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Original article

The prevalence of fungal infections in unilateral abnormal sinus imaging

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Background: Rhinosinusitis is a common disease which may involve paranasal sinuses unilaterally or bilaterally. Bilateral paranasal sinus infection is more prevalent, and mostly caused by viruses, bacteria and fungi respectively. Unilateral rhinosinusitis is found infrequently and is mostly caused by bacteria and fungi.
Objectives: We studied the prevalence and types of fungal infection, and types of rhinosinusitis, in patients with unilateral abnormal sinus imaging
Methodology: A descriptive study with prospective data collection from 44 patients with unilateral abnormal sinus imaging, who were diagnosed with rhinosinusitis in Srinagarind hospital, Khon Kaen University, Thailand between August 2005 and August 2007.
Results: The prevalence of fungal infection in unilateral rhinosinusitis was 16/41 (39.0 %, 95% CI 24.1-53.9). Bacterial infection was found in 25/41 (61%, 95% CI 46.1-75.9). Three patients were lost to follow-up. Most cases with fungal infection in our study had fungal balls which were removed by endoscopic surgery.
Conclusion: A high prevalence of fungal infection was found in patients with unilateral rhinosinusitis. This group of patients who do not respond to antibiotics require further investigations to evaluate fungal infection and early surgical intervention should be considered.

Keywords: Fungi, magnetic resonance imaging, radiography, sinusitis, tomography; X-Ray computed

Rhinosinusitis is a common disease which may involve paranasal sinuses unilaterally or bilaterally. Shin [1] reported that the latter is more prevalent. The prevalence of rhinosinusitis in Thailand has not been reported, but in the United States 14% of the population that received out-patient treatment was affected [2]. Several studies of rhinosinusitis in Thailand had reported causative organisms [3-9] but the prevalence of fungal infection is unknown. Abnormal sinus imaging can be caused by bacterial infection, fungal infection, nasal polyps and malignancies [1, 10-13]. Among these etiologies fungal infection and malignancies may lead to morbidities, such as blindness, strokes and death. Prompt investigations and management are required. Knowing the etiology, signs and symptoms of rhinosinusitis is crucial in clinical decision-making and the selection of investigations and therapy.

Kaplan and Kountakis [10] studied the imagings of patients who had unilateral maxillary sinus opacification with or without contralateral disease in the United States. There were only two patients with fungal infection, which were fungal balls. There were 28 patients with true unilateral opacification; comprising 13 mucoceles, seven inverting papillomas, seven cases of chronic rhinosinusitis without nasal polyps and only one case of fungal ball.

Rudralingam et al [14] carried out a retrospective study of maxillary sinus opacification from paranasal sinus computed tomograms (PNS CT). Twenty out of 372 patients had unilateral sinus opacification, with only one case shown to be of fungal infection (mucormycosis). Lehnerdt et al [11] reviewed the etiologies of unilateral opacification of the paranasal sinuses using CT, or magnetic resonance imagings (MRI), including tumour cases. Of 43 patients 7% had fungal infections (3/43) and 37% had tumours (16/43).

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Ikeda et al [12] conducted a prospective study in Japan of 130 patients who had unilateral sinonasal disease without bone destruction on CT or MRI, this study also included tumours. They found that six patients had fungal rhinosinusitis. There were several reports of uncommon causes of unilateral rhinosinusitis; such as Wegener's granulomatosis [15], foreign body [16], cholesterol granuloma [17], extramedullary hematopoiesis [18], silent sinus syndrome [19], periodontal disease [20], and retention cyst [21].

Fungal rhinosinusitis is an inflammatory condition with a rising incidence, possibly due to the increased usage of broad spectrum antibiotics. Furthermore, patients who are immunocompromised, have longer life expectancies. Many studies [22-25] found that fungal rhinosinusitis had unilateral involvement more than bilateral. Considering the different types of unilateral rhinosinusitis; allergic fungal rhinosinusitis and fungal balls were found to affect sinuses unilaterally [23, 26-29]. Some reported half of the allergic fungal rhinosinusitis patients to have unilateral involvement [30, 31], and acute invasive fungal rhinosinusitis can also present unilaterally [32].

The purpose of this study is to determine the prevalence of fungal infection, and the types of infections, in patients with unilateral abnormal sinus imaging in our institute.

Material and methods

Prospective data were collected from patients with unilateral abnormal sinus imaging who were diagnosed with rhinosinusitis, either from plain films of the paranasal sinus or CT or MRI, in a tertiary care, Srinagarind Hospital, Khon Kaen province, Thailand between August 2005 and August 2007.

Unilateral abnormal sinus imaging is defined by total opacification or air-fluid level or mucosal thickening (>4 mm in children or >5 mm in adult PNS plain films) of one or more sinuses on the same side. Patients' symptoms, signs, imaging and pathological results were collected. Patients were diagnosed with fungal infection by histopathologic results or sinus aspirate fungal cultures. Bacterial infections were diagnosed from sinus bacterial cultures, without histopathologic identification of fungus, or resolution of symptoms and signs after empirical antibiotics treatment. Those who were proven to be fungal infection by histopathology, but also fulfilled the diagnosis of bacterial infections, were counted as fungal infections. Those with soft tissue masses, or who were revealed to be neoplasms, were excluded from the study. Patients who were lost to follow up prior to obtaining a definite diagnosis, and those who had received previous sinus surgery, were also excluded. This study was approved by the Khon Kaen University Ethics Committee for Human Research, and informed consent was obtained from all patients. The calculated sample size was 45 patients from an estimated fungal prevalence of 40% (based on an expert opinion of the prevalence in Thailand), and a 10% dropout rate. Descriptive data is presented in percentages with 95% confidence intervals.

Results

There were 44 eligible patients, 13 males (29.5%) and 31 females (70.5%), ages ranged from 5 to 78 years (mean=43 years). Twenty-six patients had no underlying diseases, five patients had diabetes mellitus (DM), two patients had acute leukemia, one patient had a history of nasopharyngeal cancer, one had a history of a right renal calculi and another patient had asthma. There was one case each of liver cirrhosis with DM, T-cell lymphoma, breast cancer and AIDS disease. The general data and diagnosis of the patients are shown in **Table 1**.

Radiologic results showed that the right side was affected as often as the left (22:22). The most common sinus involved was the maxillary sinus (35 patients), second was the sphenoid sinus and posterior ethmoid (13 patients). Lesions in the anterior ethmoid and frontal were found in eleven and four patients respectively.

From the total of 44 patients, there were 41 patients with definite diagnoses. Three patients were excluded from the study (6.8%). One patient refused surgery, though the paranasal sinus CT revealed hyperdensity with calcification in the sphenoid sinus, which we suspected to be fungal. The second patient had chronic rhinosinusitis problem, suspected to be from bacterial infection. Both patients were lost to follow-up before reaching a definite diagnosis. The third patient excluded died from multiple-organ infection. The prevalence of fungal infection in patients with unilateral abnormal sinus imaging was 39% (16/41, CI 24.1-53.9). The prevalence of bacterial infection was 60.9% (25/41, CI 46.1-75.9). Three patients were lost to follow-up prior to obtaining a definite diagnosis.

Table 2 demonstrates the relation between the involved sinus, with abnormal imaging and the causative pathogens. Affected sinuses in the anterior group were more likely to be caused by bacteria and affected sinuses in the posterior group by fungi.

Table 1. General data, diagnosis, and unilateral sinus imaging*.

Patient no.	Gender	Age	Underlying diseases	Sinus imaging	Diagnosis
1	F	35	-	CT , MRI	Fungal ball
2	F	47	-	CT , MRI	Fungal ball
3	F	50	Well controlled DM	Plain film	Fungal ball with chronic bacterial rhinosinusitis
4	F	51	-	CT	Fungal ball
5	F	57	-	CT, MRI	Fungal ball
6	F	38	T-cell lymphoma	CT	Acute fungal rhinosinusitis with septicemia
7	F	33	HIV, disseminated MAC	CT	Fungal ball with septicemia
8	M	69	-	CT	Fungal ball
9	F	78	-	CT	Fungal ball
10	F	46	-	CT	Acute bacterial rhinosinusitis with orbital abscess with fungal ball
11	M	56	-	CT	Fungal ball with compressive optic neuropathy from ethmoid mucocele
12	F	68	DM, renal insufficiency	CT	Acute invasive fungal rhinosinusitis with fungal ball with orbital involvement
13	F	52	Hx of chronic rhinitis	CT	Fungal ball
14	F	38	Nasopharyngeal CA	CT	Fungal ball
15	F	43	Asthma	CT	Fungal ball
16	M	20	ALL	Plain film	Fungal ball, orbital cellulitis
17	F	18	-	CT	Acute bacterial rhinosinusitis
18	F	53	Breast CA	Plain film, CT	Acute bacterial rhinosinusitis
19	F	24	-	Plain film	Acute bacterial rhinosinusitis
20	F	14	AML, pulmonary aspergillosis with febrile neutropenia	Plain film	Acute bacterial rhinosinusitis
21	F	64	Liver cirrhosis, DM	Plain film	Acute bacterial rhinosinusitis
22	M	22	-	Plain film	Acute bacterial rhinosinusitis
23	M	27	Hx of chronic rhinitis	Plain film	Acute bacterial rhinosinusitis
24	F	33	DM well controlled	CT	Acute bacterial rhinosinusitis with buccal space infection, disseminated mellioidosis
25	M	61	DM	Plain film	Acute bacterial rhinosinusitis
26	M	43	-	Plain film	Acute bacterial rhinosinusitis
27	M	68	-	Plain film	Acute bacterial rhinosinusitis
28	F	39	-	Plain film	Acute bacterial rhinosinusitis
29	F	72	-	Plain film	Acute bacterial rhinosinusitis
30	F	38	-	Plain film	Acute bacterial rhinosinusitis
31	F	70	-	CT,MRI	Acute bacterial rhinosinusitis
32	M	41	DM, renal insufficiency	CT	Acute bacterial rhinosinusitis
33	M	51	Hx of chronic rhinitis	CT	Acute bacterial rhinosinusitis
34	F	68	-	Plain film, CT	Acute bacterial rhinosinusitis with orbital cellulitis
35	F	36	-	CT	Acute bacterial rhinosinusitis
36	F	10	-	Plain film	Acute bacterial odontogenic cause
37	M	5	-	Plain film	Acute bacterial odontogenic cause
38	F	9	-	CT	Acute bacterial odontogenic cause
39	F	38	Hx of chronic rhinitis	CT	Chronic bacterial rhinosinusitis
40	M	43	-	Plain film, CT	Chronic bacterial rhinosinusitis
41	F	18	-	CT	Chronic bacterial rhinosinusitis
42	M	51	-	MRI	Cavernous sinus thrombosis, suspected of non-fungal cause, loss to f/u and died due to multiple-organ failure
43	F	47	Hx of chronic rhinitis	Plain film	Chronic rhinosinusitis, suspected of bacterial cause
44	F	62	-	CT	Suspected to be fungal rhinosinusitis, loss to f/u

*ALL = Acute lymphoblastic leukemia, AML = Acute myeloid leukemia, CA = Cancer, CT = Computerized tomography, DM = Diabetes Mellitus, F = Female, M = Male, Hx = History, MAC = Mycobacterium avium complex, MRI = Magnetic resonance imaging, f/u = follow up

Table 2. Location of affected sinuses and etiology.

Location of the affected sinus	Fungal infection (N=16)	Bacterial infection (N=25)
Anterior group (25 patients)		
Maxillary alone	6	15
Anterior ethmoid alone	-	-
Frontal alone	-	-
Maxillary and anterior ethmoid	-	2
Maxillary and frontal	1	1
Anterior ethmoid and frontal	-	-
Posterior group (5 patients)		
Sphenoid	3	-
Posterior ethmoid	1	1
Anterior and posterior group (11 patients)	5	6

Our study found that in the fungal infection group, 14 patients had fungal balls, and two patients had acute invasive fungal rhinosinusitis. We found no chronic invasive fungal rhinosinusitis, nor allergic fungal rhinosinusitis in this study.

Of the patients who had fungal balls; seven patients had acute onset, one patient had sub-acute and six patients had chronic onset.

There were 17 specimens sent for fungal cultures, only three were positive. The fungi identified were *Penicillium spp.* and *Scedosporium apiospermum.* Another specimen was positive for fungus but the species was unidentifiable. The remainders of the 14 specimens were negative on fungal cultures.

The bacterial group comprised of 25 patients; 22 acute rhinosinusitis patients, and three chronic rhinosinusitis patients. None had a sub-acute onset. Three patients from the acute bacterial rhinosinusitis group were associated with odontogenic infections and all were children.

There were 26 specimens sent from both groups of patients for bacterial cultures; nine from the fungal infection group, and 17 from the bacterial infection group. In 15 specimens the following pathogens were found in **Table 3**.

Table 3. Types of rhinosinusitis and pathogens

	No. of cases
Acute bacterial rhinosinusitis	
Pseudomonas aeruginosa	1
Staphylococcus coagulase negative	1
Burkholderia pseudomallei	1
Streptococcus Gr. D non-enterococci	1
Pseudomonas aeruginosa and *Klebsiella spp.*	1
Bacillus spp.	1
Streptococcus spp.	1
No growth	5
Chronic bacterial rhinosinusitis	
Pseudomonas aeruginosa	1
Streptococcus viridans (Anaerobe)	1
No growth	3
Fungal ball	
Pseudomonas aeruginosa	2
Proteus mirabilis	1
Streptococcus Gr. D non-enterococci	1
Pseudomonas aeruginosa and *Enterobacter spp.*	1
Staphylococcus coagulase negative and *Enterobacter spp.*	1
No growth	1
Acute invasive fungal rhinosinusitis	
No growth	2

The rhinosinusitis etiologies probably related to host immune status are shown in **Table 4**. Patients were equally infected by bacterial or fungal causes, disregarding their immune status. However invasive fungal rhinosinusitis was only found in immunocompromised patients.

Twenty-five patients presented with nasal symptoms (25/44, 56.8%); the most common symptoms were nasal discharge and congestion (16/44, 36.4%). Twelve patients reported post nasal drip, the other symptoms were cacosmia, maxillary toothache and fever (15/44, 34.1%). The nasal symptoms distributed according to etiology are in **Figure 1**. Nineteen patients did not have any nasal symptoms; eleven patients were from the bacterial group, and eight patients were from the fungal group. Twenty patients had orbital symptoms (20/44, 45.5 %). The most common was eye pain (15/44, 34%), second was blurred vision (8/44, 18.2%), third was proptosis (7/44, 15.9%), fourth was diplopia (4/44, 9%) and lastly ptosis (4/44, 9%) (**Figure 2**) Three patients (6.8%) lost their vision; one due to compressive optic neuropathy from an Onodi cell mucocele, another due to cavernous sinus thrombosis in which the patient underwent endoscopic sphenoidal biopsy, antibiotics and corticosteroids. This patient was lost to follow-up prior to obtaining a definite diagnosis and died from multiple organ infection. The third patient was a diabetic patient who had acute invasive fungal rhinosinusitis with a fungal ball with orbital complications.

Table 4. Host immune status and the rhinosinusitis etiology

Immune status	Fungal infection		Bacterial infection
	Fungal ball	Invasive fungal rhinosinusitis	
Immunocompetent (30)	11	-	19
Immunocompromised (11)	3	2	6
Total	**16**		**25**

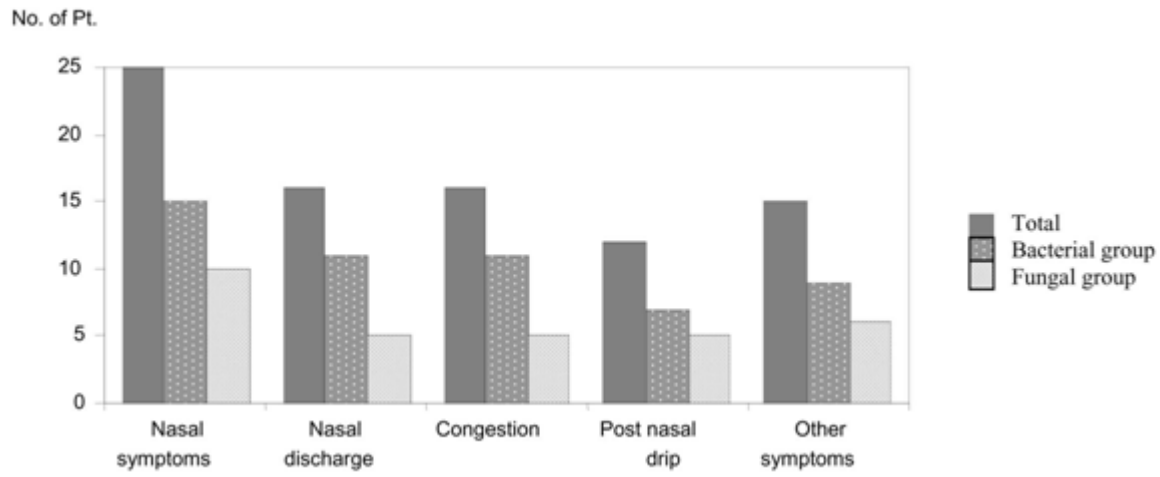

Figure 1. Nasal Symptoms in patients with unilateral rhinosinusitis

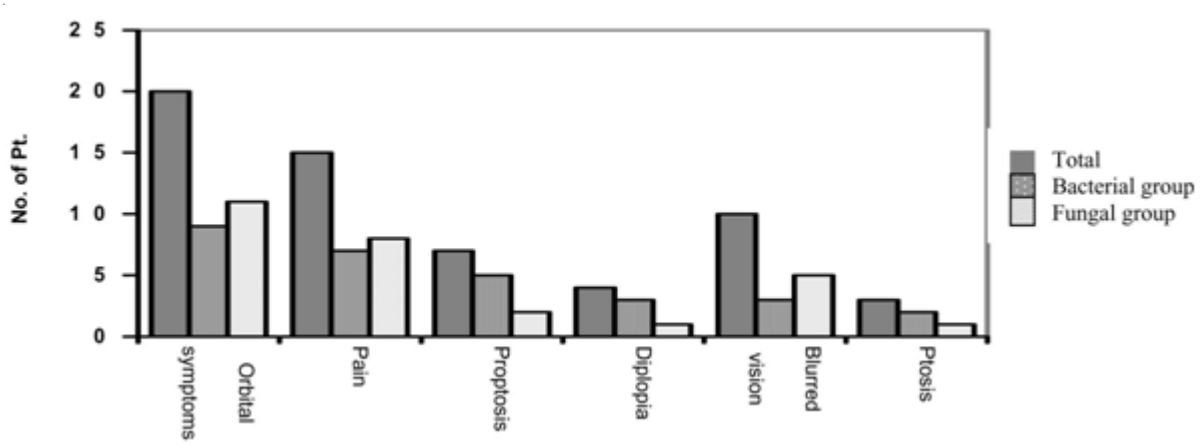

Figure 2. Orbital symptoms in patients with unilateral rhinosinusitis

Discussion

Our study demonstrated that the prevalence of fungal infection in patients with unilateral abnormal sinus imaging was 39% (95% CI 24.1-53.9). Most patients had fungal balls; only two cases were affected by acute invasive rhinosinusitis.

The prevalence of fungal infection in patients with unilateral abnormal sinus imaging in this study is much higher than in other published studies [10-14]. This could be because previous studies included cases with nasal tumours. This study focused on patients who had unilateral sinus infection. If we exclude nasal masses from the study of Kaplan and Kountakis [10], there were one in eight patients who had fungal infection (12.5%). Rudralingam et al [14] had 14 patients with unilateral maxillary opacification and only one patient had fungal infection (7.1%) Lehnerdt et al [11] studied patients who had rhinosinusitis and unilateral sinus opacification from CT or MRI, 7% were caused by fungus. All three studies concurred with the study by Ikeda et al [12] that studied unilateral sinonasal disease without bone destruction from CT or MRI. They found six of 70 patients had fungal infection (8.6%). The higher incidence of fungal infection in our series compared to other studies is possibly due to the humid tropical climate of Thailand that provides optimum conditions for the growth of fungi [33]. There was no significant correlation of occupation and fungal infection. Some patients were farmers from the rural areas and some were office workers in urban areas.

The most common type of fungal rhinosinusitis in this study is fungal ball, similar to the study by Thanaviratananich et al [34]. All cases were resolved by surgical treatment, consisting of endoscopic removal of the fungal material and widening of the affected sinus ostium. Not all of the subjects had specimens sent for cultures. We started with a step-wise treatment and some patients were treated with antibiotics and also resolved, and they did not receive surgery or other procedures such as antral punctures. In comparing the symptoms in patients with fungal infection and bacterial infection, we found that patients with fungi may not have any nasal symptoms at all. The symptoms which may indicate fungal infection are orbital pain and blurred vision. This was reported more often in patients with fungal infection and more so than in the bacterial group. These symptoms correlated with the observation that patients affected in the posterior group of sinuses alone, have a tendency to be infected by fungi. The persistence of fungal infection and delayed treatment may cause extensive destruction and may be carcinogenic [35, 36].

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