e-ISSN: 0975-5160, p-ISSN: 2820-2651

Available online on www.ijtpr.com

International Journal of Toxicological and Pharmacological Research 2023; 13(11); 296-300

Original Research Article

Clinico-Demographic Profile and Complication of Invasive Fungal Sinusitis: An Observational Study

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Received: 18-07-2023 / Revised 17-08-2023 / Accepted 28-09-2023

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Conflict of interest: Nil

Abstract:

Aim: The aim of the present study was to analyze various clinical presentation, underlying immunocompromised condition, complication of invasive fungal sinusitis.

Material & Methods: This prospective analytic study was designed including 100 patients of both types of invasive fungal sinusitis that underwent treatment as inpatient basis for the duration of 12 months, at Department of ENT were included in this study. Patients giving consent are included in this study.

Results: In this study of 100 cases of invasive fungal rhinosinusitis with a male preponderance 68% (n=68). In this study, patients having Diabetes Mellitus were more susceptible to both acute and chronic variant of invasive fungal sinusitis. In Some patients multiple underlying immunocompromised conditions were observed. The patients presented with symptoms of nasal obstruction (n=67) 67%, purulent rhinorrhea (n=45) 45%, headache (n=55) 55%, facial pain (n=21) 21%, and facial swelling (n=21) 21%, epistaxis (n=56) 56%, fever (n=33) 33%, decreased vision (n=9) 9%, diplopia (n=3) 4%. The rhinology findings like mucosal necrosis, black crust or debris, and pus in middle meatus and septum involvement were shown. Orbital cellulitis was the most common complication of invasive fungal rhino sinusitis. 12 patients had intracranial extension. Out of 100 patients 8 patients expired due to complication of fungal invasive fungal rhino sinusitis.

Conclusion: Invasive fungal sinusitis was most commonly observed in 3rdand4thdecade of life with male predominance. Prolonged uncontrolled diabetic mellitus was the most common underlying immunocompromised status. Mucor was the most common isolated fungal species. Preseptal cellulitis was the most common complication.

Keywords: Fungal rhino-sinusitis, Diabetic mellitus, HIV.

Introduction

Being one of the most serious diseases of nasal cavity and paranasal sinuses, Acute invasive fungal sinusitis is defined by fungal hyphae infiltrating the sinus mucosa, submucosa, vasculature or bone, in the setting of 4 weeks or less of sinusitis symptoms. [1] Various fungi have been reported to be pathogenic to Acute invasive fungal sinusitis including Mucor/Rhizopus, Aspergillus, Alternaria, Scedosporium, Candida, and Fusarium, among them, Aspergillus and Mucor species are the most common causative agents. These organisms are ubiquitous and are commonly inhaled into the nasal cavities and lungs by immunocompetent hosts without sequelae. Whereas Acute invasive fungal sinusitis can be a complication in immunocompromised patients with poorly controlled diabetes, malignancies, acute granulocytopenia, severe burns, long-term use of antibiotics, glucocorticoids, chemotherapy, long-term use of immunosuppressants after organ transplantation and AIDS. [2,3] These opportunistic pathogens can rapidly proliferate and invade the sinonasal mucosa.

The hypoxia environment caused by sinus obstruction may further promote the growth of fungi. The lesions involved the perivascular tissue and spread along the blood vessels, causing thrombosis, ischemia and necrosis of tissues resulting in pale, gray and even blackened mucosa. The necrotizing tissue also provides a better environment for the mass reproduction of fungi in a short period of time, thus the invasiveness is further enhanced. During this process, sinus bone destruction may occur, accompanied by intraorbital, pterygopalatine fossa and even intracranial dissemination. [4] Intracranial fungal infection and fungemia are the leading lethal factors. Despite advancements in treatment and care, the reported mortality rate in AIFR patients is

variable but consistently unfavorable, ranging from 33% to 80%. [5]

Fungal rhinosinusitis is more likely suspected when patients present with symptoms similar to chronic sinus infection resistant to conventional antibiotic therapy. [6] It can occur in any age group, but symptoms differ based on the immunity status of the individual. [7] Many severe complications like nasal deformity, visual loss, cavernous sinus thrombosis, cranial invasion, death, etc. can be found in invasive fungal sinusitis. The incidence of morbidity and mortality of invasive fungal rhinosinusitis ranged from 20 to 80%. [8] The spectrum of disease varies from allergic fungal sinusitis to acute fulminant invasive fungal sinusitis. [6]

Common reported clinical symptoms include fever, cough, black eschar, crusting of the nasal mucosa, purulent nasal discharge particularly in middle meatus, nasal obstruction, swelling over nose and face, epistaxis, headache, vision loss and diplopia. A high index of suspicion is needed for the diagnosis of fungal rhinosinusitis when patients present with symptoms similar to chronic sinus infection resistant to conventional antibiotic therapy. [9] Invasive fungal infections occur commonly among individuals who are immunocompromised with systemic illnesses, e.g., diabetes mellitus. Aspergillus is the most common pathogen in fungal rhinosinusitis. Allergic fungal rhinosinusitis results from the presence of extra-mucosal fungal hyphae in sinuses. [10]

Most commonly involved sinuses are ethmoid and sphenoid with clinical features being similar to granulomatous FRS. In the early stages, nasal endoscopic findings, particularly mucosal colour changes and the purulent discharge may be as subtle as the presenting symptoms. Alteration in mucosal appearance in nasal endoscopy, such as a discoloration, granulation and ulceration are the most consistent physical findings. Compared to allergic fungal sinusitis, invasive tends to have more focal bony erosions, lacks expansion of the sinuses, has more limited sinus disease and has more disease outside of the sinuses than within, when there is intraorbital or intracranial extension. MRI brain and orbit has more sensitivity to diagnose intracranial and intraorbital extensions. Management of invasive fungal sinusitis consists of sinonasal debridement with or without Caldwell-luc surgery followed by antifungal therapy. Long-term itraconazole or voriconazole treatment recommended after intravenous amphotericin-B therapy, for invasive fungal sinusitis. [11]

Hence the aim of this study was to analyze various clinical presentation, underlying immunocompromised condition, complication of invasive fungal sinusitis.

Material & Methods

This prospective analytic study was designed including 100 patients of both types of invasive fungal sinusitis that underwent treatment as inpatient basis for the duration of 12 months, at Department of ENT, ICARE Institute of Medical Science and Research,Haldia West Bengal India were included in this study. Patients giving consent are included in this study.

Inclusion Criteria: Patient of any age, sex; with immunocompromised status like uncontrolled diabetes mellitus, chronic renal failure, patient on prolonged systemic steroid therapy, hematological malignancies, HIV, etc. and having clinical features like fever of unknown origin, cough, black eschar, crusting of the nasal mucosa, purulent nasal discharge particularly in middle meatus, nasal obstruction, swelling over nose and face, epistaxis, headaches, vision loss and diplopia were included.

Exclusion Criteria: Patients giving negative consent to participate in study and pregnant women were excluded.

Methodology

A detailed history was obtained from all the patients, with emphasis on a history of immunocompromised status. An immunocompromised host is an individual who does not have the ability to respond normally to an infection due to an impaired immune system. Immunocompromised status includes uncontrolled diabetes mellitus, renal impairment, human immunodeficiency virus infection, malnutrition, cancers, long-term systemic steroid therapy and solid organ transplantation. Apart from anterior rhinoscopy and routine clinical examinations, detailed nasal endoscopic examinations were performed in every patient to collect fungal specimen from middle meatus and nasal cavity. Nasal swabs from the middle meatus were subjected to potassium hydroxide mount and if fungal elements were identified, then fungal culture was done. Post-operatively, tissue removed from the sinuses was sent for histopathological examinations. The data collected from the patients include age, sex, associated co-morbidities and immunocompromised status, and clinical symptoms and signs, including details of any complications the patients had at the time of presentation. The patients included in the study presented with nasal discharge, nasal obstruction, headache, or facial pain; with radiologic evidence of sinus involvement; and without any response to conventional antibiotic therapy. Statistical significance was assessed to establish if the presence of certain symptoms could be an alarming sign for the likelihood of fungal rhinosinusitis. Most of above-mentioned symptoms were part of the inclusion criteria, although other symptoms of

chronic rhinosinusitis were also taken into account. Radiographic and computed tomography imaging of nose and paranasal sinuses were done in all the cases of fungal rhinosinusitis to assess the patency of the osteomeatal complex, involvement of sinuses and erosion of bony margins or expansion of the sinus cavity or intracranial extension. Patients were categorized based on the co-morbid systemic diseases and underlying immunocompromised status.

Urgent sinonasal debridement (external and endoscopic) with or without Caldwell-Luc approach was used in all cases. Antifungal therapy included use of intravenous amphotericin-B. Parenteral amphotericin-B was the drug of choice for invasive fungal rhinosinusitis; the dose was titrated based on periodic monitoring of renal function parameters and electrolytes. The patients were discharged on oral antifungal. All the patients were instructed to perform routine alkaline nasal douching during the postoperative period. The patients were asked to follow up on 1st week, 3rd week, 6th week, 3rd month and 6th month, after surgery for suction clearance of the sinonasal cavity. The patients were evaluated clinically for improvement in symptoms, clinical examination and periodic diagnostic nasal endoscopy to assess for any relapse or recurrence of fungal infection.

Statistical Analysis: Simple proportions were calculated.

Results

Table 1: Demographic data of invasive fungal sinusitis

Total	Acute invasive fungal sinusitis (n=75)	Chronic invasivefungal sinusitis (n=25)
Sex (male:female)	50:25	18:7
Age (mean)	44 (16-78)	53 (32-71)

In this study of 100 cases of invasive fungal rhinosinusitis with a male preponderance 68% (n=68).

Table 2: Underlying immunocompromised status in invasive fungal sinusitis

Underlyingdiseases	Acute invasivefungal sinusitis (n=75)	Chronic invasive fungalsinusitis (n=25)
	N (%)	N (%)
DM	68 (90.66)	19 (76)
Renal disease	24 (32)	4 (16)
Long termsteroids	5 (6.66)	4 (16)
Malnutrition	00	1 (4)

In this study, patients having Diabetes Mellitus were more susceptible to both acute and chronic variant of invasive fungal sinusitis. In Some patients multiple underlying immunocompromised conditions were observed.

Table 3: Symptoms of acute and chronic invasive fungal sinusitis

Symptom	Acute invasive fungal sinusitis (n=75)	Chronic invasive fungalsinusitis (n=25)
	N (%)	N (%)
Headache	40 (53.34)	15 (60)
Facial swelling	33 (44)	8 (32)
Facial pain	15 (20)	6 (24)
Purulent Rhinorrhea	33 (44)	12 (48)
Nasal obstruction	53 (70.66)	14 (56)
Epistaxis	45 (60)	11 (44)
Fever	25 (33.34)	8 (32)
Decreased vision	8 (10.66)	1 (4)
Diplopia	3 (4)	0

The patients presented with symptoms of nasal obstruction (n=67) 67%, purulent rhinorrhea (n=45) 45%, headache (n=55) 55%, facial pain (n=21) 21%, and facial swelling (n=21) 21%, epistaxis (n=56) 56%, fever (n=33) 33%, decreased vision (n=9) 9%, diplopia (n=3) 4%.

Table 4: Rhinology signs of acute versus chronic invasive fungal sinusitis

	Acute invasive fungal sinusitis (n=75)	Chronic invasive fungalsinusitis (n=25)
	N (%)	N (%)
Mucosal necrosis	45 (60)	11 (44)
Black crust ordebris	15 (20)	6 (24)
Pus in middlemeatus	10 (13.34)	6 (24)
Septum involvement	5 (6.66)	1 (4)

The rhinology findings like mucosal necrosis, black crust or debris, and pus in middle meatus and septum involvement were shown.

Table 5: Complications of acute invasive fungal sinusitis versus chronic invasive sinusitis

Complications	Acute invasivefungal sinusitis (n=75) N (%)	Chronicinvasivefungal sinusitis (n=25) N (%)
Preseptal cellulitis	17 (22.66)	1 (4)
Orbital cellulitis	8 (10.66)	1(4)
Orbital abscess	3 (4)	1 (4)
Cavernous sinusthrombosis	3 (4)	0
Intracranialinvolvement	12 (16)	0
Death	8 (10.66)	0

Orbital cellulitis was the most common complication of invasive fungal rhino sinusitis. 12 patients had intracranial extension. Out of 100 patients 8 patients expired due to complication of fungal invasive fungal rhino sinusitis.

Discussion

The diagnosis of this disease is difficult, especially in the early stages. Less than 4 weeks duration separates the acute stage from the chronic stage of the disease. It is a life-threatening disease present usually in immunocompromised patients with impaired neutrophilic response. These patients include those with uncontrolled diabetes mellitus, AIDS, organ transplantation and haematological malignancies, renal impairment, patients on long-term systemic or local corticosteroids. Common reported clinical symptoms include fever, cough, black eschar, crusting of the nasal mucosa, purulent nasal discharge particularly in middle meatus, nasal obstruction, swelling over nose and face, epistaxis, headache, vision loss and diplopia. A high index of suspicion of this disease entity should be present in any immunosuppressed patients with localizing sinonasal symptoms and unilateral sinonasal involvement. Often fever of unknown origin that has failed to respond to 48 hours of broad-spectrum intravenous antibiotics may be the initial presenting symptom. Mucor, Aspergillus and Rhizopus species are most common isolated fungal pathogen. [12,13]

In this study of 100 cases of invasive fungal rhinosinusitis with a male preponderance 68% (n=68). Hazarika et al. reported three cases of rhino cerebral mucormycosis, all of whom were elderly and with diabetes. [14] Chakrabarti et al isolated fungi in 50 of the 119 patients with clinically suspected cases in North India over a 2-year period. [15] In the study of Patorn Piromchai P et al, 44.1% patients were male and 55.9% patients were female. According to Piromchai P et al. the mean age of acute group (52.27±15.2) was slightly higher than chronic group (49.86±15.2). [16] In this study, patients having Diabetes Mellitus were more susceptible to both acute and chronic variant of invasive fungal sinusitis. In Some patients multiple underlying immunocompromised conditions were observed. According to Moghadami et al [17], diabetic mellitus was the most predisposing factor followed by haematological malignancy. The patients presented with symptoms of nasal obstruction (n=67) 67%, purulent rhinorrhea (n=45) 45%, headache (n=55) 55%, facial pain (n=21) 21%, and facial swelling (n=21) 21%, epistaxis (n=56) 56%, fever (n=33) 33%, decreased vision (n=9) 9%, diplopia (n=3) 4%. Symptoms and signs such as nose ulceration, eschar of the nasal mucosa, black necrotic lesions, and perforation of the hard palate are more specific, but these findings are present only at an advanced stage. [18]

The rhinology findings like mucosal necrosis, black crust or debris, and pus in middle meatus and septum involvement were shown. Orbital cellulitis was the most common complication of invasive fungal rhino sinusitis. 12 patients had intracranial extension. Out of 100 patients 8 patients expired due to complication of fungal invasive fungal rhino sinusitis. While in Piromchai P et al [17], 76.2% have orbital complications and the most common orbital complication was cavernous sinus thrombosis.

Conclusion

Due to a high mortality rate, the diagnosis and management of invasive fungal sinusitis continues to present as challenge to the otorhinolaryngologist. Acute invasive fungal sinusitis is most common in immunocompromised patients, with the highest incidence in patients with uncontrolled diabetes mellitus. The most consistent finding of invasive fungal sinusitis was mucosal necrosis and black crust/debris. For early detection of mucosal changes one has to do endoscopic examination in all immunocompromised patients with symptoms like headache, facial or periorbital pain & swelling, purulent nasal discharge, etc. All clinician should think vigilantly in immunocompromised patients with above symptoms or in pyrexia of unknown origin not responding to antibiotics. CT scan finding of sinus wall erosion may help in diagnosis of chronic invasive fungal sinusitis. To reduce

mortality, one has to go for immediate sinonasal debridement even in local anaesthesia also.

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