

Original Article

MAGNETIC RESONANCE IMAGING AS DIAGNOSTIC TOOL FOR ACUTE INVASIVE FUNGAL SINUSITIS

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Objective: To measure the diagnostic accuracy of magnetic resonance imaging for diagnosis of acute invasive fungal sinusitis taking histopathology as gold standard.

Methods: After obtaining permission from ethical committee of hospital, 150 patients meeting the study criteria were recruited in the study which was conducted in Department of Diagnostic Radiology, Sir Ganga Ram Hospital, Lahore. Informed consent was obtained. Demographic information (name, age, gender, contact) was also obtained. Then patients underwent MRI by using 1.5T magnets by a single senior radiologist. The imaging was performed with specified sinus views and sequences including T1-weighted images in axial plane, T2-weighted images with fat saturation in axial and coronal planes, and also contrast enhanced T1-weighted images with fat saturation in axial and coronal planes. Then patients underwent biopsy by a single surgical team under general anesthesia. Histopathology was then performed on the biopsy samples obtained during sinus surgery. Reports of MRI and histopathology were compared. Out of 150 patients who were clinically suspected of having fungal sinusitis 87 were negative for fungal disease on histopathology.

Results: Sensitivity and Specificity of MRI for diagnosis of fungal sinusitis was 92.06% and 93.1% respectively. However positive predictive and negative predictive value for MRI for diagnosing fungal sinusitis was 90.63% and 94.19% respectively. Overall diagnostic accuracy of MRI was 92.67% respectively.

Conclusions: Results of this study showed high sensitivity and specificity of MRI in making the diagnosis of fungal sinusitis. Considering the results of this study MRI can be used effectively for diagnosing of fungal sinusitis.

Keywords: fungal sinusitis, magnetic resonance imaging, histopathology

Introduction

Fungal sinusitis is increasing worldwide in the past two decades. It is divided into two types including invasive and noninvasive. Noninvasive types contain allergic fungal sinusitis (AFS) and fungus ball. AFS is a hypersensitivity reaction to fungal allergens in the mucosa of the sinonasal tract in atopic individuals. The fungus ball is a different type of noninvasive fungal rhinosinusitis which is delineated as an accumulation of debris and fungal elements inside a paranasal sinus.¹ Sandeep Suresh et al found the prevalence of fungal rhinosinusitis to be 30% with mucor being the most commonly isolated species.² According to another study conducted in India the prevalence of fungal rhinosinusitis came out to be 44%.³ In Pakistan, fungal sinusitis is present in 13% patients only.⁴ It is observed that fungal infections involving the paranasal sinuses are not very common and usually occur in individuals with a compromised immune system. However according to one study, the incidence of fungal sinusitis has been increased in the immunocompetent individuals as well.⁵ The

commonest species involved are *Aspergillus* and *Mucor species*. Non-invasive as well as invasive forms of infections can be caused by *Aspergillus*. Mostly fungal infections of the sinuses tend to be noninvasive with the exception of infections occurring in immunocompromised population. But many studies have now shown invasive fungal infections in immunocompetent population as well. While non-invasive infections present with generalized symptoms of sinusitis on the other hand invasive variety tends to cause destruction of surrounding structures including the orbital walls and intracranial extension. Invasive infections produce greasy and dark coloured substance within the paranasal sinuses. Routinely the cultures obtained from the affected sinuses uncommonly show the growth of fungus. The fungal infection however is suspected when the images obtained from the computed tomography (CT) scan are reviewed and when the material removed from the affected sinus is examined.⁵ Fungal sinusitis requires early diagnosis and treatment for optimum outcome. Fungal sinusitis is a distinct clinical entity with a highly specific

Radiographic appearance based on computed tomography and magnetic resonance imaging (MRI).⁶ The diagnosis of fungal sinusitis is based upon radiological, histopathological and laboratory investigations. Fungal sinusitis is defined radiologically on magnetic resonance imaging as the detection of mucosal thickening ranging from mild to complete filling of the sinus with the presence of fungal mass which is of intermediate to low signal on T1 weighted images and T2 weighted images associated with fluid or hemorrhagic material in other paranasal sinuses as well, and enhancement of sinus mucosa with non enhancing center. No mucosal enhancement is seen in case of necrosis. Clinically suspected fungal sinusitis is defined by the presence of any one or more of these: i.e. recurring sinonasal polyposis (polypoidal masses seen to be stuffing the nasal cavity on clinical examination), non resolving chronic sinusitis, immobility of the eyes, and altered status of consciousness.

Magnetic resonance imaging (MRI) findings of fungal sinusitis:

Contrast enhanced MRI is of value in evaluation of patients with allergic fungal sinusitis and in those who are suspected to have invasive fungal sinusitis. It is also valuable in assessing spread of disease to the central nervous system in case of invasive fungal sinusitis. Low signal intensity on MRI would be more in favour of fungal disease rather than a solid mass in case of allergic fungal sinusitis.⁹

Histopathology findings of fungal sinusitis:

Allergic fungal sinusitis shows allergic mucin containing non damaged as well as deteriorated eosinophils, cellular remains, Charcot-Leyden crystals, and little amount of hyphal forms. The fungi do not cause invasion of mucus membrane in allergic fungal disease and sinus mycetoma does not contain allergic mucin. The mucosa of sinus shows infiltration by eosinophils, plasma cells, and lymphocytes and the sinus shows substance that is dense and contains hyphae which are separate from the mucosa being present adjacent to it. In acute invasive fungal sinusitis, histopathology shows invasion of the mucosa by fungal hyphae as well as invasion of submucosa and blood vessels; tissue infarction and hemorrhage; vascular inflammation and thrombosis. Carotid arteries and cavernous sinuses may also be involved. In chronic invasive fungal sinusitis there is necrosis of the mucosa, submucosa, and blood vessels, with mild inflammation. In granulomatous invasive fungal sinusitis there is granuloma formation with

multinucleated giant cells associated with erosion of sinus walls and pressure necrosis.⁹

Laboratory findings of fungal sinusitis:

In patients with allergic fungal sinusitis, raised levels of total fungus-specific IgE are frequently observed however it is uncommon in cases of sinus mycetoma.¹⁰

Rhinologists have not yet reached to any consensus upon the criteria for diagnosis of allergic fungal sinusitis.¹¹ Loury and Schaefer in 1993, put forward a diagnostic criteria, which included elevated serum eosinophils, raised total immunoglobulin E level, immunoglobulin G serum antibodies to fungal antigen or immediate skin reactivity, edematous nasal mucosa or sinonasal polyposis, characteristic MRI or CT findings and presence of allergic mucin with fungal hyphae not causing invasion histopathologically. Cody et al in 1994, made the diagnostic criteria more simple by including only characteristic allergic mucin and either cultures positive for fungus or non-invasive fungal hyphae in the obtained mucin. In the same year, Bent and Kuhn put forward a now widely accepted criteria for diagnosis. Five common characteristics were seen upon the analysis of fifteen cases. These include sinonasal polyposis, mucin containing eosinophils with no sinus tissue invasion by the fungus, Gell and Coombs type I (IgE-mediated) hypersensitivity to fungi, characteristic CT and MRI findings, and positive fungal stain of surgically removed sinus material. A similar five parameter criteria was described by DeShazo in 1997 consisting of radiological evidence of sinusitis, positive fungal stain or culture from the sinus material obtained during surgery, presence of allergic mucin (found either grossly or on histopathologic examination), no invasion by the fungus, lack of contributory factors (eg, immunodeficiencies and diabetes mellitus). Groppo et al. conducted a study on 23 patients and reported that sensitivity and specificity of MRI for diagnosis of fungal sinusitis were 86% and 75% respectively, taking histopathology as gold standard.¹² Rationale of our study was to assess the diagnostic accuracy of magnetic resonance imaging for diagnosis of fungal sinusitis taking histopathology as gold standard. Now-a-days MRI is considered to be gold standard for diagnosis / differentiation of different tumors having > 95% accuracy. Literature has shown that for confirmation of fungal sinusitis, MRI is a reliable tool but still biopsy is in practice. This may be due to lack of local evidences which would help to implement the use of MRI. The study which has been mentioned above was conducted with

very low sample size (23 patients). We conducted this study with large sample size (150 patients) to get more reliable results, so that we can implement the use of MRI for diagnosis of fungal sinusitis in future.

Methods

A sample size of 150 cases was selected by non-probability, consecutive sampling technique. Patients of age 15-50 years of either gender, presenting with clinically suspected fungal sinusitis (as per operational definition), with size of mass >10mm planned to undergo biopsy for histopathology. Patients with septal defect (on x-ray) or with history of previous surgery for fungal sinusitis (medical record) were excluded. Patients with hypertension (BP \geq 140/90 mmHg), asthma or COPD (medical record and clinical examination) were also not included.

True positive: When MRI and histopathology, both are positive for fungal sinusitis

True negative: When MRI and histopathology, both are negative for fungal sinusitis

False positive: When MRI is positive but histopathology is negative for fungal sinusitis

False negative: When MRI is negative but histopathology is positive for fungal sinusitis

After obtaining permission from ethical committee of hospital, 150 patients meeting the criteria of selection were included in the study referred to Department of Diagnostic Radiology, Sir Ganga Ram Hospital, Lahore. Informed consent was obtained. Demographic information (name, age, gender, contact) was also obtained. Then patients underwent MRI by using 1.5T magnets by a single senior radiologist. The imaging was performed with specified views and sequences for the sinuses including T1-weighted images in axial plane, T2-weighted images with fat saturation sequences in coronal and axial planes, and also contrast enhanced T1-weighted images with fat saturation sequences in coronal and axial planes. Then patients underwent biopsy by a single surgical team under general anesthesia. Histopathology was then performed on the biopsy samples obtained during sinus surgery. Reports of MRI and histopathology were compared. Out of 150 patients who were clinically suspected of having fungal sinusitis 87 were negative for fungal disease on histopathology. The obtained information was collected in proforma. Statistical analysis of the data was done with SPSS Version 20.0. Fungal sinusitis (on MRI and histopathology) was presented in terms of

frequency and percentage. A 2x2 table was formulated for the calculation of specificity, sensitivity, positive predictive value (PPV), negative predictive value (NPV) and diagnostic accuracy of MRI taking histopathology as gold standard. p-value \leq 0.05 was considered as statistically significant.

Results

Sensitivity and specificity of MRI for diagnosis of fungal sinusitis was 92.06% and 93.1% respectively. The positive predictive value and negative predictive value of MRI was 90.63% and 94.19% respectively. Overall diagnostic accuracy of MRI for diagnosis of fungal sinusitis was 92.67%. **(Table-1)**

Table-1: The baseline characteristics of mothers..

		Histopathology		Total
		Positive	Negative	
MRI	Positive	TP 58 (92.1%)	FP 6 (6.9%)	64 (42.6%)
	Negative	FN 5 (7.9%)	TN 81 (93.1%)	86 (57.33%)
Total		63 (42%)	87 (58%)	150

Sensitivity = $TP / (TP + FN) = 58 / (58 + 5) = 58 / 63 = 92.06\%$ (82.73 - 96.56).

Specificity = $TN / (TN + FP) = 81 / (81 + 6) = 81 / 87 = 93.1\%$ (85.76 - 96.8).

Positive predictive value = $TP / (TP + FP) = 58 / (58 + 6) = 58 / 64 = 90.63\%$ (81.02 - 95.63).

Negative predictive value = $TN / (TN + FN) = 81 / (81 + 5) = 81 / 86 = 94.19\%$ (87.1 - 97.49).

Diagnostic accuracy = $(TP + TN) / (TP + TN + FP + FN) = 139 / 150 = 92.67\%$ (87.35 - 95.86)

Discussion

Both the radiology and otolaryngology literature has described the radiologic features of invasive fungal sinusitis. Previously researchers focused on destruction of bone, which is depicted with CT. Destruction of bone, however, is a relatively late occurrence in the course fungal sinus disease. The high mortality of 50-80% which occurred previously may be explained to some extent by delay in the diagnosis. But now clinicians have focused more on detecting early minute features of invasive fungal infection and especially the abnormal findings in soft tissues outside the boundaries of the sinuses. There may be underestimation of the extent of invasive fungal disease when diagnosed using CT scanning alone. On this basis some researchers suggest MRI scanning early in the course of disease in patients with suspected acute fulminant invasive fungal sinusitis.¹³ A definite advantage of MRI over CT is that MRI has clearer soft-tissue contrast resolution, which defines the ability to detect even minute differences in tissues

which otherwise appear similar. Unfortunately, the ideal imaging tool for diagnosing acute fulminant invasive fungal sinusitis in immune-compromised patients has yet to be established.^{13,14,15} Invasive fungal sinusitis is a rather common disease and it has a high rate of mortality if diagnosis is delayed however it is often misdiagnosed. An early diagnosis is required for successful treatment, which can be achieved with radiologic imaging including CT and MRI each having its own advantages.¹⁶ Whereas CT is better to assess for bone changes, MR imaging is superior in evaluating intracranial and intraorbital extension of the disease.¹⁶ In our study 64 patients showed typical features of fungal sinusitis on MRI i.e. low signal intensity mucosal thickening and fungal mass on T1 and T2 weighted images and signs of intraorbital and intracranial extension. On histopathology 63 patients were positive for fungal sinusitis showing features of mucosal infiltration by eosinophils, plasma cells, lymphocytes and fungal hyphae. Findings of this study regarding sensitivity and specificity for MRI for diagnosis of fungal sinusitis were in line with the study of Groppo et al.¹² However the obtained sensitivity and specificity of MRI in this study was a bit higher as that of reported by Groppo et al.¹² Another study conducted by Kadri et al showed high sensitivity and specificity of MRI in diagnosing fungal sinusitis with intracranial extension however their sample size was of fifty patients with 30 females and 20 males, having mean age of 40 years.¹⁷ It is recommended that incidentally made findings on MRI should be reported normal as these findings do not suggest that children whose MRI is performed for causes unrelated to sinus disease require sinus treatment.¹⁸ MRI has an additional advantage that it does not involve use of ionizing-radiation, which is critical for patients who are undergoing frequent studies over their lifetime given the multiple co-morbidities and especially of

importance for children. The use of computerized tomography is in planning surgery and image-guided navigation during surgery.¹⁹ MRI sharply differentiates mass from adjacent inflammatory tissue and sinus secretions. It is to note that MRI has better soft tissue resolution, but it is inferior when it comes to evaluation of bones. On MRI the appearance of edematous membrane and mucus is distinct hyperintensity on T2-weighted images. The nasal polyps on the other hand return intermediate signals. A disadvantage of MRI is its inability to highlight bony anatomy for which CT scan can be used. Vascular and CNS complications (e.g. vascular invasion with infarction, pseudoaneurysm formation, intracranial invasion with enhancement of the meninges and cerebral grey and white matter involvement) are better assessed on MRI with contrast.²⁰ There is devascularization of mucosa in acute invasive fungal sinusitis which leads to no enhancement of mucosa after IV contrast and this is one of the earliest MRI findings of AIFRS. Moreover, invasion of the fungal disease into the orbit and post-maxillary fat pad can be clearly depicted. Additionally MRI is helpful in depicting disease extension in the orbit (extraocular muscles, extraconal post-septal fat, and intraconal fat) as well as intracranial extension (cavernous sinus, involvement of pachymeninges, leptomeninges and brain).²¹

Conclusion

It is concluded that magnetic resonance imaging can be used with significant diagnostic accuracy for the diagnosis of fungal sinusitis, taking histopathology as gold standard. Moreover magnetic resonance imaging is investigation of choice because of its lack of radiation hazards.

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