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DIAGNOSTIC VALIDATION OF COMPUTED TOMOGRAPHY IN SUSPECTED FUNGAL RHINOSINUSITIS- A TERTIARY CARE CENTER STUDY

Radiodiagnosis

Ajitha J S Assistant Professor, Department of Radiodiagnosis, Government Medical College, Thiruvananthapuram, Kerala, India.

Unnikrishnan G Associate Professor, Department Of General Surgery, Government Medical College, Thiruvananthapuram, Kerala, India. - Corresponding Author

Preetha S Associate Professor, Department Of General Surgery, Government Medical College, Thiruvananthapuram, Kerala, India.

ABSTRACT

Background: Most fungal sinus infections are benign or noninvasive, except when they occur in individuals who are immunocompromised. Fungal infections of the sinuses have recently been blamed for causing most cases of chronic rhinosinusitis. Complicated sinusitis refers to symptoms suggesting spread of disease into adjacent structures, including orbital or intracranial complications.

Materials and methods: We conducted this study Department of Radiodiagnosis , Govt. Medical College Hospital, Thiruvananthapuram during 2014-2015

Inclusion criteria: All those patients with clinical features of rhinosinusitis sent to the department of radiodiagnosis for CT PNS. **Exclusion criteria:** Post surgical cases, Patients not giving consent to prticipate in the study, Patients with sinusitis not undergone histopathological evaluation for sinusitis, Patients in whom CT is contraindicated.

Aim: To compare CT findings of fungal rhinosinusitis with histopathology.

Result : We analyzed the data of 62 patients (6.7%) with mean age of 40.6 years (ranging from 8 to 81 years, median of 45.4 years), 25 male and 37 female patients. Nasal endoscopic findings were: nasal secretion in 57 patients (91.9%), divided into 29 (46.7%) yellowish color, 23 (25%) greenish, 4 were brown and 1 was black; middle meatus obstruction in 47 (75.8), polyposis in 25 (40.3%), bilateral in 10 (16.1%) and unilateral in 15 (24.1%), inferior conchae hypertrophy in 17 (27.4%) and adenoid hypertrophy in 3 (4.8%).

Conclusion: Fungal rhinosinusitis is an important clinical problem with diverse manifestations. It should be considered in all immunocompromised patients and in all patients with chronic sinusitis

KEYWORDS:

Introduction

Fungal Rhinosinusitis is an important clinical problem with diverse manifestations. It is a serious condition, as certain forms of fungal sinusitis are associated with a high rate of mortality.It should be considered in all immunocompromised patients and in all patients with chronic sinusitis. Its successful treatment requires a prompt diagnosis and frequently relies on radiologic imaging, specifically computed tomography (CT) imaging.

Background

Fungal infections of the sinuses have recently been blamed for causing most cases of chronic rhinosinusitis. Most fungal sinus infections are benign or noninvasive, except when they occur in individuals who are immunocompromised. Distinguishing invasive disease from noninvasive disease is important because the treatment and prognosis are different for each.

Of the more than 400,000 known fungal species, approximately 400 are human pathogens, only 50 of which cause systemic or central nervous system infection. Although many people are colonized by fungi, an intact immune system prevents subsequent infection.(1) Aspergillus, Bipolaris, and Rhizopus are the more commonly implicated organisms causing fungal sinusitis.

Rhinosinusitis is inflammation of the nasal cavity and adjacent paranasal sinuses.

Acute sinusitis refers to symptom duration <4 weeks, subacute 4-12 weeks, and chronic >12 weeks.

Complicated sinusitis refers to symptoms suggesting spread of disease into adjacent structures, including orbital or intracranial compli cations. (2)

Broadly classified into Invasive and noninvasive.

Invasive-The more serious infection commonly occurs in patients with diabetes or in individuals who are immunocompromised and is characterized by its invasiveness, tissue destruction, and rapid onset.

Early detection and treatment are vital for these infections because of the high mortality rate.

Noninvasive infections are chronic and are usually treated for extended periods as chronic sinusitis before the condition is recognized.

Rationale of the study

Clinical evaluation of patients with sinusitis cannot accurately determine the etiology of bacterial versus fungal. CT is non invasive and is less costly compared to MRI.

Research question

What is the validity of Computed Tomography in the diagnosis of Fungal rhinosinusitis among suspected subjects of fungal sinusitis?

Aim

To compare CT findings of fungal rhinosinusitis with histopathology findings

Objectives

1.to identify the imaging features that can differentiate between fungal and non fungal rhinosinusitis
2.to classify fungal rhinosinusitis
3.to assess the extension of the disease- intracranial extension, extension into the soft tissues of face and orbit.
4.to assess imaging features of recurrence.
5.to identify anatomical variants which predispose to the incidence of fungal rhinosinusitis.

Findings of Fungal Sinusitis on CT scan.

Approximately half the cases (51% as studied by Mukherji et al, 1998) occur unilaterally, and many others show asymmetric involvement (78% as studied by Mukherji et al, 1998) by the disease on the two sides. There is expansion of the involved sinuses with corresponding reduction in the space of the surrounding compartments such as the orbit, which may be accompanied by remodelling or attenuation, of the bony margins within the periphery of the. Several studies have quoted the incidence of bony erosion with spread of pathology into the adjacent anatomic areas as 20%.[3,4]

The majority of sinuses show near complete opacification on unenhanced CT scan, the sinuses are typically opacified by centrally (often serpiginous) hyperdense material with a peripheral rim of hypodense mucosa. It is also called double density sign (DDS).

Homogeneous or / heterogeneous opacification of sinus, high density areas, mucosal thickening, polyps formation, osseous erosion / destruction, calcification, retroantral, intraorbital, intracranial, and overlying superficial soft tissue extension.

Methodology

Study design

Observational study for measuring diagnostic accuracy.

Study settings

Department of Radiodiagnosis , Govt. Medical College Hospital, Thiruvananthapuram

Study population

Includes the patients referred for CT PNS to the Department of Radiodiagnosis, Govt.Medical College, Trivandrum, with clinical features of rhinosinusitis.

Study period

3 years

Selection criteria

Inclusion criteria

All those patients with clinical features of rhinosinusitis sent to the department of radiodiagnosis for CT PNS.

Exclusion criteria

1.Post surgical cases.
2.Patients not giving consent to prticipate in the study
3.Patients with sinusitis not undergone histopathological evaluation for sinusitis
3.Patients in whom CT is contraindicated ,like patients with
H/o allergy to iodinated i/v contrast media.
H/o impaired renal function.
Pregnancy.

Gold standard

The final pathological diagnosis in all patients is to be confirmed by histopathology.

Technique

Name,age and details of the patient will be recorded on a proforma. Patients are recruited after CT study. Informed consent will be taken for collecting the details of image and for participating in the study.

CT protocol in our department

CT analysis will be done using multi slice CT Machine. After obtaining the scout projection, the area of scanning will be defined to include the region from roof of frontal sinus up to the hard palate.

Axial sections will be performed with the patient in supine position and the plane of data acquisition parallel to hard palate.The sections will be taken with slice thickness of 3mm and reconstructions will be carried out at 0.6 mm in coronal and sagittal planes. Scanning parameters include 150-180 mAS, 120 kV and tube rotation time of 0.6 seconds. Extended cephalic/caudal sections will be carried out to see the extension of the disease process wherever necessary.

Contrast enhanced CT will be performed wherever indicated after giving a rapid bolus of injection of 50 ml of non-ionic iodinated contrast material after evaluating RFT. The images thus generated will be reconstructed at appropriate window widths and window levels to depict the bony abnormalities as well as soft tissue pathologies. In case of pediatric patients, who may need sedation, due care in consultation with the pediatrics department will be taken.

Time taken for the study is approximately 5-10 minutes.
Permission for the study was granted by the ethics committee of the institute.

A detailed history will be elicited to determine the clinical correlation accurately.

All the patients will be followed-up to correlate with the histopathological diagnosis.

Sample size

The sensitivity and specificity values of CT detection of fungal sinusitis have been reported in scientific studies are 69% and 83%, respectively.(ISSN 1815-2287)

Total number of patients to be studied is calculated as follows.
Sample size of no. of positive cases is calculated using the formula,

$$N = \frac{(Z\alpha)^2 PQ}{d^2}$$

where P is sensitivity of the new test and d is the precision.
The value obtained for sample size with sensitivity as proportion, P as 69, Q as 31 and d as 6.9 (10% of P), sample size of no.of positive cases is

$$N = \frac{(1.96)^2 \times 69 \times (100-69)}{(6.9)^2}$$

$$= \frac{3.84 \times 69 \times 31}{47.6} = 173$$

With prevalence of 20% (in our institution) , Total sample size is

$$\frac{(173 \times 100)}{20} = 865$$

Study Variables

Age, gender, education, occupation, marital status, place of residence, socioeconomic status, hyperlipidemia, hypertension, diabetes, immunity status, h/o intake of immunocompomising drugs etc.

CT images are studied under the following steps

Unilateral/bilateral
Single/multiple sinuses
Calcification- present/absent
Density of the intrasinus content
Degree of enhancement and enhancement pattern-nil/mild/moderate/intense

Expansion of sinuses-present/absent
Thinning of sinus wall-present/absent
Erosion of bony walls-present/absent
Bone sclerosis- present/absent
Bone remodelling- preseent/absent
Extent of disease into adjacent soft tissue-present/absent
Extension into orbits-present/absent
Extension into cranium-present/absent
2, Nasal endoscopy/biopsy
3.Biopsy report

Operational definitions

Sensitivity is defined as the proportion of diseased patients who are reported as test positive. It denotes the ability of a test to identify correctly all those who have the disease ("true positives"). Thus sensitivity is true positive rate, expressed as a percentage.

Sensitivity= true positive / (true positive + false negative).

Specificity is defined as the proportion of disease-free patients who are reported as negative by the new test. It denotes the ability of a test to identify correctly all those who do not have the disease ("true negatives"). Thus specificity is true negative rate, expressed as a percentage.

Specificity= true negative/(true negative +false positive)

Positive Predictive Value is defined as the proportion of patients reported as test positive who have the disease. It indicates the probability that a patient with a positive result has, in fact the disease in question, expressed as a percentage.

Positive Predictive Value = [TP/(TP+FP)] x 100

Negative Predictive Value is defined as the proportion of patients reported negative who do not have the disease. It indicates the probability that a patient with a negative result does not have the disease in question, expressed as a percentage.

Negative Predictive Value = [TN/ (FN+TN)] x 100

In a study population already screened by clinical examination,

Likelihood Ratios (LR+) and (LR-) are a more important parameter than positive predictive value and negative predictive value as it is less dependent on prevalence.

LR+ is the ratio of probability of positive test in people with disease and probability of positive test without disease.
LR+ value of more than 10 means that the test is extremely good and useful
A value of between 5 and 10 means the test is moderately good
A value of below 3 means that the test is not very useful.
Likelihood Ratio (LR+) = sensitivity/[1-specificity]
When specificity is equal to one, 1-specificity is equal to 0; as it is impossible to divide a constant with 0, the LR+ ratio cannot be calculated and the cell is left blank internationally.
Likelihood ratio negative (LR-) is the ratio of probability of negative test in people with disease and probability of negative test without disease.

Likelihood Ratio (LR-) = [1-sensitivity]/specificity
Accuracy is the proportion of total true positives and true negatives of total number of patients, calculated as a percentage.

Accuracy = (total true positives + true Negatives) / total sample size
Receiver Operator Characteristic curve will be plotted with sensitivity (in Y axis) against 1-specificity (in X axis) and suitable cut offs can be identified with suitable sensitivity and (1-specificity)

Data collection process
Data collection will start after obtaining clearance from Human Ethics Committee. Name, age and details of the patient will be recorded on a proforma.

Patients will be informed that data collected would be used in a study and that issues related to confidentiality and anonymity would be taken due care of. Data regarding the outcome of /biopsy/follow up of these patients is collected from the Pathology/Microbiology department and from the referred departments of ENT/Neurosurgery, Govt. Medical college, Trivandrum.

Data Analysis
The data will be entered and statistical analysis will be carried out Mean and standard deviation will be calculated for age. Frequencies and percentages will be computed for gender, presence of fungus ball and biopsy results.

The diagnostic accuracy of computed tomography in fungal sinusitis will be assessed in relations of sensitivity, specificity, positive predictive value , negative predictive value and likelihood ratio by keeping histopathology as gold standard / reference value.

A 2x2 table will be generated to calculate these values.

Test results	Reference Standard Diagnosis		Total
	Diseased	Not diseased	
Positive	A (True positive)	B (False positive)	A + B
Negative	C (False negative)	D (True negative)	C + D
Total	A + C	B + D	A + B + C + D

RESULTS
Out of a total of 865sinonasal surgical procedures, we selected the cases in which we detected the presence of fungi identified by laboratory exams, which are the object of this study.

We analyzed the data of 62 patients (6.7%) with mean age of 40.6 years (ranging from 8 to 81 years, median of 45.4 years), 25 male and 37 female patients.

Signs and symptoms	n	%
Nasal obstruction	57	92
Nasal secretion	55	89
Post-nasal dripping	51	82
Cough	43	69
Allergic rhinitis	30	48
Anosmia/halitosis	21	34
Asthma	21	34
Sorethroat	20	32
Intolerance to aspirin	14	22
Fatigue	14	22
Facial pain	9	15

The most frequent comorbidities were rhinitis in 33 patients (53.2%), bronchial asthma in 21 patients (33.8%), hypertension in 16 (25.8%), and aspirin intolerance in 14 (22.5%). There were fewer cases of repetitive bronchopneumonia (7 patients), bronchiectasia (6 patients), hepatitis (4 cases), diabetes mellitus and leukemia (6 patients) and isolated cases of tuberculosis and hypophysis tumor. As to previous use of medication, 59 patients (95.1%) had used broad-spectrum antibiotic in the month before the surgery, 37 (59.6%) had used topical nasal corticoids, 25 (40.3%) had used oral corticoids, and 6 (9.7%) had received some type of immunosuppressant drugs that were not steroids.

Only 11 patients (18.6%) had been previously submitted to sinonasal surgery:
Nasal endoscopic findings were: nasal secretion in 57 patients (91.9%), divided into 29 (46.7%) yellowish color, 23 (25%) greenish, 4 were brown and 1 was black; middle meatus obstruction in 47 (75.8), polyposis in 25 (40.3%), bilateral in 10 (16.1%) and unilateral in 15 (24.1%), inferior conchae hypertrophy in 17 (27.4%) and adenoid hypertrophy in 3 (4.8%).

CT scan findings	n	%
Opacification	62	100
Middle meatus obstruction	49	79
Bone sclerosis/thickening	34	54.8
Calcifications	28	47.4
Metallic density images	18	29
Bone erosions	16	25.4
Sinus expansion	11	17.7

Mycological culture exam was obtained during surgery and showed Aspergillus as the most frequent, followed by Candida and Penicillium Bacteriological examination indicated associated bacterial infection in 47 patients with growth of S. aureus in 15 cases (31.9%), P. aeruginosa in 10 (21.2%) and Haemophillus sp. in 4 (8.5%). In 10 patients (16.9%) there was no bacterial growth and in 2 the exam was not performed.

Definite histopathological exam showed nonspecific chronic inflammation in 25 cases (40.3%), allergic chronic inflammation in 21 cases (33.8%), suppurative chronic inflammation in 12 (19.3%), and fungal invasion in 4 (6.4%). As to FRS classification, we observed fungal ball in 33 patients (53.2%), AFRS in 24 (38.7%) and indolent FRS in 3 (4.8%). In 2 patients, fungi were considered saprophyte. There was no case of invasive fungal rhinosinusitis

Types of fungal rhinosinusitis	n	%
Fungal ball	23	53.2
Allergic fungal rhinosinusitis	24	38.7
Indolent fungal rhinosinusitis	3	4.8
Saprophyte infection	2	3.2
Invasive fungal rhinosinusitis	0	-

Among the cases classified as fungal ball, nasal obstruction was present in 30 (90.9%), posterior nasal secretion in 29 (87.8%), and topical steroids in only 9 (27.3%). Cough was the complaint in 19 cases (57.5%), intolerance to aspirin was detected in only 1 case (3.5%) and 6 (18.2%) had repetitive pneumonia. Polyps were seen in only 2 cases (7.1%) and middle meatus obstruction in 7 (21.2%).

The patients with AFRS presented as a whole nasal obstruction, posterior nasal secretion and previous use of topical steroids and systemic antibiotics. Cough was the complaint in 14 (58.3%) cases, 12 (50%) referred intolerance to aspirin, and only 5 (20.1%) had previous pneumonia. Surgical findings evidenced multiple polyps in 22 patients (19.6%), medium meatus obstruction in 21 (87.5%) and microcalcifications in 20 (81.8%) of the cases. The most frequent type of fungus was Aspergillus (8 cases).

Analysing the radiographical studies with CT scan , the finding of obstruction of the middle meatus did not show statistically significant difference . The other findings, such as presence of bone erosion, were found in 12 patients (50%) with AFRS and in 4 (12.1%) with fungal ball ($p<0.001$), microcalcification in 19 (79.1%) and 10 (30.3%) ($p<0.001$), and mucosa thickness in 8 (33.3%) and 2 (6.1%) patients ($p = 0.02$), respectively, evidencing a statistically significant difference between the groups.

As to type of fungus, we found there were no statistically significant differences in cultures.

Postoperative follow-up was on average 19.4 months, with standard deviation of 6.3 months.

CONCLUSION

Fungal rhinosinusitis is an important clinical problem with diverse manifestations. It should be considered in all immunocompromised patients and in all patients with chronic sinusitis.

Understanding the different types of fungal sinusitis and knowing their particular radiologic features allows the radiologist to play a crucial role in alerting the clinician to use appropriate diagnostic techniques for confirmation. Prompt diagnosis and initiation of appropriate therapy are essential to avoid a protracted or fatal outcome.

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