

# Orally inhaled fluticasone propionate improved chronic rhinosinusitis with co-morbid asthma: report of a case

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## Summary

**Chronic rhinosinusitis and asthma are expressions of airway inflammatory diseases that frequently coexist, especially in the case of adult-onset asthma. Both conditions have similar pathological features, while one affects the upper airways and the other the lower airways. Whether the treatment of bronchial inflammation affects the severity of sinus disease remains an unanswered question. We report a case of refractory chronic rhinosinusitis with co-morbid adult-onset asthma that effectively improved upon treatment with a daily dose of 200 µg (100 µg *b.i.d.*) of inhaled fluticasone propionate (FP). (*Asian Pac J Allergy Immunol* 2013;31:84-7)**

**Key words:** *chronic rhinosinusitis, adult-onset asthma, inhaled corticosteroid, eosinophils, one airway one disease*

## Introduction

Chronic rhinosinusitis is a chronic inflammatory disease of the upper airways characterised by accumulation of eosinophils. Patients with chronic rhinosinusitis often have co-morbid asthma. Asthma is also present in more than 50% of patients with sinus disease,<sup>1</sup> and studies using computed tomography (CT) have indicated that 80~90% of adult patients with asthma have sinus abnormalities.<sup>2</sup> The severity of sinus abnormalities in patients with chronic rhinosinusitis complicated by asthma correlates with the eosinophil counts in the sputum and blood.<sup>3</sup> As with asthma, chronic

rhinosinusitis is associated with local production of helper T type 2 cytokines, such as interleukin (IL)-5, and eotaxin.<sup>4</sup> In addition, cysteinyl leukotrienes (CysLTs) play key roles in the pathogenesis of asthma, and they are strongly expressed in the nasal polyps of patients with co-morbid asthma.<sup>5</sup> Taken together, it is increasingly thought that the relationship between chronic rhinosinusitis and asthma represents an airway inflammatory condition that fits the concept of ‘one airway, one disease.’

The concept of ‘one airway, one disease’ as applied to allergic rhinitis and asthma is supported by the following observations. Patients with allergic rhinosinusitis with co-morbid asthma who were treated with a corticosteroid nasal spray (in addition to their asthma medications) showed improvement of their asthma symptoms indicating that treating allergic rhinitis can improve asthma. Similarly, allergic rhinitis patients treated with steroid inhalation therapy for their asthma showed an improvement of their nasal symptoms.<sup>6,7</sup>

However, in the case of chronic rhinosinusitis with co-morbid asthma, there are no studies showing the effects of steroid inhalation therapy (given for their asthma) on chronic rhinosinusitis. Here, we report a case of chronic rhinosinusitis with adult-onset asthma that effectively improved upon treatment with inhalation steroid therapy, namely, fluticasone propionate.

## Case Report

A female patient aged 55 with a 10-year history of asthma presented with anosmia and nasal obstruction of 6 years’ duration. Endoscopic examination demonstrated multiple nasal polyps bilaterally. Computed tomography (CT) of the sinuses revealed striking sinus cavity shadows in the bilateral ethmoid sinuses and olfactory clefts, but almost none in the maxillary sinus. Total IgE was 396 IU/ml. Specific IgE antibodies to 3 allergens (Japanese cedar, Japanese cypress and ragweed) were detected using the capsulated hydrophobic carrier polymer-radioallergosorbent tests. Endoscopic

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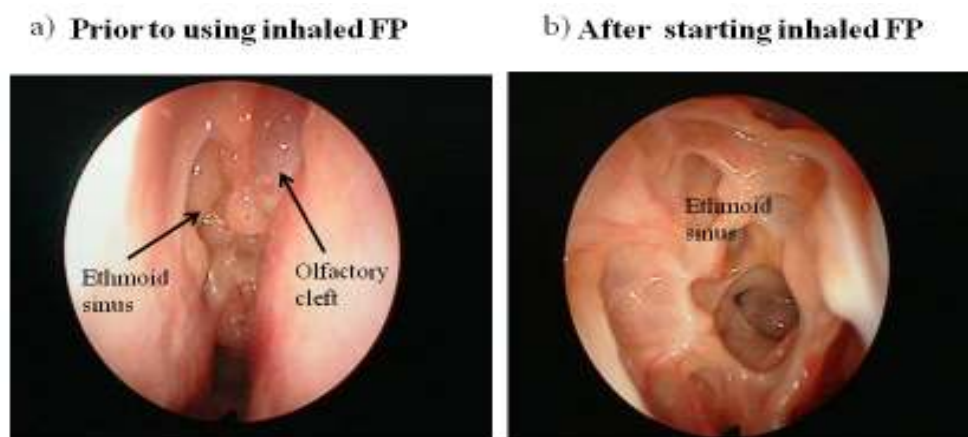


sinus surgery (ESS) was performed. The nasal polyp tissues showed striking eosinophil infiltration. Soon after the operation, combined treatment with topical fluticasone propionate (FP), and montelukast, 10 mg daily, was started. Peripheral blood eosinophil rate prior to ESS was 14.1%, and the CT score according to the Lund-Mackey system score was 21 points. One year following the ESS, the eosinophil rate was still high at 19.0%, endoscopic examination revealed multiple sites of mucosal swelling in the bilateral ethmoid sinuses (Figure 1a) and the CT score was 20 points (Lund-Mackey system) based on the CT image (Figure 2a). Treatment also comprised of inhaled FP at a daily dose of 200 µg (100 µg *b.i.d.*), which was started 10 years earlier, but the patient herself had discontinued this one year before her first visit to our institution. Following that discontinuation, she sometimes experienced bouts of coughing and/or wheezing. She was then diagnosed as having asthma by a respiratory medicine specialist on the basis of comprehensive consideration of her history of repeated bouts of coughing, wheezing, etc., and the findings of chest auscultation, pulmonary function tests, etc. Since spirometry showed FEV<sub>1.0</sub> 1.67 L, FEV<sub>1.0</sub>%-G 68.72%, %FEV<sub>1.0</sub> 84.3%, we reinstated the inhaled FP 100 µg *b.i.d.* therapy. Subsequently, there was improvement in her subjective symptoms, and after 6 months, the circulating eosinophil rate had normalised at 3.7%. Six months after re-starting inhaled FP, endoscopic examination showed that the ethmoidal mucosal swelling had disappeared (Figure 1b), and the mucosa of the olfactory clefts had also

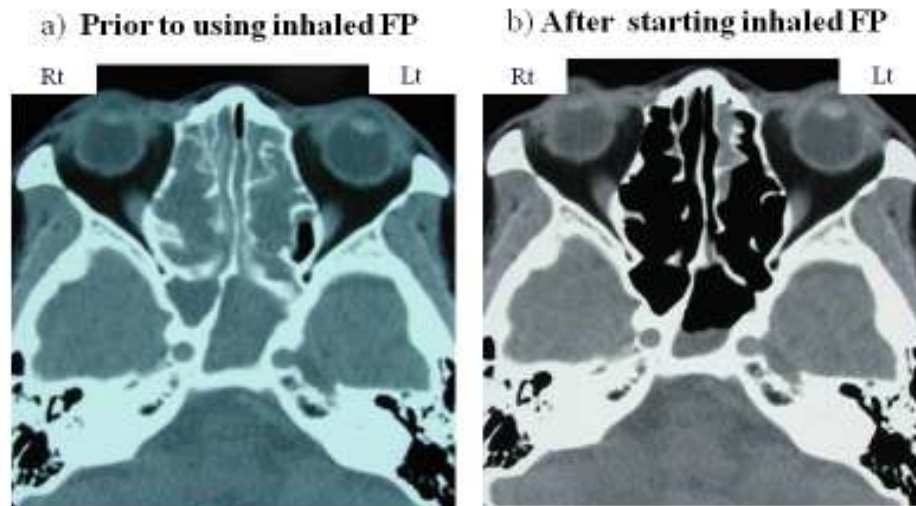
become normal. CT examination showed improvement in the nasal sinus shadows (Figure 2b), and the CT score had decreased to 5 points. A Visual Analogue Scale had shown no sense of smell at the initial visit or following the ESS, but remarkable improvement was seen following the reinstatement of the inhaled FP therapy. At the time of writing this case report, more than 2 years thereafter, there is no recurrence of mucosal swelling in the nasal sinuses or in the olfactory clefts, no increase in circulating eosinophil rate, and the patient has reported no subjective symptoms of impaired sense of smell.

### Results

Chronic rhinosinusitis and asthma are conditions that frequently coexist and are characterised by accumulation of eosinophils in the sinus mucosa as well as in the peripheral blood.<sup>1,3</sup> More than 50% of patients with sinus disease have asthma.<sup>1</sup> Eighty to ninety per cent of adult patients with asthma have sinus abnormalities on computed tomography (CT).<sup>3</sup> The CT characteristics in chronic rhinosinusitis accompanied by asthma are the presence of opaque shadows in the ethmoid sinus and olfactory cleft, and less dense shadows in the maxillary and sphenoid sinuses.<sup>8</sup> Our present case also showed eosinophil infiltration of nasal polyps and blood eosinophilia, and the CT images revealed opaque shadows in bilateral ethmoid sinuses and olfactory clefts. However, the maxillary sinuses were nearly devoid of any shadow. Those findings were thus in close agreement with the clinical characteristics of



**Figure 1.** Endoscopic findings (r. nose) a) Prior to the inhalation therapy for asthma (i.e., prior to using inhaled FP). b) Post-inhalation therapy for asthma (i.e., 6 months after starting inhaled FP).



**Figure 2.** CT images (horizontal) a) Prior to the inhalation therapy for asthma (i.e., prior to using inhaled FP). Soft-tissue shadows are seen in the ethmoid sinuses, olfactory clefts and sphenoid sinuses on both sides. b) Post-inhalation therapy for asthma (i.e., 6 months after starting inhaled FP). The soft-tissue shadows are reduced.

the more refractory type of chronic rhinosinusitis that is accompanied by asthma.

As with asthma, chronic rhinosinusitis is also associated with activation of Th2 cytokines like IL-5 and eosinophil-attracting chemokines, such as eotaxin.<sup>4</sup> Eosinophils are an additional source of these cytokines, suggesting that chronic rhinosinusitis has become a disease of up-regulated eosinophil infiltration, with eosinophils themselves providing the cytokines necessary for their own recruitment and activation. Cysteinyl leukotrienes (CysLTs) are factors that are also known to be chemotactic for eosinophils, promote adhesion molecule expression and inhibit eosinophil apoptosis, thereby contributing to eosinophilic inflammation. Chronic hyperplastic eosinophilic rhinosinusitis showed increased levels of CysLTs which were associated with asthma and correlated with the blood eosinophil count.<sup>5</sup> Chronic rhinosinusitis and asthma can also be considered to fall within the same concept of airway inflammatory diseases as ‘one airway, one disease.’

Allergic rhinitis and asthma frequently occur together. The epidemiologic, pathophysiologic and clinical data are so compelling that the concept of ‘one airway, one disease’ is accepted.<sup>9</sup> Although several mechanisms have been held responsible for the interaction between the upper and lower airways, recent data provide ample evidence of existence of a systemic pathway. In patients with allergic rhinitis, segmental bronchial provocation, as well as nasal

provocation, induced allergic inflammation in both the nasal and bronchial mucosa.<sup>10,11</sup> Furthermore, allergen provocation resulted in increased levels of circulating inflammatory cells and inflammatory mediators.<sup>10,11</sup> Presumably, absorption of such inflammatory mediators as IL-5 and eotaxin from sites of inflammation into the systemic circulation results in the release of eosinophils and their progenitor cells from the bone marrow.<sup>12</sup> Interestingly, in seasonal allergic rhinitis patients, an orally inhaled steroid reduced eosinophilia in both the peripheral blood and the nose, and attenuated the nasal symptoms.<sup>7</sup>

Topical nasal steroid treatment is widely advocated for the control of nasal polyp inflammation and growth, but the response to this treatment is often only partial.<sup>13</sup> LT-receptor antagonists have also been used to treat chronic rhinosinusitis associated with asthma, but their efficacy is also limited.<sup>14</sup> The numbers of the non-responders to both treatments are not negligible. In fact, following ESS our present patient was also started on treatment using an FP nasal spray plus montelukast, but the CT score for chronic rhinosinusitis remained unchanged as compared to that before that therapy.

Inhaled corticosteroids are also widely accepted as first-line preventive treatments for asthma. Their risk-to-benefit ratio is based on their relative potencies for airway and systemic glucocorticoid activity. Although it is reported that inhaled FP

causes suppression of adrenocortical activity even at clinically recommended doses, the dose of inhaled FP (100 µg *b.i.d.*) used in our patient is not considered to provoke any systemic effects in adults.<sup>15</sup> We instructed this patient to breathe through the mouth for at least 10 seconds after each dosing to avoid nasal deposition of inhaled FP. Thus, it is unlikely that direct nasal deposition of the inhaled FP was responsible for any of the effects of the therapy. Accordingly, we speculate that inhaled FP reduces lower airway Th2 type inflammation and that communication between the bronchial airways and bone marrow (involving cytokines like IL-5), potentially promoting a 'pan-airway' eosinophilia, might have been abrogated by the inhaled FP. The beneficial effect of the inhaled FP in this case might have been due to attenuation of that eosinophilia.

We experienced a case of refractory chronic rhinosinusitis with co-morbid adult-onset asthma, which was treated ineffectively with only an intranasal corticosteroid and montelukast, but subsequently improved upon addition of inhaled steroid therapy for asthma. Treating asthma with inhaled steroid therapy appears to be important in treating refractory chronic rhinosinusitis associated with asthma.

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