this is that the fungal elements must be removed to control the allergic response. The patient may have unilateral or bilateral disease. In cases of the former extent

of surgery should be limited to the side of involvement, partial surgery in this situation is unlikely to be lasting benefit ***(Marks, 2000)***. Owing to re-exposure to the inciting organism, the pathogenic process is not curable and, despite initial excellent result, eventual relapse is likely ***(Kuperferberg et al., 1997)***. For this reason other authors consider that complete endoscopic spheno-ethmoidectomy with wide middle meatus antrostomy and frontal sinusotomy, is warranted in most cases ***(Marks, 2000)***.

Overall, the mechanisms behind polyp formation are believed to be multifactorial. Recent evidence suggests an important role for proinflammatory cytokines, chimokines, and chemotactic factors in the pathogenesis of inflammatory polyps ***(Lane and Kennedy, 2003)***, along a variety of environmental, genetic, and biochemical factors that have previously been proposed ***(Shin et al., 2000)***.

Albu et al. (2004) stated that patients presenting NSAID intolerance or asthma are at risk for the development of recurrences after endonasal surgery for nasal polyposis.

Aim of the work

1- To determine the incidence of fungal sinusitis among the patients of nasal polyposis.

2- To study the role of fungi in the etiology of the nasal polyposis.

3- To study the effect of antifungal treatment in prevention of recurrence nasal polyposis after surgical removal.

Review of literature

Nasal polyps can be defined as mucosal sacs containing edema, fibrous tissue, vessels, inflammatory cells, and glands. Although endoscopic and microscopic surgical techniques have been popular treatment methods for nasal polyps in recent years, there has been less attention given to the origin of nasal polyps ***(Selner, 1988)***.

However, as far as 1882, Zuckerkandl pointed out that the nasal polyps most commonly originated from the lateral nasal wall in the region of the ethmoidal clefts ***(Zuckerkandl, 1882)***.

Nasal polyposis represents a chronic inflammatory disease of the lateral wall of the nose and the anterior ethmoidal air cell. In the last decade, a truly significant effort has been made to understand the pathogenesis, growth, persistence, and recurrence of nasal polyps ***(Mygind and Lildholdt, 1977).***

The condition of nasal polyposis has been an enigma in the recorded history of mankind. It is found in a wide number of diseases and has varied histological components determined by the basic disease state. Thus, it may represent a common pathologic end point in a number of disease processes and offers a spectrum of severity ranging from discrete localized lesions to massive diffuse mucosal

change, producing significant facial deformity ***(Bernstein, 2001 and Settipane et al., 1977)***.

The history of nasal polyps goes back for a period of over 4,000 years to ancient Egypt. This condition may perhaps be the earliest disease on record for which we know the name of both the patient and the physician ***(Bernstein 2001).***

INCIDENCE

There are many studies to evaluate incidence of occurrence of nasal polyposis in chronic rhino-sinusitis patients or in autopsies.

Site of origin

By surgical investigation, ***Stammberger (1991)*** evaluated the site of nasal polyps in reported 200 consecutive patients underwent functional endoscopic sinus surgery. He noted that in 80% of patients there were polyps originated from the middle meatal mucosa, uncinate process, and infundibulum. In 65%, polyps originated from the ethmoidal bulla and hiatus semilunaris. In 48%, polyps originated from the frontal recess. Polyps were found inside the ethmoidal bulla in 30%.

By autopsy evaluation, ***Larsen and Tos (2001)*** evaluated the origin of nasal polyps in three cadaveric studies [Table R. 1]. In the first study, conventional anterior rhinoscopy was performed for 300 autopsies and nasal

polyps were noted in six nasoethmoidal specimens ***(Larsen and Tos, 1991)***. In the second study, the nasoethmoidal complex was removed transcranially in 19 autopsy specimens and examined directly; anterior rhinoscopy was not performed. Polyps were found in 5 of 19 specimens, a frequency of 26% ***(Larsen and Tos, 1995 and Larsen et al., 1994)***. In the third study, 31 autopsy specimens were evaluated with endoscopic dissection. Polyps were noted in 13 of 31 (42%) specimens ***(Larsen and Tos, 1996).***

Important characteristics of nasal polyps were noted in the aforementioned studies. Polyps were found mainly in the transition space between the nose and sinuses. It was found that 75% of polyps were related to ethmoidal recesses and clefts [Table R. 2]. Most of the polyps were unilateral [63%], and bilateral nasal polyps were found in 37% of the cadavers [Table R. 3] ***(Larsen and Tos, 2001)***.

Continuous postmortem studies in autopsy materials and systematic endoscopic examinations for silent, asymptomatic nasal polyps in various groups of patients indicate that the frequency of nasal polyps is high and most of the polyps originate from the mucosa of the ostia, clefts, and recesses in the ostiomeatal complex where the initial stage of sinonasal polyposis seems to take place ***(Larsen and Tos, 2004).***

The high frequency of nasal polyps seems to show that nasal polyps often are small and do not always reach a