










## Pediatric allergic fungal rhinosinusitis: case report and literature review

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### Abstract

Allergic fungal rhinosinusitis is typically described as a condition involving nasal polyposis and eosinophilic mucin in which fungal hyphae are entrapped within enlarged sinus cavities, accompanied by an immune hypersensitivity response to fungi. There are rare reports in the pediatric literature. Early diagnosis and management with surgery represent the primary therapeutic approach, complemented by corticosteroid therapy and long-term follow-up to prevent relapse. In addition, novel biologic therapies have been investigated in recent years for the treatment of allergic fungal rhinosinusitis. Here, we report the case of a child with allergic fungal rhinosinusitis and summarize the literature review of data published.

### Keywords

allergic fungal rhinosinusitis, chronic rhinosinusitis in children, pediatric sinusitis, case report

### Introduction

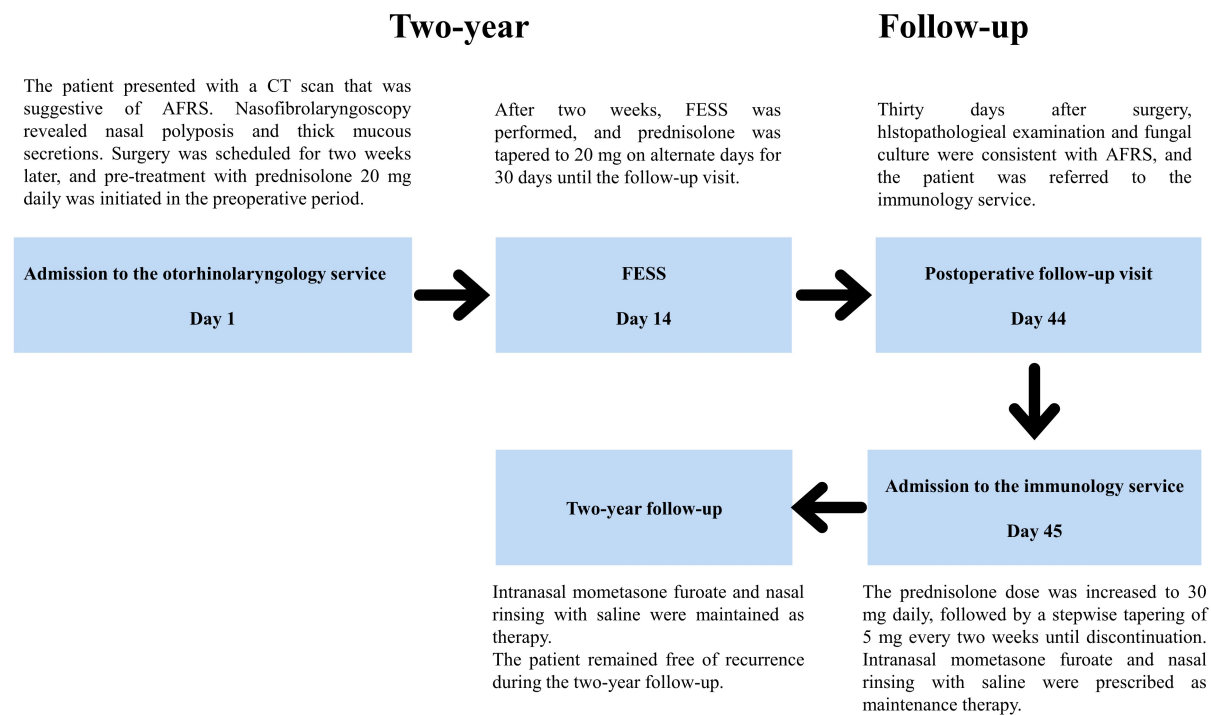
Allergic fungal rhinosinusitis (AFRS) is an endotype of chronic rhinosinusitis with nasal polyps (CRSwNP). It is typically described as a condition involving nasal polyposis and eosinophilic mucin in which fungal



hyphae are entrapped within enlarged sinus cavities, accompanied by an immune hypersensitivity response to fungi [1–4]. Although AFRS has been well characterized in adult patients, there are rare reports in the pediatric literature [2, 3]. Here, we report the case of a pediatric patient with AFRS and summarize a literature review of published data.

### Timeline

Figure 1 shows the timeline of treatment for a 12-year-old male patient with normal immune function.

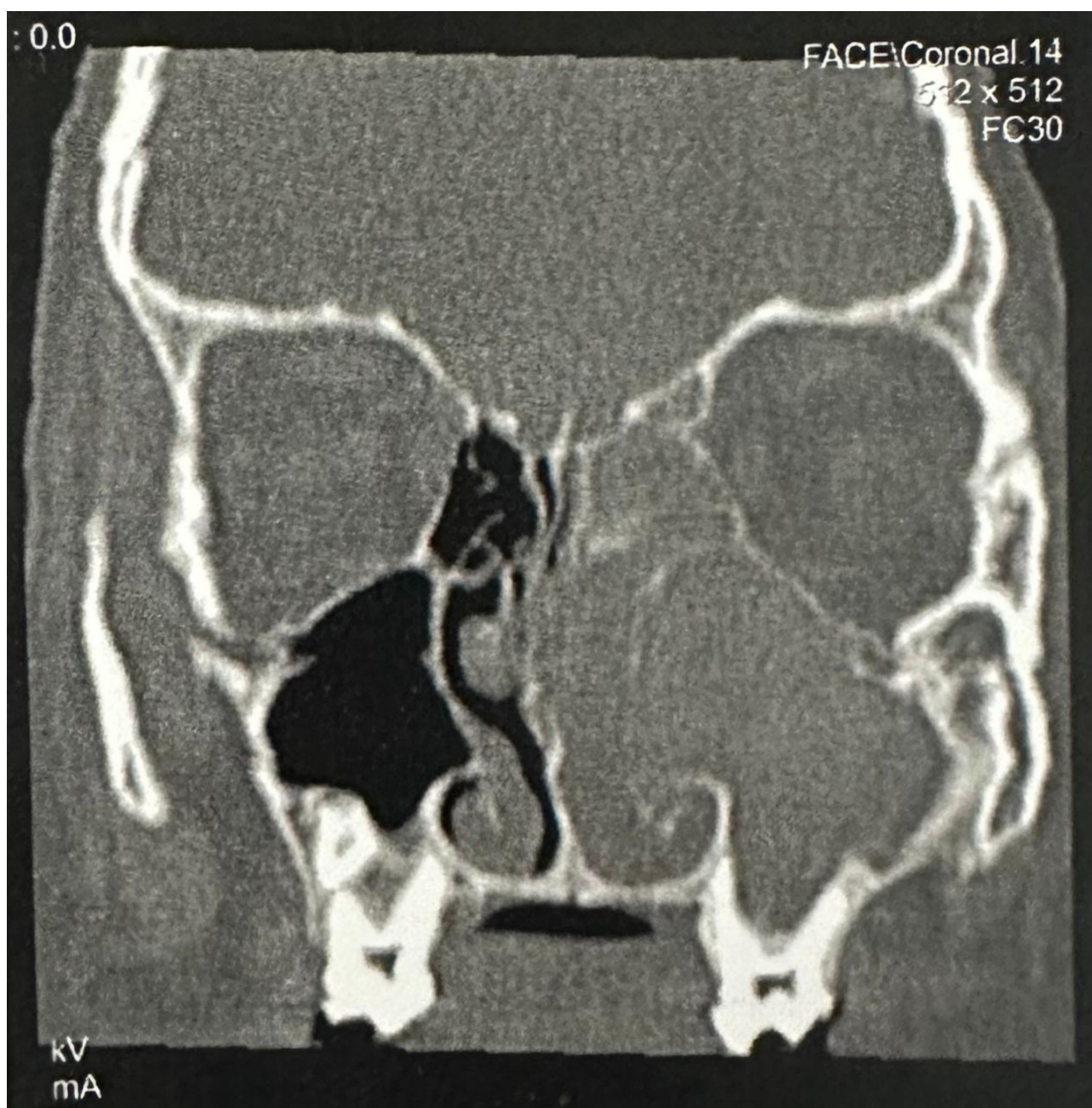


**Figure 1. Timeline.** AFRS: allergic fungal rhinosinusitis; FESS: functional endoscopic sinus surgery.

### Narrative

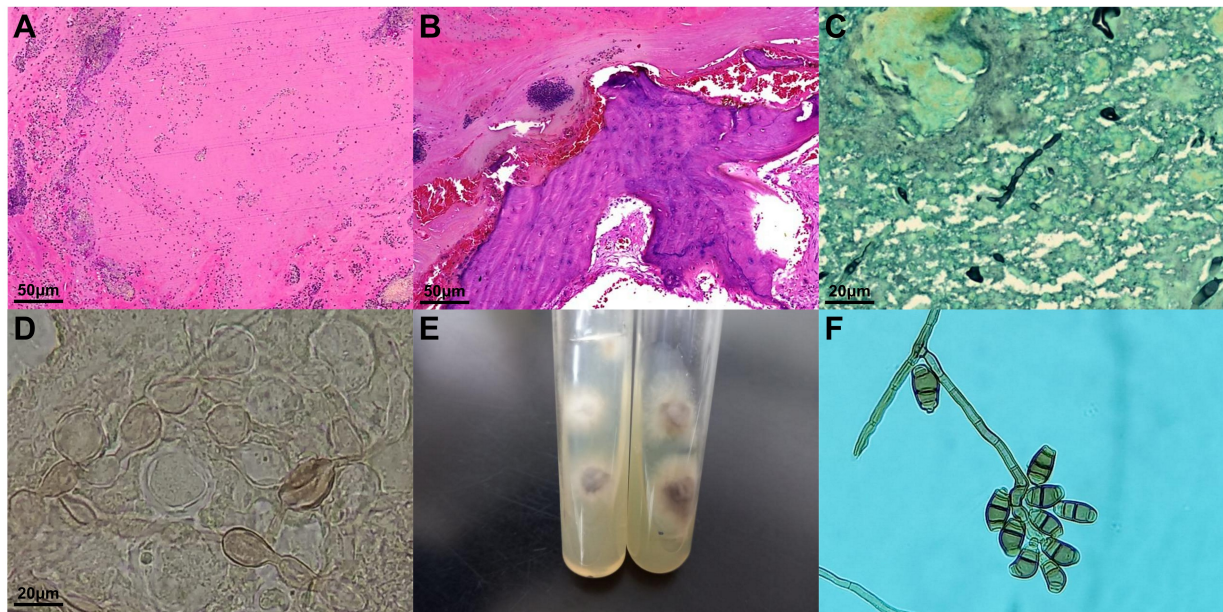
A 12-year-old immunocompetent male patient was admitted to our department (Figure 1) with a 3-month history of left-sided nasal obstruction for which he had received systemic therapy with antihistamine and steroids without improvement. He had a personal and family history of allergic rhinitis and initiated allergen-specific immunotherapy at 5 years of age. However, the treatment was discontinued after 6 months. No symptoms of asthma were reported, and spirometry demonstrated normal values. He also complained of left periorbital swelling with eye ipsilateral proptosis. Computed tomography (CT) showed opacification of the frontal sinuses, left maxillary sinus, and increased density of left ethmoid cells, as well as evidence of bone remodeling with bulging of the medial wall of the left maxillary sinus, bulging of the left orbital lamina, thinning of the left ethmoidal trabeculae, and mucosal thickening in the sphenoidal sinus. There was also a deviation of the nasal septum to the right and extensive involvement of the frontal sinuses, left maxillary sinus, and ethmoid cells, extending into the nasal fossa, with an expansive appearance and dense content, causing ipsilateral anterior bulging at the medial anterior ethmo-orbital margin, displacing the retro-medial muscle and adjacent orbital fat, impinging upon the eyeball. Consideration should be given to benign tumors, fungal sinusitis, and esthesioneuroblastoma. There was a slight external deviation of the left eyeball (Figure 2). He was started on prednisolone 20 mg daily for two weeks in the preoperative period, and the dose was subsequently tapered to 20 mg on alternate days until the postoperative follow-up visits at 30 days. Patient underwent functional endoscopic sinus surgery (FESS) and polypectomy. Histopathological analysis showed eosinophilic amorphous material with associated inflammatory infiltrates and degenerated epithelial cells, adjacent to bone fragments (Figure 3A and B). Grocott's

methenamine silver (GMS) revealed fungal elements (Figure 3C). The direct microscopic examination showed the fungus (Figure 3D). A fungal culture grew *Curvularia* species (Figure 3E and F). In addition, the patient's serum IgE was markedly elevated at 1,963 IU/mL (normal < 200 IU/mL), blood eosinophil counts were 51 cells/L, fungal-specific IgE and mite-specific IgE were positive. During the postoperative follow-up visit, the prednisolone dose was increased to 30 mg daily, followed by a stepwise tapering of 5 mg every two weeks until discontinuation. In addition, the patient was prescribed intranasal mometasone furoate and nasal rinsing with saline as maintenance therapy. No adverse events were observed in the patient. After surgery, he was symptom-free, and the frontal/maxillary sinus mucosa maintained its normalized state. The patient remained free of recurrence over a two-year follow-up period.



**Figure 2. Coronal CT showed opacification of the frontal sinuses, left maxillary sinus, and increased density of left ethmoid cells, as well as evidence of bone remodeling.** There was also a deviation of the nasal septum to the right and extensive involvement of the frontal sinuses, left maxillary sinus, and ethmoid cells, extending into the nasal fossa, with an expansive appearance and dense content causing ipsilateral anterior bulging at the medial anterior ethmo-orbital margin, displacing the retro-medial muscle and adjacent orbital fat, impinging upon the eyeball.





**Figure 3. Histopathology and direct examination for fungi.** (A) Hematoxylin-eosin stain of the obtained allergic mucin, demonstrating eosinophilic amorphous material with associated inflammatory infiltrates and degenerated epithelial cells (scale bar = 50  $\mu$ m, magnification  $\times 100$ ). (B) Haematoxylin and eosin staining of necrotic cellular debris and amorphous eosinophilic mucin adjacent to bone fragments (scale bar = 50  $\mu$ m, magnification  $\times 100$ ). (C) Grocott's methenamine silver (GMS) revealed fungal elements (scale bar = 20  $\mu$ m, magnification  $\times 400$ ). (D) Direct microscopic examination with KOH 20% + Parker Ink (Quink<sup>®</sup>) showed dematiaceous septate branched hyphae, with swollen cells, as well as hyaline septate hyphae (scale bar = 20  $\mu$ m, magnification  $\times 400$ ). (E) Culture on Sabouraud-dextrose agar 2% (BD-DIFCO<sup>™</sup>) and Mycosel agar (BD-BBL<sup>™</sup>), after five days at 30°C, showed the growth of brown to gray woolly surfaced colonies with dark reverse. (F) Slide cultures on Potato-Dextrose agar (BD-DIFCO<sup>™</sup>), after seven days, better revealed the typical microscopic characteristics, such as large curved septate dematiaceous conidia, mostly four-celled, with a swollen and darker central cell, as well as dark septate branched hyphae and geniculate conidiophores.

## Diagnostics

CT showed opacification of the frontal sinuses, left maxillary sinus, and increased density of left ethmoid cells, as well as evidence of bone remodeling with bulging of the medial wall of the left maxillary sinus, bulging of the left orbital lamina, thinning of the left ethmoidal trabeculae, as well as mucosal thickening in the sphenoidal sinus. There was also a deviation of the nasal septum to the right and extensive involvement of the frontal sinuses, left maxillary sinus, and ethmoid cells, extending into the nasal fossa, with an expansive appearance and dense content, causing ipsilateral anterior bulging at the medial anterior ethmo-orbital margin, displacing the retro-medial muscle and adjacent orbital fat, impinging upon the eyeball. Consideration should be given to benign tumors, fungal sinusitis, and esthesioneuroblastoma.

## Patient perspective

The patient and his family were anxious about the persistence of symptoms and particularly alarmed by the eye swelling. After surgery, they felt relieved with the resolution of symptoms and reassured by the clear diagnosis and follow-up. During two years of monitoring, the patient remained healthy and resumed normal daily activities without limitations.

## Discussion

AFRS is more common in temperate regions with high humidity [1, 3]. The most common AFRS-etiological molds reported are dematiaceous (such as *Bipolaris*, *Curvularia*, and *Exserohilum*) and *Aspergillus* (a hyaline mold) [5]. The genus *Curvularia* comprises a group that encompasses more than 35 species. Mostly, they are facultative plant and soil pathogens of tropical areas and subtropical [6]. The types of fungi cultured in the sinus cavities are similar in children as in adults, and the most commonly encountered genus in AFRS is *Aspergillus* [7, 8].

Typically, patients with AFRS have been described in the third decade of life. Children with AFRS appear to differ from adults in some aspects of their clinical presentation [2, 3, 9]. Pediatric AFRS is thought to have a more aggressive nature, with higher serum immunoglobulin E and more frequent bone erosion and malformation of facial bones [9]. However, the periosteal layers are generally preserved, and fungal invasion of the intracranial compartment is exceedingly rare, even in cases where the mass extends through the orbit.

Most patients initially present with gradual nasal obstruction, nasal discharge, anosmia, and headaches. In children with AFRS, unilateral disease occurs more frequently than in adults, and alterations of the facial skeleton are also more prevalent in the pediatric population, with over half of the cases presenting with manifestations such as proptosis, telecanthus, or malar flattening secondary to bone erosion [2, 9]. In pediatric patients, AFRS often appears more severe, likely due to the incomplete development of the facial skeleton, which predisposes them to extensive bone expansion, regional spread, and erosion, with potential complications such as telecanthus, proptosis, malar flattening, ophthalmoplegia, medial canthal bulging, and widening of the nasal pyramid [7, 10]. In the case reported, the patient presented initially with mild, insidious symptoms and developed hypertrophic disease, causing proptosis and bone erosion.

Endoscopic examination may reveal nasal polyps and allergic mucin. Histological analysis of allergic mucin typically demonstrates eosinophilic aggregates containing Charcot-Leyden crystals and fungal hyphae. Pediatric patients with AFRS have radiographic features similar to those in adult patients [10]. The mucin causes increased attenuation on CT without contrast material [8, 11]. Mucin accumulation and local inflammation may induce sinus expansion with osseous erosion or remodeling. The ethmoid sinus is the most commonly involved. In AFRS, bone loss is more frequent than in other chronic rhinosinusitis forms, typically reflecting pressure from mucin rather than invasive disease. The high protein concentration of allergic mucin causes a T1 central low signal and a T2 central signal void [11, 12].

While the pathophysiology of AFRS is still being elucidated, disruption of the epithelial cell barrier allows fungi within the paranasal sinuses to upregulate type 2 immune responses, leading to the characteristic type I hypersensitivity, eosinophilic inflammation, and type 2 cytokine profile associated with the disease [1, 13].

In 1994, Bent and Kuhn developed a set of major and minor criteria for the diagnosis of AFRS, these were: (1) type I hypersensitivity to fungi confirmed by history, skin tests, or serology; (2) nasal polyposis; (3) characteristic CT signs; (4) eosinophilic mucus without fungal invasion into sinus tissue; and (5) positive fungal stain of sinus contents removed during surgery. Minor features included (1) radiographic bone erosion; (2) positive fungal cultures; (3) unilateral disease predominance; (4) Charcot-Leyden crystals; and (5) peripheral eosinophilia. A patient had to fulfil all five major features to receive the diagnosis [1–4, 9, 13]. Although Bent and Kuhn's criteria were originally developed for adults, they are also applied in pediatric patients [2, 9]. In the case reported, the patient presented 5 major criteria and 3 minor criteria.

Surgical intervention, together with topical and systemic corticosteroids, constitutes the standard treatment. FESS to open the paranasal sinuses allows for the removal of eosinophilic mucin and debris [1]. Oral antifungal therapy and immunotherapy have not demonstrated clear benefit and are consequently not recommended by recent guidelines [10]. Omalizumab, dupilumab, and mepolizumab are currently approved for treating CRSwNP in general, but clinical trials to date with these biologics did not involve AFRS patients [1, 4, 9, 10, 14]. Biologic agents may offer a future therapeutic option for AFRS, but limited evidence and high costs currently restrict their use in both adults and children. Further studies are required to confirm efficacy and assess long-term safety in pediatric populations [9].

## Conclusions

Pediatric chronic rhinosinusitis has a significant clinical impact, constituting both a large economic and healthcare resource burden. AFRS needs to be considered in children with nasal polyps, unilateral sinus

disease, and facial bone malformations. Early diagnosis and management with surgery represent the primary therapeutic approach, complemented by corticosteroid therapy and long-term follow-up to prevent relapse. Biologics may represent an important therapy for AFRS in the future. Additional studies are needed for the development and testing of new therapeutic options.

## Abbreviations

AFRS: allergic fungal rhinosinusitis

CRSwNP: chronic rhinosinusitis with nasal polyps

CT: computed tomography

FESS: functional endoscopic sinus surgery

GMS: Grocott's methenamine silver

## Declarations

### Author contributions

DASM: Conceptualization, Investigation, Writing—original draft, Writing—review & editing, Formal analysis, Visualization. SDDJ: Conceptualization, Investigation, Writing—original draft, Writing—review & editing, Supervision. FCC: Conceptualization, Investigation, Supervision. GB: Conceptualization, Investigation, Writing—review & editing. ACB: Conceptualization, Investigation, Writing—review & editing. SORV: Conceptualization, Investigation, Writing—original draft, Writing—review & editing. PNF: Conceptualization, Investigation, Supervision. All authors read and approved the submitted version.

### Conflicts of interest

The authors declare that there are no conflicts of interest.

### Ethical approval

This study was approved by the Comitê de Ética em Pesquisa do Hospital Universitário Clementino Fraga Filho (HUCFF/UFRJ), number CAAE 03685518.5.0000.5262, and complies with the Declaration of Helsinki.

### Consent to participate

Informed consent to participate in the study was obtained from the participant's guardians.

### Consent to publication

Informed consent to publication was obtained from the participant and the participant's guardians.

### Availability of data and materials

Requests for accessing the datasets should be directed to Daniela de Abreu e Silva Martinez ([daniela.dasm@gmail.com](mailto:daniela.dasm@gmail.com)).

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