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Case report

A case report of allergic fungal rhinosinusitis managed with Dupilumab

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ABSTRACT

Introduction: Allergic fungal rhinosinusitis (AFRS) is a subtype of chronic rhinosinusitis with nasal polyps. It is characterized by eosinophilic mucin, which results from an inflammatory reaction to non-invasive fungal hyphae in the rhino-sinuses. It is clinically recognizable due to the criteria set by Bent and Kuhn. The treatment approach is multimodal, and the main treatment approach is surgical debridement, followed by a course of oral and/or topical corticosteroids to decrease recurrence post-surgery. This case report aims to illustrate the effect of Dupilumab, on the number of relapse episodes in a patient and the associated parameters.

Case presentation: Herein we report a case of a 40-year-old woman referred to our institution as a case of refractory AFRS for which she underwent four functional endoscopic sinus surgeries (FESS) and was on maximum medical treatment. She presented with complaints of facial fullness and pain, headache, and purulent discharge. After another trial of surgery which did not control her symptoms, she was assessed for criteria to start biological treatment. The symptoms were successfully controlled after initiation of the agent, and she was followed up using multiple subjective and objective measures.

Conclusion: AFRS is a non-invasive immune-mediated sub-clinical entity of chronic rhinosinusitis. A multimodal approach to its treatment based on surgical debridement with medical therapy has shown positive outcomes. In this case we present significant improvement after administering Dupilumab; therefore, suggesting its addition to the treatment regimen of refractory AFRS.

1. Introduction

Allergic fungal rhinosinusitis (AFRS) is a subtype of chronic rhinosinusitis with nasal polyps (CRSwNP). It is characterized by eosinophilic mucin (i.e., allergic mucin), which results from an inflammatory reaction to non-invasive fungal hyphae in the rhino-sinuses [1,2]. While sensitization to the fungi is present in CRSwNP, the distinguishing feature with AFRS is the high IgE levels. Although the pathophysiology of this entity is not adequately understood, it is clinically recognizable due to the criteria set by Bent and Kuhn (Table 1) [3,4]. AFRS remains an uncommon disease, as only a few countries have reported multiple cases, accounting for 5–10% [5] of all chronic rhinosinusitis (CRS) cases [1,2]. The treatment approach is multimodal, and the main approach is surgical debridement, followed by a course of oral and/or topical corticosteroids to decrease recurrence post-surgery. This is shown in a clinical study where only 15.2% of their patients had recurrence after receiving a full course of topical and oral corticosteroids post-operation [1,6]. It is also important to note that little evidence that demonstrates the effectiveness of topical and oral antifungals [1]. Some research supports the use of biologic agents to target this kind of inflammation reaction [1,7]; however, many of the studies are not specific to AFRS [1]. This case report aims to illustrate the effect of Dupilumab, an interleukin-4 (IL-4) receptor antagonist [8], on the number of relapse episodes in a patient and the associated parameters. We report a case of a patient who presented with persistent disease even with maximum medical treatment and multiple surgeries then was managed with a course of Dupilumab in a tertiary hospital.

This case report has been written in line with 2020 SCARE criteria [15].

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Table 1
AFRS clinical criteria as set by Bent and Kuhn.

Major	Minor
Type I hypersenstivity	Asthma
Nasal polyposis	Unilateral disease
Characteristic CT findings	Bone erosion
Eosinophilic mucin without invasion	Fungal cultures
Positive fungal stain	Charcot-Leyden crystals
	Serum eosinophilia

2. Presentation of the case

We present a case of a forty-year-old female referred to our institution as a known case of refractory AFRS for five years. At the time of presentation, she had undergone four functional endoscopic sinus surgeries (FESS), with the most recent one a year before presentation as well as maximum medical treatment. The patient still complained of facial fullness and pain, headache, and intermittent recurrent purulent nasal discharge. She denied any history of atopy or allergy to any foods or medications; she also has mild intermittent bronchial asthma requiring albuterol as per needed. On examination, nostrils and chest were clear. Investigations such as computer tomography (CT scan) showed bilateral maxillary signs of AFRS, and rigid nasal endoscopy showed nasal polyps, grade III on the Meltzer clinical scoring system [9]. The histopathology sample showed allergic mucin with fungal elements, consistent with allergic fungal sinusitis.

In the follow-up, magnetic resonance imaging showed suspicion of allergic fungal sinusitis; therefore, she underwent revision FESS in our institution. The post-operative period was uneventful until seven months post-operation when she presented to the clinic with a decreased sense of smell, rhinorrhea, and frontal headache – all of which manifested after an upper respiratory tract infection. Moreover, imaging (Fig. 1) also showed bilateral opacification and signs mucosal inflammation of ethmoidal and maxillary sinuses. Based on a shared decision with the managing multidisciplinary team, composed of otolaryngologists, pulmonologists and immunologists, she was deemed a suitable candidate for treatment with Dupilumab. Criteria was met for starting biologic treatment due to significant loss of sense of smell, need for more than two courses of oral corticosteroids, and evidence of type II inflammation [1]. Before treatment initiation, she underwent several lab tests, such as IgE serum levels and Eosinophil levels; and her Sino-Nasal Outcome Test (SNOT-22) [10] scores were calculated to follow treatment progression. Provided are post-treatment nasal endoscopy images to visualize the progression (Figs. 2 and 3).

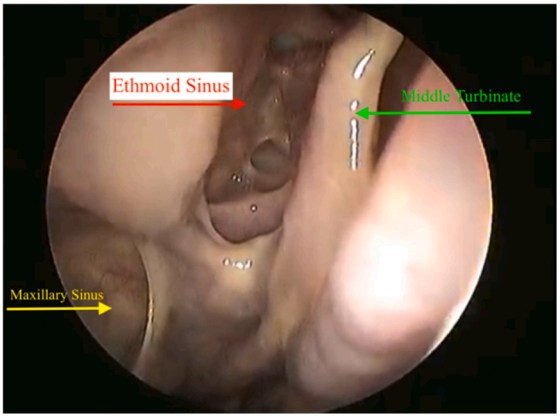
IgE levels at presentation were 13,360 kU/L, and the most recent levels were 305 kU/L. As for Eosinophils, they decreased from 400 cells/μL to 160 cells/μL. Her SNOT-22 score decreased from 87 to 21. Furthermore, her smell diskettes test score [11] at presentation was 4/8 and the most recent assessment showed that it is now 7/8. The patient showed good response following the criteria set defining response to biologic treatment in CRSwNP [1], and she is satisfied with the results of the planned care.

3. Discussion

AFRS is defined as an inflammatory reaction to fungi in the nasal and paranasal sinuses, with clear diagnostic criteria. It is an identified subtype of CRSwP, which is characterized by eosinophilic type 1 hypersensitivity reaction to the colonizing mold [11]. As understanding of the pathogenesis evolves; so, do the treatment modalities. A multimodal approach to the treatment of AFRS has proven to be the most beneficial, with surgical treatment remaining the foundation for this recurring disease [3]. Dupilumab inhibits the effect of IL13 and IL4 through blocking IL-4Rα. These two cytokines play a key role in type 2 inflammation responsible for the disease pathology in AFRS [12]. The usage of Dupilumab for the management of atopic dermatitis and asthma [13], both are types of type 2 inflammation, supported the rationale that it can be used to limit the recurrence of AFRS, decrease IgE levels and act as a steroid-sparing agent [8]. Dupilumab may act via different possible mechanisms including suppression of B-cell and IgE production and inhibition of cellular trafficking in inflamed tissue through the endothelium. Additionally, it is found to reduce type 2 inflammation markers in peripheral blood and nasal polyp tissue. These biomarkers include Eosinophilic cationic protein (ECP), eotaxins, IgE and cytokines like IL-13 [14]. The U.S. Food and Drug Administration has approved the usage of Dupilumab for chronic rhinosinusitis [16] but further specifications are needed for its usage in subtypes such as AFRS. There are ongoing trials expected to yield more results regarding the usage of Dupilumab to reduce the need for rescue therapy with systemic corticosteroid or surgery in patients who have chronic history of AFRS [17].

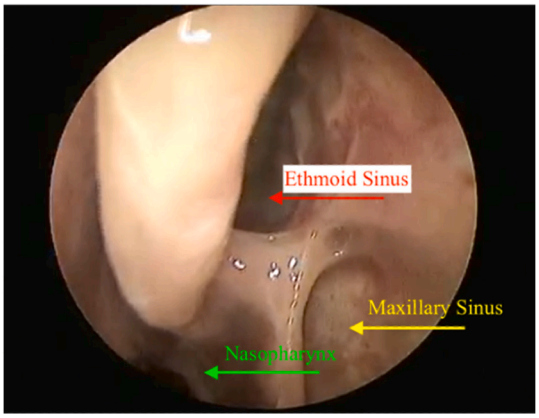
In a similar case presented by Rachelle et al. [12], we considered starting Dupilumab for the following reasons; recurrence of symptoms

Fig. 1. CT scan of paranasal sinuses prior to treatment.



Right nostril endoscopy post-dupilumab

Fig. 2. Right nostril endoscopy post-dupilumab.



Left nostril endoscopy post-dupilumab

Fig. 3. Left nostril endoscopy post-dupilumab.

despite medical and surgical treatment and high IgE and Eosinophil levels (Table 2). In this case, the clinical benefit was reached after treatment with Dupilumab, but the exact duration of treatment is unknown with prolonged treatment possibly contributing to the sustained effect. The treatment was tolerated, and the patient was satisfied with the treatment outcomes. Further studies, with a higher level of evidence, are needed to investigate the effectiveness, safety and appropriate treatment duration of Dupilumab in AFRS.

4. Conclusion

AFRS is a non-invasive immune-mediated recognized sub-clinical entity of chronic rhinosinusitis. A multimodal approach to its treatment based on surgical debridement with medical therapy has shown positive outcomes. Here we report a case of refractory AFRS that showed significant improvement post-Dupilumab administration. We measured both subjective (e.g. SNOT-22) and objective (e.g. IgE, Eosinophils) outcomes for the patient. By presenting this case we are suggesting its addition to the treatment regimen of resistant AFRS.

Source of funding

None.

Ethical approval

This study has been approved by Research Advisory council at King Faisal Specialist hospital in Riyadh, Saudi Arabia (RAC# 2200308).

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Registration of research studies

King Faisal Specialist hospital in Riyadh, Saudi Arabia (RAC# 2215219).

Guarantor

Dr. Naif H. Alotaibi MD, Associate professor, College of Medicine, Alfaisal University, Department of Otolaryngology, King Faisal Specialist Hospital and Research Canter, Riyadh, Saudi Arabia.

Table 2
Pre and post dupilumab treatment levels of serum IgE, serum Eosinophils, SNOT-22 and smell diskettes test. There is improvement of these parameters after treatment with Dupilumab.

	Pre-Dupilumab	Post-Dupilumab
Serum IgE	13,360 kU/L	305 kU/L
Serum Eosinophils	400 cells/μL	160 cells/μL
SNOT-22	87	21
Smell diskettes	4/8	7/8

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CRediT authorship contribution statement

First author: writing, editing, and supervising.
Second author: corresponding author, writing, review, editing, data collection, and finalizing manuscript.
Third author: reviewing manuscript and data analysis.
Fourth author: writing, review and data analysis.

Declaration of competing interest

The first author reports having received lecture fees from Smith & Nephew and fees for serving on an advisory board from Sanofi.

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