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Radiological Evaluation of Allergic Fungal Sinusitis: Novel Findings

Alerjik Fungal Sinüzitin Radyolojik Değerlendirmesi: Yeni Bulgular

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Abstract

Aim: Fungal sinusitis is a disease that was previously considered a rare disease, but has recently been reported with increasing frequency in warm climates. Fungal sinusitis classification has evolved over the past two decades and is said to include five subtypes. Discrimination of different subtypes and knowing their radiological features are important for accurate and rapid diagnosis and initiation of appropriate treatment. In our study, we aimed to investigate whether there is a difference between the radiological findings of allergic fungal sinusitis (AFS) with a newly defined finding that may help the diagnosis of AFS; serrated turbinate and those reported in the literature.

Material and Method: Our study included 120 patients who underwent paranasal sinus computed tomography examination in our center between January 2019 and September 2021. Patients diagnosed with AFS as a result of allergic tests and/or fungal culture examinations were included in the first group, and patients diagnosed with non-AFS rhinosinusitis were included in the second group. Presence of serrated turbinate appearance, polyps, bone erosion, CT hyperdensity were evaluated in the images.

Results: The radiological features of AFS and non-AFS were compaired and serrated turbinate appearance was found to be statistically signifant in AFS ($p<0.05$). Bone erosion, presence of polyps and CT hyperdensity did not differ between the groups ($p>0.05$).

Conclusion: Our findings showed that serrated turbinate appearance may be a useful radiological marker in the diagnosis of AFS. Bone erosion should be evaluated seperately from other morphological and structural changes in the bone structure, and the bone density measurements should be specified for sinus opacification.

Keywords: Allergic fungal sinusitis, serrated turbinate, bone erosion, radiology

Öz

Amaç: Fungal sinüzit daha önceleri nadir görülen bir hastalık olarak kabul edilen, ancak son zamanlarda sıcak iklimlerde artan sıklıkta bildirilen bir hastalıktır. Fungal sinüzit sınıflandırması son yirmi yılda gelişmiştir ve beş alt tip içerdiği söylenmektedir. Farklı tiplerinin anlaşılması ve bunların radyolojik özelliklerinin bilinmesi doğru ve hızlı tanı ile uygun tedavinin başlatılması açısından önemlidir. Çalışmamızda Alerjik Fungal Sinüzit (AFS) tanısına yardımcı olabilecek yeni bir bulgu olan serrated konka varlığı ile ılıman iklim kuşağında yer alan ülkemizde AFS'nin radyolojik bulgularının literatürde belirtilenler ile farklılığının bulunup bulunmadığını araştırmayı amaçladık.

Gereç ve Yöntem: Çalışmamıza Ocak 2019 – Eylül 2021 tarihleri arasında merkezimizde paranazal sinüs BT incelemesi yapılan 120 hasta dahil edilmiştir. Hastalardan alerjik testler ve/veya fungal kültür incelemeleri sonucu AFS tanısı konulanlar birinci grup, AFS dışı rinosinüzit tanısı konulan hastalar ikinci gruba dahil edilmiştir. Görüntülerde serrated konka görünümünün varlığı, polip varlığı, kemik erozyon varlığı ve CT hiperdansitesi varlığı araştırılmıştır.

Bulgular: Çalışmamızda AFS'nin radyolojik özellikleri diğer rinosinüzitlerle karşılaştırılmış olup serrated konka görünümünün AFS için istatistiksel farklılığını tespit ettik ($p<0.05$). Kemik erozyon, polip mevcudiyeti ve CT hiperdansitesi ise farklılık göstermemekteydi ($p>0.05$).

Sonuç: Ortaya koyduğumuz bulgular AFS tanısı için serrated konka görünümünün ayırıcı tanıda faydalı bir belirteç olabileceğini göstermiştir. Kemik erozyonun kemik yapıdaki diğer şekil ve yapı değişikliklerinden ayrı değerlendirilmesi, sinüs opasifikasyonu için de dansite değerinin belirtilmesi gerekmektedir.

Anahtar Kelimeler: Alerjik fungal sinüzit, serrated konka, kemik erozyon, radyoloji

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INTRODUCTION

Fungal sinusitis is a disease that was previously considered a rare disease, but has recently been reported with increasing frequency, especially in warmer climates such as the Southern USA and Australia.[1-3] The fungal sinusitis classification has evolved over the past two decades and includes 5 subtypes. Acute invasive fungal sinusitis, chronic invasive fungal sinusitis, chronic granulomatous invasive fungal sinusitis constitute the invasive group whereas allergic fungal sinüsitis (AFS) and fungal ball (fungal mycetoma) are classified as non-invasive fungal sinusitis.[1,4] These five subtypes have different clinical and radiologic features. The treatment strategies and prognosis of each type are also different.[1] Differentiation of fungal sinusitis subtypes with their specific radiological features is important to distinguish them from bacterial sinusitis subtypes and to initiate correct, rapid diagnosis and treatment.[1,5]

The idea of AFS first appear when Safirstein et al described a clinical picture in allergic bronchopulmonary aspergillosis in 1976 in with nasal polyposis, nasal mucosal crust formation resembling sinusitis and Aspergillus was isolated in sinus cultures.[6] The same clinical picture was described by Millar et al as allergic aspergillosis of the paranasal sinuses in 1981, and as allergic aspergillus sinusitis by Katzenstein et al in 1983.[7,8] However, the pathology first expressed by Robson et al with the term allergic fungal sinusitis (AFS) showing that it can also be caused by non-aspergillus fungi, is a newly defined disease that is generally seen in atopic individuals and is different from other types of sinusitis.[9] As a result, AFS is an Ig-E mediated hypersensitivity reaction to fungal elements, not an infection of the mucosa, and is the most common form of fungal sinusitis.[10,11]

AFS diagnostic criteria established by Bent and Kuhn in 1994 are positive allergy tests, nasal polyposis, characteristic computed tomography (CT) scan findings, presence of eosinophilic mucin, and detection of fungus in the culture. However, as stated by the authors, first of all, there should be suspicion about the presence of AFS in the patient.[5] In later studies on the subject, heterogenous mucin-induced areas in the paranasal sinuses in CT examinations were accepted as relatively characteristic features of the disease, although they were not specific for AFS.[12,13] It is stated that in magnetic resonance (MRI), hypointense appearance in the centre in T1W sequence, presence of central signal gap and peripheral signal increase in T2W sequence are significant for AFS when compaired with invasive fungal sinusitis subtypes, and combined CT and MRI findings provide a radiographic appearance that is highly specific for AFS.[14] However, recently there are opinions that radiological findings alone are not significant in the diagnosis of AFS.[15]

Although Bent and Kuhn diagnostic criteria for AFS is extremely useful, according to the information that we have gained in recent years about AFS, this disease is much more common than expected in some parts of the world and there may be a need for a re-evaluation in the radiological diagnostic criteria due to increased number of diagnoses of AFS.[5] In our study, we aimed to investigate the presence of serrated turbinate, which is a new radiological finding that can help the diagnosis of AFS, and whether there is a difference between the radiological findings among AFS and non-AFS in our study.

MATERIAL AND METHOD

This study was conducted in accordance with the ethical principles stated in the Declaration of Helsinki and was approved by the Ethical Committee of noninvasive Clinical Research of the Mardin Artuklu University (2021/2). Our study included 120 out of 186 patients who underwent paranasal sinus CT examination with a preliminary diagnosis of sinusitis in our center between January 2019 and September 2021. 26 patients under 18 years age, 32 patients who had a previous operation involving paranasal sinuses, 8 patients with a mass or invasive pathology were excluded from the study. Patients diagnosed with AFS as a result of allergic tests and/or fungal culture examinations were included in first group, and patients diagnosed with non-AFS rhinosinusitis were included in the second group. The CT examinations were performed with General Electric IQ™ 32-Detector Spiral MSCT device with 120–130 kV tube voltage using 80-160 mAs value within 0,625 mm section thickness. The images taken in axial plane and evaluated together with coronal and sagittal reformat images by an otolaryngologist experienced in radiological anatomy and a radiologist retrospectively. Presence of serrated turbinate morphology, presence of polyps, presence of bone erosion and hyperdensity in the sinus are investigated on CT images (**Figure 1-4**).

Figure 1. Serrated turbinate (white arrowheads)

Figure 2. Polypoid lesion (white arrow)

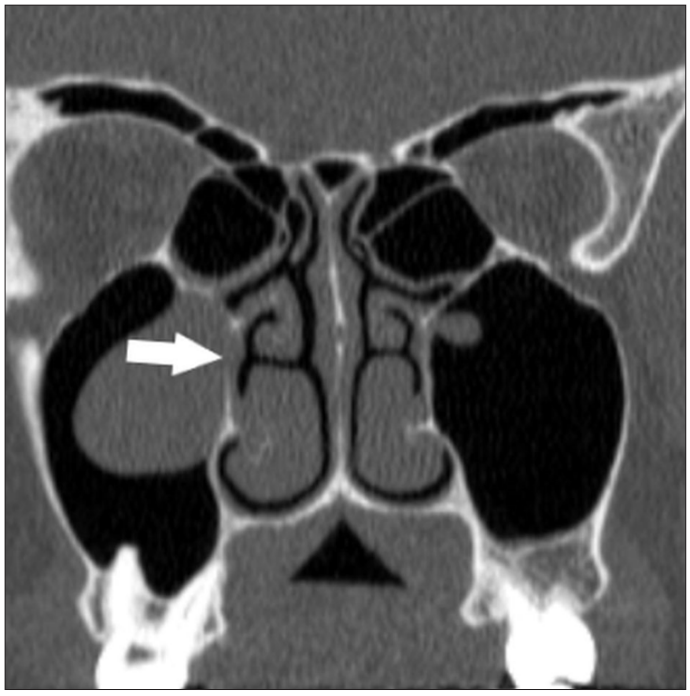

Figure 3. Bone erosion (white arrow)

Statistical Analysis

Data were analyzed using the Statistical Package for the Social Sciences (SPSS) software, version 22 (IBM Corp. Armonk, NY). Distribution of variables, were analyzed using Shapiro Wilk test. Variables were not found to be distributed normally in Shapiro Wilk test. Categorical data were also analyzed by chi-square test. A p value of <0.05 was considered significant.

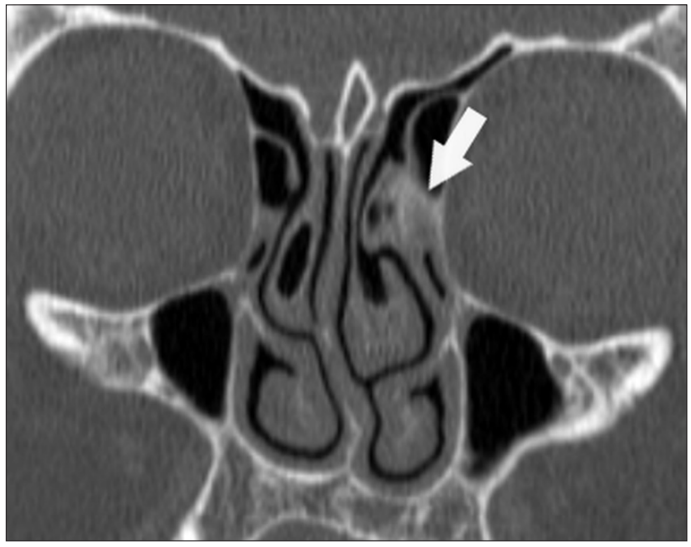

Figure 4. Hyperdense lesion (white arrow)

RESULTS

120 adult patients (50% male, 50% female; 18 to 63 years old) met the inclusion criteria for our study. The distribution of age is normal with mean of 36.81 years and standard deviation (SD) 11.24 years. Of the 120 patients; 86 patients (72%) are AFS (-) and 34 patient (28%) are AFS (+). Among AFS (+) patients; 19 patients (16%) are female and 15 patients (12%) are male.

AFS (+) patients are compaired with AFS (-) patients among gender, polyp formation, serrated concha appearance, bone erosion and hyperintensity on CT. None of the parameters were found to be statistically significant except serrated concha morphology on CT (p<0.05) (**Table 1**).

Polyp formation, bone erosion and hyperdensity on CT is compaired between serrated concha positive and negative patients. Statistical difference was found between serrated concha positive and negative patients. However there were no statistically significant relation between positive and negative patients in bone erosion and hyperdensity parameters on CT (p>0.05) (**Table 2**).

Table 1. Comparison of AFS (+) and AFS (-) patients according to gender, presence of polyp, serrated concha, bone erosion and hyperdensity.

	AFS		p
	Positive	**Negative**	
Female	19 (15.8%)	41 (34.2%)	p>0.05
Male	15 (12.5%)	45 (37.5%)	
Polyp			p>0.05
Positive	15 (12.5%)	26 (%21.7)	
Negative	19 (15.8%)	60 (50%)	
Serrated Turbinate			p<0.05*
Positive	19 (15.8%)	5 (4.2%)	
Negative	15 (12.5%)	81 (67.5%)	
Bone Erosion			p>0.05
Positive	2 (1.7%)	1 (0.8%)	
Negative	32 (26.5%)	85 (70.8%)	
Hyperdensity			p>0.05
Positive	5 (4.2%)	6 (5%)	
Negative	29 (24.2%)	80 (66.2%)	

Chi-square test.

Table 2. Comparison of serrated concha morphology on CT between polyp formation, bone erosion and hyperdensity.

	Serrated		p
	Positive	Negative	
Polyp			p=0.021*
Positive	13 (10.8%)	28 (23.3%)	
Negative	11 (9.2%)	68 (56.7%)	
Erosion			p=0.1
Positive	2 (1.7%)	1 (0.8%)	
Negative	22 (18.3%)	95 (79.2%)	
Hyperdensity			p=0.6
Positive	2 (1.7%)	9 (7.5%)	
Negative	22 (18.3)	87 (72.5%)	

Chi-square test.

DISCUSSION

AFS is a type of chronic sinusitis associated with the presence of eosinophilic mucin with fungal hyphae in the sinuses and type I Ig E-mediated hypersensitivity to fungi.[16] Pathological findings in AFS may vary due to eosinophil predominant inflammation, Charcot-Leyden crystals, and inflammatory response to various fungal species.[17] The most common fungal species seen in AFS Aspergillus, Alternaria, Bipolaris and Curvularia (18). The rate of AFS in chronic sinusitis was found to be between 4-24% in various studies, and it is said to be even higher in temperate climates.[19,20]

Although AFS is a relatively newly defined disease, there are many studies in the literature, especially on radiological imaging features. Studies provide very useful information about CT and MRI images in AFS.[4,21] Bent and Kuhn criteria consisting of major and minor criteria are used in diagnosis of AFS. The main criteria are history, history of type I hypersensitivity by skin test or in vitro test, nasal polyposis, characteristic CT scan findings (areas of serpiginous hyperattenuation), presence of eosinophilic mucin without evidence of invasion, and presence of fungal cell in the operation material removed during surgery. Patients must meet all the major criteria for diagnosis except the positive fungal cell culture. Minor criteria include unilateral predominance of disease, history of asthma, Charcot-Leyden crystals, and peripheral eosinophilia. Minor criteria support the diagnosis but are not diagnostic.[5] Although CT is also useful in diagnosis of sinusitis and in demonstrating bone erosion, it was not found to be sufficient to determine the etiology of sinusitis.[21] Although ''starry-sky'' ''ground-glass'' or ''serpiginous'' patterns, but commonly referred to as the ''double-density'' images in CT scan are associated with AFS, it has been reported that this appearance is also seen in other fungal pathologies.[22] Three findings in particular (nasal polyps, hyperattenuation foci in the sinuses on CT scan, and high Aspergillus-directed IgE antibody titers) were identified as reliable and specific indicators for the preoperative diagnosis of AFS in subsequent studies.[23] All AFS patients had polyposis and hyperattenuation on CT reported by Bent and Kuhn.[5] It has been reported that nasal polyps are not associated with allergies, but may be associated with AFS.[2] The most likely cause of hyperdensity in CT is the presence of heavy metal (eg iron and manganese) deposits and calcium salt precipitation in the allergic fungal mucin.[12] The presence of hyperattenuation and polyp formation was not statistically significant in our study. Although the CT finding was named hyperdensity in the literature review, no specific Hounsfield Unit (HU) value was given in any study. We can not use the term sinus opacification which we used to evaluate sinus radiographs because the inflammatory sinus contents are in soft tissue density. We think that this proportional difference may be due to the difference in the use of terminology, it may be useful to give specific HU values in subsequent studies to overcome this issue.

Although AFS is accepted among non-invasive sinusitis, bone erosion and expansion are still included in radiological imaging findings.[24] The incidence of bone erosion is between 20-80% in various studies.[12,25,26] It is speculated that as the amount of mucin in the sinus increases, decalcification may occur with mucocele formation and bone remodelling in the involved paranasal sinus.[24] Presence of mucin and local inflammatory changes can cause enlargement of the sinuses thereby causing remodelling.[27] Local bone resorption is much more common in AFS than in other forms of chronic rhinosinusitis, and bone erosion does not always denote invasive disease. It may be caused by pressure effects of mucin.[27] Therefore, in this context it is incorrect to accept bone erosion as a indicator of AFS. In fact, as Bent and Kuhn said it is unfortunately not possible to disagree with the authors who stated that there are many misunderstandings about AFS due to the novelty of disease, and misdiagnosis of AFS is prevalent despite the intervening 27 years.[5] The incidence of bone erosion was also not statistically significant in our study. This may be due to the fact that we did not consider remodelling as erosion in our study.

Serrated turbinate appearance, one of the incidental findings in paranasal sinus tomographies shared by Zain-Alabdeen and El Khateeb in their article attracted our attention.[28] During discussions about serrated turbinate with clinicans, serrated turbinate appearance might be interpreted as the cobblestone appearance of the mucosa. However, we noticed that this morphology was not mentioned as a radiological finding in the literature. We included serrated turbinate morphology in our study, and surprisingly, we found the statistical association of this morphology with AFS ($p<0.05$). However, since our study only focus on AFS, larger series of studies are needed about the relation of serrated turbinate morphology with other allergic rhinitis and fungal sinusitis subtypes.

Our current opinion, like Pillai et al, is that CT imaging alone will not be sufficient to accurately diagnose one subtype of fungal sinusitis, perhaps only helping us to differentiate it from non-fungal sinusitis.[15] Combined CT and MRI findings have also been reported to provide a radiographic appearance that is highly specific for AFS.[14]

Our study has some limitations. MRI images were not included in our study, as it is a retrospective study and MRI images of the patients were not available. In addition, the low number of patients diagnosed with AFS are another drawback of our study. This study is the first study analyzing paranasal serrated turbinate morphology with AFS and more research is needed for further evaluation with larger patient groups.

CONCLUSION

Although AFS is a clinical entity that has been recently described, the presence of fungal infection in immunocompetent individuals should be suspected in order to diagnose AFS, and it should be evaluated radiologically, immunologically, microbiologically and histopathologically with ENT examination. In our study, no diagnostic criteria was found in cases treated as AFS, that is consistent with the literature. We argue that we need large and objective studies that will fully demonstrate the value of radiological findings including serrated turbinate for the diagnosis of AFS.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was approved by the Ethical Committee of Noninvasive Clinical Research of the Mardin Artuklu University (2021/2).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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