Spontaneous Nasal Polypectomy Proceeded by Fluticasone Propionate (XHANCE®) and Zileuton (Xyflo®) Application

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Abstract:
Background: Nasal polyps (NPs) are inflammatory outgrowths of paranasal sinus mucosa that occur in one to four percent of the population and most commonly cause congestion, obstruction, or hyposmia. Intranasal corticosteroids, along with short courses of oral corticosteroids, are most often recommended for symptomatic nasal polyposis, prior to consideration of surgical intervention. We present the first reported case of spontaneous nasal polypectomy, occurring after use of fluticasone propionate (XHANCE®) and zileuton (Xyflo®).

Methods: A 43-year-old Asian-Indian male with history of allergic rhinitis, asthma, and nasal polyposis had been prescribed subcutaneous immunotherapy for five years without effectiveness before another polypectomy was scheduled. After the polyps resurfaced, the patient was prescribed prednisone and underwent another polypectomy. He later presented with persistent NPs and congestion, as well as diffuse lymphadenopathy and pruritic eyes and ears. Fluticasone Propionate was continued as maintenance therapy and Zileuton was prescribed in place of Montelukast (Singulair®).

Results: After several weeks of the new treatment regimen, the patient reported polyp irritation and movement, as well as influenza-like symptoms. Epistaxis soon occurred, followed by a spontaneous polypectomy. Three more polyps were expelled with bloody discharge. The patient reported resolved hyposmia and reduced symptoms thereafter. The treatment regimen was continued without change or further episodes of epistaxis and polypectomy.

Conclusion: Few case reports in the literature describe polyp autoamputation. We report the first instance of spontaneous nasal polypectomy in the literature, induced by Fluticasone Propionate and Zileuton.

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Introduction:
Chronic rhinosinusitis with nasal polyposis (CRSwithNP) develops in approximately 25 to 30% of CRS patients, who demonstrate at least three months of persistent rhinosinusitis symptoms, but is still associated with significant morbidity and decreased quality of life.¹² NPs are inflammatory lesions that originate from sinus outlets, grow most often bilaterally into the nasal airway, and provoke bone remodeling and sclerosis.²³ Intranasal corticosteroids delivered via traditional nasal sprays have served as first-line treatment but commonly demonstrate suboptimal symptom control, polyph regression, and unpleasant side effects.⁴ A newly approved exhalation delivery system with the potent steroid fluticasone propionate (EDS-FLU) aims to improve outcomes by significantly increasing delivery to superior/posterior nasal passages.⁴⁵ Autopolypectomy has occurred in cases of antrochoanal, vocal cord, bronchial, gastric, and
colorectal polyps, but we describe the first reported NP autoamputation induced by short-term application of an EDS-FLU (XHANCE®) and Zileuton (Xyflo®).

**Case Description:**

A 43-year-old Asian-Indian male referred by otolaryngology presented in an allergy/immunology office for evaluation of recurrent NPs. His history was significant for since adolescence, allergic rhinitis, moderate persistent asthma, and persistent nasal and sinus congestion. His two surgical nasal polypectomies resulted in NP regrowth with worsening symptoms, including diffuse cervical lymphadenopathy, nasal congestion, sneezing, and ocular pruritus. The second polypectomy was advised for management of restricted mouth breathing and NP regrowth into the sinuses and near the eyes. He also reported worsening NPs after a recent pulmonology prescription of omalizumab (XOLAIR®), tiotropium (Spiriva Respimat®), and Montelukast (Singular®).

A CT scan and nasal endoscopy conducted prior to the second nasal polypectomy and ethmoidectomy, which removed ethmoid bone to enlarge the sinus and improve drainage, had confirmed extensive NPs (Figure 1). Otolaryngology had described obstructive right and left nasal contents prior to the patient's second polypectomy. The respiratory mucosa was eosinophilic and chronically inflamed around the inflammatory polyps with retention cysts. Bilateral intranasal ethmoidectomy enabled respiration of anterior and posterior ethmoidal air cells. Nasal polypectomy bilaterally and extensively removed polyps extending into the nasopharyngeal cavity and partly trimmed the inferior turbinate. Bilateral intranasal sphenoid sinusotomy, maxillary antrostomy, and opening of the frontoethmoidal recess cleared the sinuses and extensively removed polyps.

The physical examination revealed bilateral turbinate edema (+1) and unilateral (left) NPs. The patient was prescribed fluticasone propionate nasal exhaler suspension (93 mcg, two sprays BID) and zileuton (600 mg, two extended-release tablets BID) as maintenance therapy.

![Computed Tomography scans of the paranasal sinus.](image)

The patient followed-up a month later with resolution of anosmia and hypogeusia and photographic evidence of an autopolypectomy episode. He explained that he noticed NP movement and experienced flu-like symptoms and epistaxis from his left nostril several weeks after commencing his new maintenance therapy. A NP spontaneously ejected the next day. Then three more NPs were naturally expelled (Figure 2). NP regrowth had not occurred since this autopolypectomy episode. The
patient was recommended to continue fluticasone propionate and follow-up in several months.

**Figure 2: Autopolypectomy Episode**

Nasal polyp in tissue seen in picture above collected after autopolypectomy episode.

**Discussion:**

Rhinosinusitis is one of the most commonly diagnosed diseases among adults in the nation (10-15%) and accounts for over $22 billion of indirect and direct annual health care costs.\(^1\)\(^,\)\(^4\) Middle-aged males account for the largest cohort of patients.\(^2\) NPs identified in patients younger than 20 or older than 80 years of age may indicate cystic fibrosis or neoplasm, respectively.\(^2\) CRSwNP is diagnosed after at least 12 weeks of persistent rhinosinusitis symptoms, including nasal congestion/obstruction, rhinorrhea, postnasal drainage, hyposmia or anosmia, facial pain/pressure, headache, halitosis, fatigue, dental pain, cough, throat clearing, ear pain, or vague facial or sinus fullness.\(^1\) Patients with CRSwNP demonstrate increased prevalence of rhinosinusitis, allergic rhinitis, chronic rhinitis, gastroesophageal reflux disease, sleep apnea, and asthma (26-48%).\(^2\)

NPs develop among the chronically inflamed mucosa investing the ostiomeatal complex, ethmoid infundibulum, and uncinate process, and, thus, often exacerbate ventilation and sinus drainage blockage.\(^3\)\(^,\)\(^4\) CRSwNP pathogenesis was originally classified as a Type-II inflammatory response with increased eosinophilia but is now further complicated by impaired, undefined innate and adaptive immune responses.\(^2\) The defective sinonasal epithelial barrier increases tissue permeability, decreases epithelial resistance, and causes acanthosis and acantholysis.\(^2\) Bilateral widening of the ethmoid infundibulum and truncation of the more distal, bulbous part of the middle turbinate may be consequential of subtle bone remodeling and sclerosis of sinus architecture.\(^3\)

Treatment options for CRSwNP initially include topical corticosteroids and nasal saline irrigants.\(^2\) Surgical intervention is only indicated for CRSwNP when NPs persistently inhibit sinus drainage or cause significant nasal congestion, as well as when medical therapy fails to resolve recurrent infectious rhinosinusitis.\(^1\) Intranasal steroids have been effective at decreasing NP size or preventing regrowth of NP after surgical removal.\(^1\) However, current studies have not determined the extent of intranasal steroid use that is effective to prevent the need for sinus surgery or regrowth of NPs.\(^1\) Leopold et al. and Palmer et al. conducted Phase 3 clinical trials for the newly approved EDS-FLU that delivers high-potency, topically acting steroid fluticasone propionate higher and deeper into the nasal passages than ordinary nasal sprays, including to the ostiomeatal complex, where sinus ostia normally ventilate and drain and where polyps usually originate in CRSwNP.\(^4\)\(^,\)\(^5\) Palmer et al. reported significant mean SNOT-22 scores and polyp grade improvement (~21.5, 83.3%) and NP elimination (54.2%), over one-year treatment with EDS-FLU (372 µg BID). Leopold et al. documented “much” or “very much” improvement in the majority (68%) of study participants, as well as a substantial decrease (by 62-67%) in surgical polypectomy referrals.\(^5\) The present case support the efficacy of EDS-FLU in significantly improving treatment of CRSwNP and offering an effective and well-tolerated option, particularly for patients who do not obtain satisfactory relief with standard intranasal corticosteroids.\(^4\)\(^,\)\(^5\)

Autopolypectomy is rarely reported in the literature. The earliest and most common natural polyp amputation cases describe pedunculated polyps located in the antrum.\(^6\) Peristalsis-induced torsion and traction of polyps may culminate with necrosis and amputation or peduncle ulceration.\(^6\) Choi et al. postulated that nonsteroidal anti-inflammatory drug-induced gastric injury at the peduncle of a 1.8-cm polyp on the lesser curvature of the prepyloric antrum may have ulcerated and, subsequently, led to its detachment.\(^6\) The 73-year-old female patient’s higher risk for H. pylori infection may have increased her susceptibility to...
this natural polypectomy. Shah and Shahidullah described another spontaneous polyp expulsion of gastrointestinal origin. A 60-year-old male defecated “a piece of flesh” and bright red blood per rectum, proceeded by lower abdominal pain and constipation for several weeks and increased dosing of magnesium citrate.

Spontaneous polypectomies have also occurred in the respiratory tract. A case of right lower lobe alectectomy resolved in an 18-year-old female, after spontaneously coughing up a tissue mass previously detected via fiberoptic bronchoscopy. Ahmed et al. discussed a 62-year-old male with a three-month history of vocal hoarseness that immediately improved after he coughed out a tissue chunk during his morning walk. Videolaryngoscopy indicated a raw mucosal area on the superior surface of the anterior one-third of the right vocal cord.

Most similar to the present case of spontaneous nasal polypectomy are case reports by Ole-Lengine and Manni, Rashid et al., and Pruna et al. describing total strangulation and autoexpulsion of antrochoanal (Killian) polyps, respectively. Pruna et al. accounted a 41-year-old male with nasal polyposis remitted to the hospital 15 days after a vigorous sneezing fit and fleshy mass expulsion through the left nostril. A CT scan following this incident indicated chronic residual inflammation, a hypoplastic and medically displaced middle turbinate, and ethmoidal infundibulum enlargement but no remaining mass lesion of the antrochoanal polyp. These polyps are generally benign, solitary, unilateral lesions originating in a maxillary sinus; passing through ethmoidal infundibulum or accessory ostium, between middle turbinate and lateral nasal wall, and posteriorly into the choana; and expelling anteriorly through nasal passages or posteriorly through the mouth. Simple NPs differ in their bilateral growth and higher association with allergic rhinitis, mucus glands, and elevated eosinophils.

Conclusion:

CRSwNP patients experience significantly decreased quality of life and productivity, as well as missed school and/or work days. It is imperative that physicians treating this chronic disease be cognizant of the latest pathophysiology, diagnosis, and treatment research and standards. The newly approved EDS-FLU that provided maintenance therapy, along with zileuton, in this CRSwNP case demonstrated clinical improvement in all diagnostically defining disease symptoms, polyp grade, and quality of life in patients with CRSwNP.

However, we acknowledge further studies are necessitated to determine if this combination is statistically significant. We report the first instance of spontaneous nasal polypectomy in the literature by this application of fluticasone propionate and zileuton.

Author Contributions:

All authors contributed to the conception or design of the work and the acquisition, analysis, critical revision of the case report. MR drafted the manuscript. All authors approval the final version of the manuscript to be published.

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