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Short Report

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Is there a link between chronic allergic fungal rhinosinusitis and alpha-1 antitrypsin deficiency? A case report

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Abstract

Diagnosis of AAT deficiency starts with clinical suspicion and it is confirmed through serum levels and phenotyping/genotyping. AAT deficiency represents a potential contributing factor to chronic allergic fungal rhinosinusitis. We report a case of chronic fungal allergic rhinosinusitis associated with alpha-1 antitrypsin deficit. A 40-year-old female patient was referred to an Otolaryngology Consultation due to chronic rhinosinusitis with nasal polyps. Clinically, she exhibited resistance to muiltiple medical and surgical treatments. A culture of nasal secretions identified *Aspergillus fumigatus*. She received treatment with corticosteroids and antifungal therapy. An allergological study confirmed sensitization to *Aspergillus fumigatus* and *Cladosporium herbarum.* She subsequently underwent sublingual immunotherapy to *Aspergillus fumigatus*, which led to clinical improvement. However, her condition later deteriorated, prompting a more thorough etiological investigation that revealed an alpha-1 antitrypsin deficiency.

Keywords: Chronic allergic fungal rhinosinusitis; Alpha-1 antitrypsin deficiency; Nasal polyposis.

Introduction

Chronic Allergic Fungal Rhinosinusitis (AFRS) is a non-invasive subtype characterized by typical CT and MRI findings, specific IgE to fungal antigens and eosinophilic mucin, indicating an anti- inflammatory reaction to fungal hyphae in the sinuses [1]. Some features suggestive of this diagnosis include a young immunocompetent patient with unilateral or asymmetric involvement of the paranasal sinuses; a history of atopy, nasal polyps and the presence of nasal casts and a lack of significant pain [2]. Current treatment protocols for this condition typically involve a combined medical and surgical approach. Alpha-1-Antitrypsin (AAT) deficiency is a genetic disorder caused by mutations in the SERPINA1 gene, typically with lung and/or liver involvement. Patients can present different genotypes and phenotypes. Diagnosis is confirmed by decreased serum levels of antitrypsin protein along with a deficient phenotype. Despite being one of the most prevalent genetic disorders, it remains underdiagnosed [3].

Case report

We present the case of a 40-year-old woman referred to an Otolaryngology Consultation for severe nasal obstruction, purulent secretions, and progressive anosmia, which began at the age of 23. She underwent rhinoscopy, which identified the presence of bilateral polyposis. Her personal history is relevant only for mild rhinitis since childhood. A CT scan identified sinonasal bilateral polyps. At 27 years old, she underwent a polypectomy. The removed fragments were analyzed, and the histopathological examination revealed bilateral sinonasal inflammatory polyps. Two months later, she underwent a MRI, which revealed

a lesion localized in the nasal fossae, involving the ethmoidal cells and the left maxillary sinus. She underwent a second polypectomy and the histopathologic analysis of fragments of the lesion revealed inflammatory sinonasal polyps. Nasal secretion culture identified *Aspergillus fumigatus.* However, two months after the second surgery, her symptoms recurred. A new CT scan was performed (Figures 1 and 2) and showed complete filling of the paranasal sinuses and nasal fossae. She was treated with deflazacort and intravenous fluconazole for two weeks and was referred to the Allergy and Clinical Immunology Consultation. Skin testing showed positive results for *Aspergillus fumigatus* (9 mm) and *Cladosporium herbarum* (4 mm). Laboratory tests revealed a total IgE of 1560 IU/ml, a specific IgE for *Aspergillus fumigatus* of 41.1 IU/ml, and for *Alternaria alternata* of 0.9 IU/ml.

Based on these findings, to improve her quality of life, she started sublingual immunotherapy for *Aspergillus fumigatus* (TOL forte Leti®) for three years. Her symptoms were controlled for three years, but they relapsed after the treatment period. A new CT scan of the paranasal sinuses revealed filling of the sinus cavities. Additionally, a more extensive study was performed, which did not reveal any immunological dysfunction other than a decrease in A1T (61 mg/dL). The study confirmed the diagnosis of Pi* MPalermo-S genotype. She has no family history of AAT deficiency. C-reactive protein showed a slight elevation (0.93 mg/dL). Although she presented no symptoms of pulmonary or liver disease, she underwent pulmonary function tests and a thoracic CT scan, which showed no relevant findings. Despite daily treatment with nasal irrigation and nasal budesonide, she still experiences nasal obstruction.

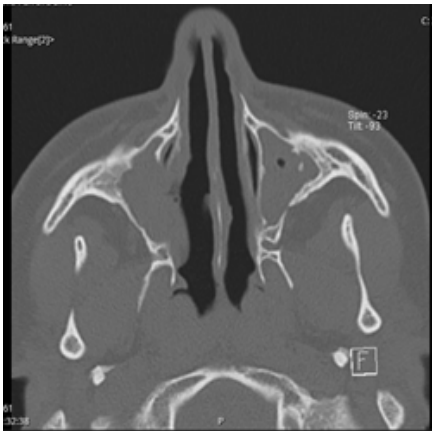

Figure 1: CT scan in axial plane shows complete filling of the paranasal sinuses and nasal fossae.

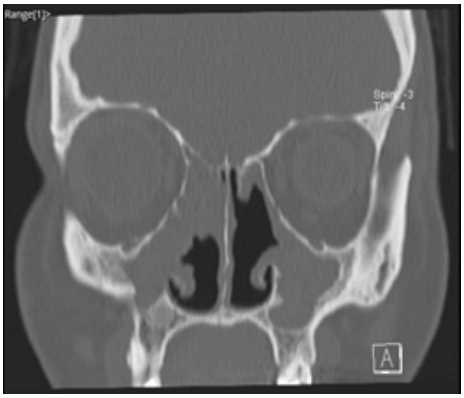

Figure 2: CT scan in coronal plane shows complete filling of the paranasal sinuses and nasal fossae.

Discussion

This case highlights the complex approach of severe recurrent fungal allergic rhinosinusitis where multiple factors can contribute: type I hypersensitivity, mucosal inflammation, nasal microbiome dysregulation, surgical anatomical changes, and potentially AAT deficiency. AAT, a serine protease inhibitor, regulates different inflammatory cascades within the body [4]. This clinical case raised some questions: What is the importance of AAT associated microorganism infection in the pathogenesis of chronic allergic rhinosinusitis to fungi? Are we in front of a patient with concomitant different diseases or may AAT deficiency have a role in pathogenesis and susceptibility to fungal infections and chronic inflammation? We hypothesize that this patient's severity of AFRS may be partially due to AAT deficiency. Insufficient AAT contribute to poor control neutrophil elastase activity, perhaps contributing to sinus disease in this patient. To date, study results regarding the efficacy of immunotherapy in fungal rhinosinusitis are controversial, which can explain symptom relapse after treatment.

Conclusion

The potential interplay between AAT deficiency and chronic fungal sinusitis requires further investigation. We suggest screening patients with recurrent or severe AFRS for AAT deficiency and, eventually, evaluation of rhinosinusal disease in diagnosed AAT deficiency patients. Given the limitations in the currently available literature, further controlled studies are essential to evaluate the prevalence of AAT deficiency in patients with AFRS, to understand the role of ATT deficiency and development or severity of AFRS and evaluated specific therapeutic strategies.

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