Suez Canal University Medical Journal Vol. 25 (3), 2022
Pages 89-95

Could Fungal Infection be demonstrated among Some Nasal Polyposis Cases?

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Abstract

Background: Nasal polyposis is one of the common chronic inflammatory diseases of the paranasal sinuses and nasal mucosa. Allergic fungal sinusitis (AFS) should be suspected in patients who have sinusitis and nasal polyposis. Tissue examination can provide an accurate diagnosis of fungal infection by studying the histomorphology of fungus. *Aim:* to identify the presence of fungal infection in nasal polyps' by studying specimen histopathology. *Patients and Methods:* The study was designed as prospective and carried out on 96 patients with nasal polyposis and functional endoscopic sinus surgery was done for all patients. The resected tissue was processed for light microscopy with hematoxylin and eosin stain to identify the presence of fungus infection. *Results:* Histopathological examination for nasal polyposis revealed that 24 patients (25%) had fungus infection when staining with Periodic Acid-Schiff (PAS) revealed dense eosinophilic rounded fungal rod structures in the center of granuloma. In addition, lamina propria shows basophilic aggregates with surrounding chronic inflammation with focal granulomatous inflammation. *Conclusion:* The antifungal drugs could be used as adjuvant therapy in the treatment and prevention of nasal polyposis recurrence

Keywords: Polyp; Nasal; Fungus; Investigation; Histopathology

Introduction

Nasal polyposis is one of the chronic inflammation of the nose and paranasal sinuses mucosa, the clinical picture is characterized by protrusion of edematous polyps from the middle & superior meatus with demonstrated eosinophilic tissue infiltration and a variety of pro-inflammatory cytokines and chemokines in the polyps' epithelium and lamina propria of the nose[(1)]. Clinical as well as experimental studies indicate that the formation and growth of the nasal polyp are enhanced and perpetuated by a cascade of the process of mucosal epithelium, lamina propria, and inflammatory cells, which, in turn, may be started by both infectious and non-infectious inflammation[(1)]. Despite surgery having had better results for nasal polyposis management for a long time, a change in the management policy in the last years has greater use of medications, especially topical corticosteroids, antibiotics, and anti-fungal[(2)]. Allergic Fungal Sinusitis (AFS) may be expected in persons with sinusitis and nasal polyposis depending on the long history of symptoms present before the presentation and these patients usually have atopy and

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have had many sinus surgeries[3]. This category is demonstrated by the presence of fungal forms invading the sinonasal submucosal tissue with frequent angioinvasion and rapid management is important and often needs surgical and medical treatment[4]. The tissue examination is the only method to demonstrate the fungal infection by studying the fungus histomorphology and the sound tissue reaction to the fungus[5]. Infectious agents (including viruses, bacteria, or fungi) may be strong primary factors that stimulate the nasal epithelial cells' growth and stimulation of fibroblasts to produce nasal polyps[6]. Our study aims to identify if the fungal infection could be present in nasal polyposis histopathological examined specimens.

Patients and Methods

A prospective study was carried out to evaluate the presence of fungus in histopathological spacemen from nasal polyposis in the Suez Canal university hospital from august 2018 to august 2021. All 96 patients with nasal polyposis of more than 2 years duration and subjected to endoscopic sinus surgery were included in our study while Cystic fibrosis, primary ciliary dyskinesia, the presence of bronchial asthma, lower airways obstruction manifestation, aspirin allergy were excluded from our study. All patients fulfilling the inclusion criteria were subjected to complete medical history, nasal endoscopic examination, and CT paranasal sinus. Symptoms score system presence of nasal symptoms and nasal polyps (anosmia, sneezing, rhinorrhea, obstruction, and itching) the score is zero for the patient who has no symptoms, score one for the patient who has mild symptoms, score two for moderate symptoms, and three for severe symptoms, so that the maximal global nasal symptom score was 15 according to Tsicopoulos et al. (2004)[7]. Nasal endoscopy: The nasal endoscopy was done in a sitting position by a rigid endoscope of 0°C and 30°C (Storz, Tuttlingen, Germany). scored according to Johansson et al. The grades of nasal polyps are demonstrated according to fixed anatomical landmarks in four steps 0="no polyposis", 1="mild polyposis" ("small polyps not reaching the upper edge of the inferior turbinate"), 2="moderate polyposis" ("medium-sized polyps reaching between the upper and lower edges of the inferior turbinate"), 3="severe polyposis" ("large polyps reaching below the lower edge of the inferior turbinate")[8]. Computerized Tomography (CT) of the nose and paranasal sinuses. The results of CT scans were classified according to the Fokkens et al.[9] score. The mucosal changes were graded as zero (no abnormality), one (partial opacification), or two (total opacification) of the frontal, maxillary, anterior ethmoid, posterior ethmoid, and sphenoid sinus, bilaterally. The ostiomeatal complexes were scored bilaterally as zero (not occluded) or two (occluded). The maximal CT grading score is 24. The Functional Endoscopic Sinus Surgery was done for all patients under general anesthesia in each patient after obtaining informed consent. Standard surgical steps were done in each case according to the extent of the disease. In the postoperative stage medications in form of steroid drop, oral antihistamines, and antibiotics with regular nasal wash and cleaning of nasal adhesions and crusting was done on each post-operative follow-up visit. The resected nasal polyposis tissue was examined under light microscopy. The specimens of tissue were fixed in 10% neutral buffered formalin, dehydrated in graded alcohol series, cleared in xylene, and enmeshed in paraffin wax. Then 5µm thick paraffin sections were

stained with Hematoxylin and Eosin stain and examined under the light microscope. Ten sections were examined for each patient, under the high power field (×40)[10]. They were also examined under Leica DM 1000 light microscope, in the Center of Excellence in Molecular & Cellular Medicine, Faculty of Medicine, Suez Can University, Ismailia, Egypt. Assessment was performed by the examination of 10 sections from each patient, high power field

Ethical considerations

The local ethics committee approved the study. Written consent was obtained from all study participants. Written informed consent for the publication was obtained from all participants.

Statistical analysis

The collected data were processed using SPSS version 15 [SPSS Inc., Chicago, IL, USA]. Quantitative data were expressed as means ± SD while qualitative data were expressed as numbers and percentages [%]. The student t-test was used to test the significance of the difference for quantitative variables that follow a normal distribution.

Results

Ninety-six patients presented with nasal polyposis with a mean age of 39.7±4.1 years and including 67 males (69.8%) and 29 females (30.2%) who were subjected to FESS. The preoperative Global Nasal Symptom Score domains include obstruction (2.41±0.74), anosmia (2.53±0.71), sneezing (2.1±0.61), rhinorrhea (2.5±0.9), itching (1.7±0.79) Table (1). The preoperative endoscopy score for the left nasal cavity score (2.12±0.74) for the right nasal cavity (2.6± 0.11) and the total score (4.72±0.85) Table (2).

Table 1: The basic Global Nasal Symptom Score among the study population

	GNSS
Obstruction	2.41±0.74
Anosmia	2.53±0.71
Sneezing	2.1±0.61
Rhinorrhea	2.5±0.9
Itching	1.7±0.79

Data are presented as mean and standard deviation, GNSS= Global Nasal Symptom Score

Table 2: Basic endoscopy score and the basic CT score among the study population

	Endoscopy score	CT score
Left Nasal Cavity	2.12±0.74	6.19±1.98
Right Nasal Cavity	2.6±0.11	6.9±3.1
Total	4.72±0.85	13.09±5.08

Data are presented as mean and standard deviation, (×400).

The CT score either for the left nasal cavity score (6.19±1.98) for the right nasal cavity (6.9±3.1) or the total score (13.09±5.08) Table (2). All patients were subjected to FESS without major reported complications, 7 patients had adhesions and were treated with lysis and stent for 2 weeks. Histopathological examination for nasal polyposis specimen revealed that 72 patients (75%) without any evidence of fungal infection as tissue revealed polypoid fragments lined with uniform non-keratinized stratified squamous epithelial lined with mucus-secreting pseudostrati-

fied columnar epithelial covering and overlying edematous lamina propria with mild chronic inflammation with lymphoid aggregate (Figure 1, 2 and 3). While 24 patients (25%) had fungus infection as histopathological examination for nasal polyposis specimen revealed polypoid fragments lined with thickened uniform non-keratinized stratified squamous epithelial covering, with dipping into underlying chronically inflamed lamina propria with congested blood vessels and focal erosions, the underlying chronically inflamed lamina propria shows basophilic aggregates with surrounding chronic inflammation with focal granulomatous inflammation in the underlying lamina propria when staining with PAS revealed dense eosinophilic rounded fungal rod structures in the center of granuloma (Figure 4,5,6 and 7).

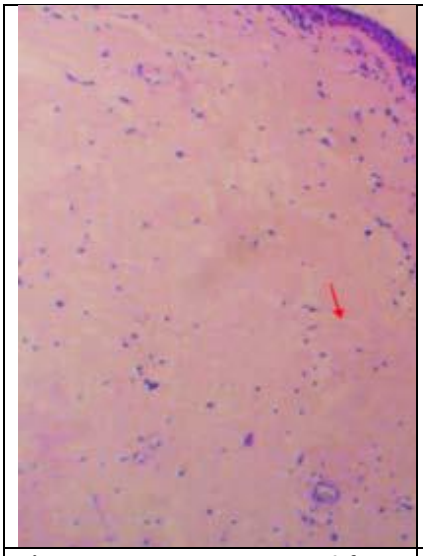

Figure 1: Sections examined from paraffin-embedded tissue revealed polypoid fragments lined with uniform non-keratinized stratified squamous epithelial covering (Black arrow), overlying edematous lamina propria with mild chronic inflammation (Red arrow). There was no evidence of fungal infection (H&E, 10x).

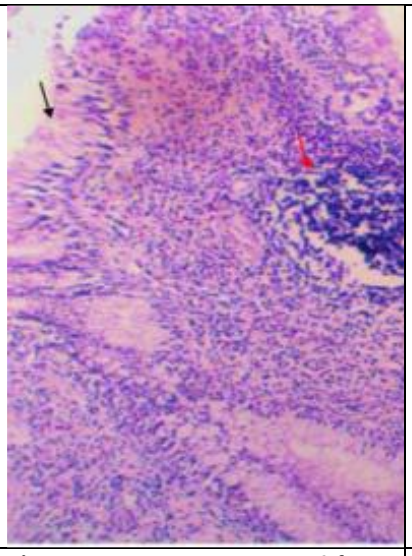

Figure 2: Sections examined from paraffin-embedded tissue revealed polypoid fragments lined with mucus-secreting pseudostratified columnar epithelial covering (Black arrow), overlying densely chronically inflamed lamina propria with lymphoid aggregate (Red arrow). There was no evidence of fungal infection (H&E, 10x).

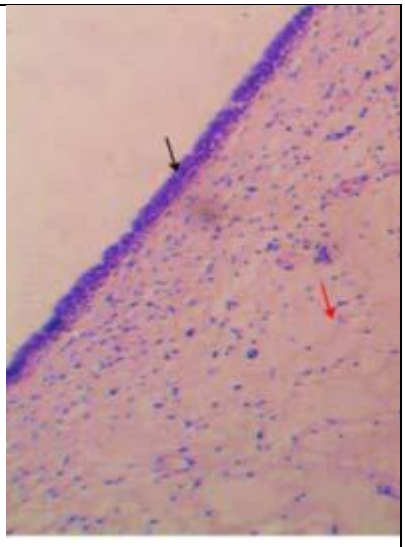

Figure 3: Sections examined from paraffin-embedded tissue revealed polypoid fragments lined with uniform non-keratinized stratified squamous epithelial covering (Black arrow), overlying edematous lamina propria with mild chronic inflammation (Red arrow). There was no evidence of fungal infection (H&E, 10x).

Discussion

Chronic Rhino Sinusitis (CRS) is one of the chronic inflammatory disorders of the upper airways with two major phenotypes present, CRS unassociated Nasal Polyps (CRSsNP) and CRS associated Nasal Polyps (CRSwNP)[11]. The prevalence of CRSwNP ranges between 0.2 and 4%. Up to 15% of patients with asthma have nasal polyps and up to 45% of patients with nasal polyps have asthma[12]. Nasal polyps are a common disease with different causes and allergic fungal sinusitis which is the effect of fungal antigens leading to nasal polyp's formation as Kuhn and Javer found specific IGE to fungal species was higher to total IGE[13]. Bee-See *et al.* (2005) show that the incidence of AFS in adult Malaysian patients with refractory rhinosinusitis was 26.7%, they found fungus

in secretions in only 5 patients (16.7%) and in nasal secretions and in surgical specimens in 11(36.7%)[14]. The study by Ferguson demonstrates the recurrence of AFS post-surgery is very high[15]. The allergic fungal sinusitis associated with nasal polyps previously considered rare is now being reported with increasing frequency worldwide and should be one of the differential diagnoses in all patients who have chronic sinusitis, allergic rhinitis, asthma, and nasal polyposis[16]. Diagnosis of fungal hyphae by direct microscopical examination and histopathology of tissue is the best for the diagnosis of fungal infection and this helps in the identification of the etiologic agent, in addition, Histopathological examination is important to distinguish the invasive from the non-invasive type[17,18].

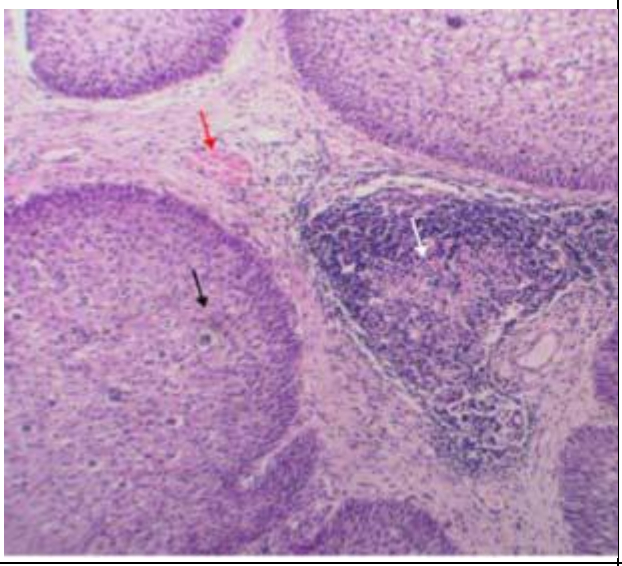

Figure 4: Sections examined from paraffin-embedded tissue revealed polypoid fragments lined with thickened uniform non-keratinized stratified squamous epithelial covering (Black arrow), with dipping into underlying chronically inflamed lamina propria with congested blood vessels (Red arrow). There was focal granulomatous inflammation in the underlying lamina propria (White arrow) (H&E, 10x).

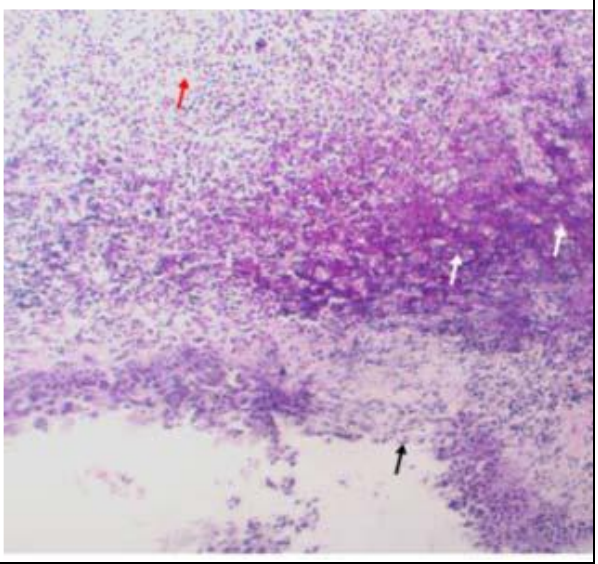

Figure 5: Sections examined from paraffin-embedded tissue revealed polypoid fragments lined with uniform non-keratinized stratified squamous epithelial covering, with focal erosions (Black arrows). The underlying chronically inflamed lamina propria (Red arrows) show basophilic aggregates with surrounding chronic inflammation (White arrows) (H&E, 10x).

In this study, fungus infection was 25% whereas Panda *et al*. found the fungal ball in 60% of their study population[19]. Aspergillus species were reported by Srivani *et al*. as the most common isolated fungi (17.3%) from the nasal polyps which are comparable with other studies in contrast to the western studies where dematiaceous fungi are more common causative agents[20]. The exact pathology of AFS is incompletely unclear. Perhaps, fungi become entrapped in the sinuses of allergic patients with ostiomeatal complex stenosis, more thick mucus, or a mucociliary clearance dysfunction. The ensuing immune response exacerbates the disease[21]. Perhaps, there may be a future big role for topical antifungal drugs, which could hypothetically decrease antigen load. In vitro analysis of fungal liability indicates that the common AFS pathogens are sensitive to many antifungals available in irrigation solutions[22]. We focused in our study on the histopathological as-

sessment for the presence of fungus infection, but etiological factors could be investigated in another study in addition utilization of antifungal therapy could be a solution in some cases preventing the recurrence. Amphotericin B is an antifungal medication used for serious fungal infections and leishmaniasis.

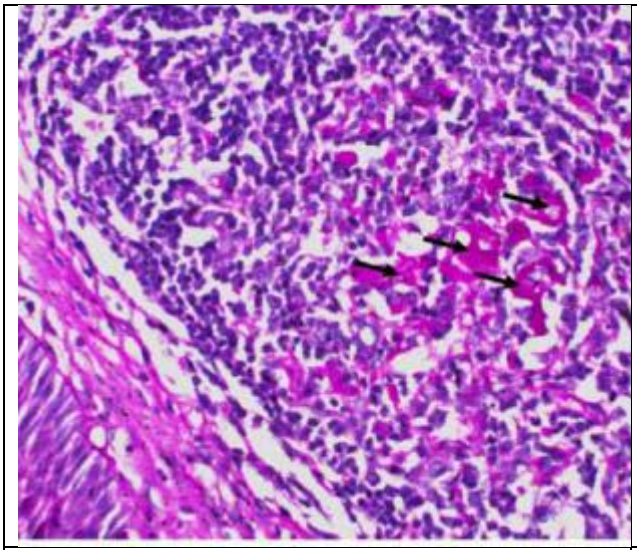

Figure 6: Staining with PAS revealed dense eosinophilic rounded fungal structures (Black arrows) in the center of granuloma (PAS, 40x).

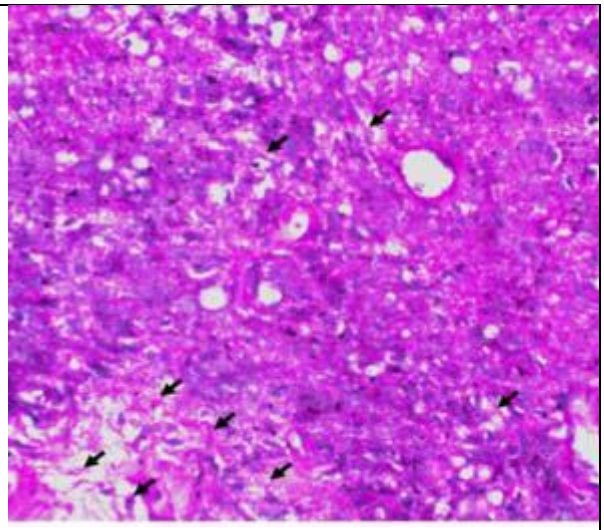

Figure 7: Staining with PAS revealed dense eosinophilic fungal rod structures (Black arrows) in the lamina propria aggregate (PAS, 40x).

Conclusion

Fungal infection could be present in some cases of nasal polyposis and antifungal drugs could be used as an adjuvant therapy to improve surgical outcomes.

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