



Polypoid change of middle turbinate is associated to an increased risk of polyp recurrence after surgery in patients with chronic rhinosinusitis with nasal polyps

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Abstract

Background Chronic rhinosinusitis with nasal polyps (CRSwNP) affects approximately 4% of general population. Patients with CRSwNP have greater burden of CRS symptoms and higher rate of relapse after either medical or surgical treatments. The aim of this study was to evaluate the association between polypoid change of anterior free border of middle turbinate and rate of relapse in patients with CRSwNP.

Methods A controlled prospective cohort study was performed. Seventy-seven adult patients with CRSwNP in whom their MT polypoid change was proved and 77 patients without MT polypoid change were recruited. Allergy, asthma, aspirin hypersensitivity, Lund Kennedy and Lund Mackay scores and eosinophilic scores of polyp and middle turbinate were recorded. Patient's health-related quality of life was assessed using the 22-item Sino-Nasal Outcome Test (SNOT-22) questionnaire. All patients were evaluated 12 months after ESS. Polyp relapse, Lund Kennedy scores and SNOT-22 scores were documented.

Results The relapse rate in patients with MT polypoid change was significantly higher than the control group (37.14 vs. 20.58, p value = 0.03). Eosinophil score of nasal polyps and MT specimens were significantly higher in patients with MT polypoid change than patients without polypoid change. The postoperative Lund Kennedy and SNOT-22 scores in patients with MT polypoid change were significantly higher than the control group.

Conclusion This study showed a significant association between polypoid change of anterior free border of middle turbinate and nasal polyp relapse. This new and simple criterion of severity of CRSwNP could have clinical implications.

Keywords Nasal polyp · Chronic rhinosinusitis · Middle turbinate

Introduction

Chronic rhinosinusitis with nasal polyps (CRSwNP) is a subgroup of chronic rhinosinusitis (CRS) that affects approximately 4% of general population [1]. CRSwNP is clinically defined as thickening of the nasal and paranasal sinus mucosa present for > 3 months and endoscopically visualized polyps. Clinical studies have demonstrated that patients with CRSwNP have greater burden of CRS symptoms and higher rate of relapse after either medical or surgical treatments [2, 3].

The etiology of CRSwNP is not completely understood. Allergy, asthma, aspirin sensitivity, fungal infection and genetic factors are associated with development of nasal polyps [4]. In asthmatic patients a prevalence of 7–15% has been reported [5]. The prevalence of nasal polyps in patients with aspirin hypersensitivity was reported to be as high as 60% [6].

Intranasal glucocorticoids have a documented effect on polyp size, nasal blockage, discharge and sneezing [7]. Systemic glucocorticoids are reserved for advanced cases particularly when allergy is present. There are some evidences for adjunctive use of leukotrienes antagonist, anti-IgE, anti-biotic and antimycotic [8].

Surgery is now the mainstay of treatment for medically resistant nasal polyps. Endoscopic sinus surgery (ESS) restores mucociliary function of the nose and sinuses and allows delivery of anti-inflammatory medications to surgical cavity. Although there is a high level of satisfaction

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with ESS and overall symptomatic improvement, 23–87% of patients need revision surgery because of polyp recurrence [9, 10]. Asthma, aspirin and NSAID hypersensitivity, stage of polyps, previous surgery, percentage of eosinophils in polyps, mast cell localization in polyps, serum IgE level and eosinophilia are known predictors of relapse [11, 12].

In our practice, we observed that polypoid change of anterior free border of middle turbinate (MT) was linked to higher risk of relapse in patients with CRSwNP. Therefore, this study was designed to evaluate the association between polypoid change of anterior free border of MT and rate of relapse in patients with CRSwNP.

Methods

Study population

This study was designed as a controlled prospective cohort study to compare the relapse rate of nasal polyps in patients with and without polypoid changes of anterior free border of MT who underwent endoscopic sinus surgery. The study was conducted at Otolaryngology Head and Neck Surgery Department of Imam Khomeini Hospital Complex from September 2015 to April 2017. Full ethical approval was granted by the research ethics committee of Tehran University of medical sciences. Voluntary written informed consent was obtained from each participant. Patients were always permitted to withdraw from the study without concern about further treatment.

The study included 77 adult patients with CRSwNP in whom their MT polypoid change was proved under endoscopy and 77 patients without MT polypoid change. Patients with > 3-month CRS symptoms with endoscopic evidence of polyps and/or mucosal change on CT scan, who did not respond to the standard treatment regimes, including nasal saline irrigation combined with intranasal

corticosteroids and antibiotics, and were candidates for ESS were recruited. Exclusion criteria included previous sinus surgery, cystic fibrosis, congenital mucociliary problems, immune deficiency, systemic vasculitis, allergic fungal rhinosinusitis and fungal rhinositis.

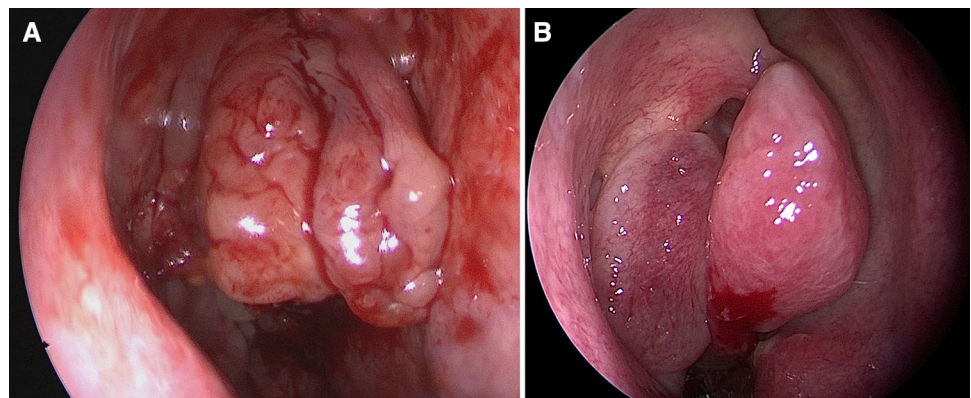
Clinical evaluation

After a comprehensive history and physical examination, baseline clinical data were recorded. Allergy symptoms and history of allergy, asthma or aspirin hypersensitivity were recorded. Patients with positive allergy symptoms or a positive history were recommended to undergo allergy testing for documentation. The nasal cavity was examined with a rigid nasal endoscope. Endoscopic grading was based on Lund Kennedy scores, range from 0 to 10 [13].

Polypoid change was defined as edematous or polypoid change of mucosa covering anterior free border of turbinate (Fig. 1). This assessment was performed by senior authors. Patients were consecutively entered the study and allocated in two groups. CT scan of the paranasal sinuses was conducted and scored using the Lund Mackay scoring system [14]. Patient's symptoms and health-related quality of life were assessed using the 22-item Sino-Nasal Outcome Test (SNOT-22) questionnaire [15].

All patients underwent full ESS using the standard technique under general anesthesia including antrostomy, ethmoidectomy, sphenoidectomy and if necessary frontal recess approach. All patients received pre-op oral steroid for 10 days (prednisolone, 20 mg, daily). The surgery was bilateral in almost all patients. The surgical specimens from the nasal polyp and middle turbinate were sent for pathology examination. Under the light microscope, at a magnification of 400×, the number of eosinophils present within epithelial cells and in the submucosa was scored as follows: 0 (none); 1 (1–2 eosinophils); 2 (3–10 eosinophils); 3 (11–30 eosinophils); or 4 (> 30 eosinophils).

Fig. 1 Middle turbinate with (a) and without (b) polypoid change



Follow-up

All patients underwent nasal endoscopy postoperatively at 4 week, 3, 6 and 12 months. Presence of polyp (not cobble stoned, polypoid or edematous mucosa) at 12-month endoscopic examination was defined as polyp relapse. Lund Kennedy scores and SNOT-22 scores were documented at 12-month visit.

In each visit debridement of surgical cavity from discharge and polyps were performed. Regarding severity of mucosal disease, steroid therapy included topical steroid, budesonide in normal saline or oral steroid were recommended. Antibiotics were given in case of frank nasal purulence.

Statistical analysis

All statistical analyses were performed with the computer software (SPSS, version 15; IBM Corp, Armonk, NY). Distribution of continuous variables was analyzed using the Kolmogorov–Smirnov test for normality. Continuous variables were expressed as mean (SD). Means were compared using the *t* test. Difference between preoperative and postoperative measurements was tested using the paired *t* test. Nominal variables were tested using the χ^2 test. A *p* value less than 0.05 was considered statistically significant. Logistic regression analysis was used to explore any possible association between MT polypoid change and polyp relapse, adjusted for other potential confounding factors.

Results

A total of 154 patients with CRSwNP who fulfilled the inclusion criteria were recruited; although 138 patients completed the study. Seven patients with MT polypoid change and 9 patients without polypoid change were lost to follow-up.

The mean age of patients ($N = 154$) was 42.43 ± 10.87 . 135 patients (87.66%) were male. 27 patients (17.53%) were asthmatics, 29 patients (18.83%) had aspirin hypersensitivity and 52 patients (33.76%) had positive allergy test. Mean SNOT-22 score was 36.35 ± 13.74 . Mean score of Lund Mackay was 17.75 ± 4.93 . No significant difference was found between two groups in terms of age, sex, asthma or aspirin hypersensitivity. Baseline values of SNOT-22, Lund Kennedy and Lund Mackay scores showed no significant differences between the two groups. The patients' baseline characteristics are summarized in Table 1.

The mean eosinophil scores of nasal polyp and middle turbinate specimens were significantly higher in patients with MT polypoid change than patients without polypoid change (3.47 vs. 3.08, *p* value = 0.001 and 3.59 vs. 0.93, *p* value < 0.001, respectively).

All patients were evaluated 12 months after ESS. The comparison of postoperative variables is summarized in Table 2. 26 of 70 patients (37.14%) with MT polypoid change and 14 of 68 patients (20.58%) without polypoid

Table 1 Patients characteristics at enrollment

Characteristic	Total $N = 154$	CRSwNP with MT polypoid change, $N = 77$	CRSwNP without MT polypoid change, $N = 77$	<i>p</i> value
Age (years), mean (SD)	42.43 (10.87)	41.24 (10.43)	43.63 (11.52)	0.18
Male gender, <i>n</i> (%)	135 (87.66)	65 (84.44)	70 (90.9)	0.22
Asthma, <i>n</i> (%)	27 (17.53)	17 (22.07)	10 (12.98)	0.10
Allergy, <i>n</i> (%)	52 (33.76)	32 (41.55)	20 (25.97)	0.03
Aspirin hypersensitivity, <i>n</i> (%)	29 (18.83)	16 (20.7)	13 (16.8)	0.53
SNOT-22, mean (SD)	36.35 (13.74)	37.5 (13.04)	35.2 (14.17)	0.29
Lund Mackay, mean (SD)	17.75 (4.93)	17.4 (5.07)	18.1 (4.88)	0.37
Lund Kennedy, mean (SD)	8.9 (2.26)	9.1 (2.49)	8.7 (2.14)	0.28
Eosinophil score of polyp, mean (SD)	3.27 (0.71)	3.47 (0.65)	3.08 (0.84)	0.001
Eosinophil score of middle turbinate, mean (SD)	2.26 (0.59)	3.59 (0.64)	0.93 (0.57)	< 0.001

Table 2 Postoperative relapse rate, SNOT-22 scores and Lund Kennedy scores

	CRSwNP with MT polypoid change, $N = 70$	CRSwNP without MT polypoid change, $N = 68$	<i>p</i> value
Relapse rate, <i>n</i> (%)	26 (37.14)	14 (20.58)	0.03
SNOT-22, mean (SD)	29.75 (9.56)	12.03 (7.31)	< 0.001
Lund Kennedy, mean (SD)	3.4 (2.08)	2.7 (1.58)	0.02

change had polyp relapse. The relapse rate in patients with MT polypoid change was significantly higher than the control group (37.14 vs. 20.58, p value = 0.03). The postoperative Lund Kennedy score in patients with MT polypoid change was significantly higher than the control group (3.4 vs. 2.7, p value = 0.02). The postoperative SNOT-22 scores were improved from baseline significantly in both groups, but the postoperative SNOT-22 scores in patients with MT polypoid change was significantly higher than patients without MT polypoid change group (29.75 vs. 12.03 p value < 0.001). Using the multiple logistic regression analysis, we found no significant association between MT polypoid change, allergy, eosinophil score of polyp and eosinophil score of middle turbinate.

Discussion

CRSwNP is a common chronic problem, which significantly reduces patient's quality of life. Studies have shown that patients with CRS have lower QOL than patients with angina, congestive heart failure or chronic back pain [16]. Curative treatment is hard to achieve in nasal polyposis. Nasal polyps are associated with high rate of recurrence. Medical and surgical treatments have not been shown to be consistently effective compared with different controlled groups. Different etiological factors, mechanisms and triggers have been proposed to promote the chronic inflammation and post-surgical relapses in CRSwNP. Aspirin and NSAID hypersensitivity, asthma, staging of polyp, previous nasal polypectomy, percentage of eosinophils in polyps, mast cell localization in polyps, serum IgE level and eosinophilia are known predictors of relapse, but there is a weak association between atopy and risk of nasal polyps development and relapse [17, 18].

Brunner et al. have found that polypoid changes of middle turbinate in patients without evidence of CRS has been associated with allergic rhinitis [19]. Hamizan et al. reported that middle turbinate edema is an endoscopic feature to predict presence of inhalant allergy [20]. White et al. performed a prospective study in 25 patients with isolated MT polyps [21]. All 16 patients who underwent allergy testing were positive for inhalant allergy. They reported that polypoid edema or frank polyps isolated to the middle turbinate is highly associated with allergic rhinitis and positive allergy testing.

Benamara et al. reported that the origin of nasal polyps was middle meatus (98%), superior meatus (61%), posterior olfactory fossa (75%), and anterior olfactory fossa (41%). The middle turbinate (free border or medial side) was the origin of nasal polyp in 50% of cases [22]. Based on our personal experience, we hypothesized that patients with CRSwNP who have polypoid change of *anterior free*

border of middle turbinate experience more relapses comparing to CRSwNP patients with normal looking anterior free border of middle turbinate. We have presumed that in patients with CRSwNP polypoid change of middle turbinate in medial and lateral surfaces are common, but involvement of anterior free border is less common and may reflect a more severe inflammatory process of nasal and paranasal sinuses.

This study showed that, there was no significant difference between two groups except in two items. There were more eosinophils in polypoid middle turbinate compared to normal appearing turbinate, and the eosinophil score in nasal polyp of patients with middle turbinate change was significantly more than patients with normal appearing middle turbinate.

Postoperatively symptomatic improvement reflected as decrease in SNOT 22 score was significantly better in patients with normal appearing anterior free border of middle turbinate. On endoscopic examination, the incidence of nasal polyp relapse was significantly greater in patients with polypoid changes of middle turbinate. Lund Kennedy score which is a good representative of degree of inflammation in postoperative surgical cavity was significantly lower in patients with no evidence of polypoid change in middle turbinate. We did not find any significant correlation between allergy and MT polypoid change in patients with CRSwNP.

Considering significance of polypoid change of MT as a new and simple criterion for severity of CRSwNP, this finding could have clinical implications. Finding polypoid change of MT, surgeon faces a more severe CRS and more resistant patient. In order to get better results, more extensive surgery is needed on MT (turbinoplasty, MT resection), maxilla (mega antrostomy, prelacrimal), frontal (II, III) or sphenoid (trans-septal). Also postoperatively, these patients need close observation and frequent courses of budesonide in normal saline would be helpful.

In conclusion, this study showed a significant association between MT polypoid change and nasal polyp relapse. Although we did not find any correlation between allergy and MT polypoid change, the role of allergy in CRSwNP patients with MT change should be given more consideration. Local indices of eosinophilic inflammation and IgE level may be more accurate markers. Further studies are required to determine: (1) the prevalence of middle turbinate polypoid change in CRSwNP; (2) the possible role of middle turbinate polypoid change as a predictor factor of relapse; (3) the surgical implication of this finding and the role of middle turbinate resection in this subgroup of CRSwNP.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval This study has been approved by the research ethics committee of Tehran University of medical sciences and has been performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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