Original Research Article

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Isolated sphenoid sinus disease; a retrospective review of underlying pathologies and their clinicopathological implications

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ABSTRACT

Background: Isolated sphenoid sinus disease (ISSD) includes a small cohort of patients evaluated for sinus disease which tend to be diagnostically challenging and may lead to devastating complications. This study aims to evaluate the spectrum of etiological factors and to analyze clinic-radiological characteristics of ISSD

Methods: It is a retrospective review of cases of ISSD managed by the department of otolaryngology of a tertiary care medical centre between January 2017 and December 2019. A total of 21 patients were included and their demographic details, co-morbidities, symptomatology, cross-sectional imaging, treatment received and follow-up details were retrieved from medical records for analysis and comparison.

Results: The most common diagnoses in our cohort were invasive fungal sinusitis (n=9), chronic non-specific sinusitis (n=7) and allergic fungal sinusitis (n=3) in that order, with mean duration of symptoms 58.2 days, 300 days and 260 days respectively. Cases of invasive disease had a shorter course, more frequent cranial nerve involvement, with radiological features of heterogenous soft tissue densities and bone erosion. Cases of chronic non-specific sinusitis and allergic fungal sinusitis had more long-standing disease with a milder course and less ominous radiological features. Biopsy report from one of the patient's was that of squamous cell carcinoma while the other patient was diagnosed with a sphenoid mucocoele.

Conclusions: ISSD is an uncommon entity in clinical practice with non-specific symptoms and a potential for grave complications. Therefore, the condition must be borne in mind by clinicians and prompt treatment must be initiated.

Keywords: Sphenoid sinusitis, Endoscopic sinus surgery, Holocranial headache, Ophthalmoplegia, Sphenoidotomy

INTRODUCTION

The term ISSD is used to denote those conditions that affect the sphenoid sinus on one side or both sides, without involving the other paranasal sinuses.1-3 It represents a small proportion of diagnostically challenging conditions that have a tendency to complicate if not detected early. 4,5 Anatomically, sphenoid sinus is peculiarly proximal to critical neurovascular elements, and any pathological condition that affects the sphenoid sinus can potentially spread to involve these surrounding structures leading to significant morbidity and even mortality. In this case series, we evaluated the cases of ISSD treated over three years at a single tertiary care centre with primary objective of defining demographics, clinical manifestations, etiopathological associations, radiological characteristics, differential diagnoses, and therapeutic approach and outcomes of ISSD. Although a few of the earlier reports have analyzed above-mentioned features of this condition, present study has uniquely compared clinico-radiological characteristics of the condition as per pathological nature of underlying cause.

METHODS

This is a retrospective chart review of ISSD managed by the department of otolaryngology of a tertiary care medical centre between January 2017 and December 2019. All cases of sinus disease restricted to the sphenoid region who were treated in this centre during the time period were included in the study. Cases with multiple sinus disease, previous nasal surgeries, or incomplete medical records were excluded from the study. The demographic details, clinical manifestations, and the patho-microbiological characteristics of each of the included patients were collected from the medical records of the hospital. Also, the archived radiological images of these patients were retrieved, and the individual management principles and the outcomes were noted separately. Date analysis was done using the SPSS 22 version software. We applied descriptive statistics for defining the clinicopathological characteristics of ISSD. Categorical data was represented in the form of frequencies and proportions. Continuous data was represented as mean and standard deviation. ANOVA was used as test of significance to identify the mean difference between more than two quantitative variables. We also compared these factors between the subgroups as per the aetiology. The study was cleared by the institutional ethical committee (IEC Project No.: 371-2020) before commencement.

RESULTS

A total of 21 cases were recruited into the study, out of which 12 (57.1%) were females, and the remaining 9 were males. The mean age of the study population was 54.7 years, ranging from 23 to 85 years of age. Fifteen of the included patients gave a history of type 2 diabetes mellitus, and six patients were hypertensive. Other preexisting conditions noted in our study were hypothyroidism (n=2) and rheumatoid arthritis (n=1). Also, two of the cases had a prior history of malignancy (buccal carcinoma in one and breast malignancy in the other), for which both had received complete treatment and were disease-free for more than five years at the time of diagnosing with ISSD. The most common presenting complaint in our cohort was holocranial headache (n=13, 61.9%) followed by diminished vision (n=11, 52.3%), double vision (n=9, 42.8%), and hemifacial or retroorbital pain (n=4, 19%). In other words, 11 of 21 patients had weakness of cranial nerve II, nine patients had involvement of one or more of III, IV and VI nerve palsy, and four patients had trigeminal neuropathy features. Nasal symptoms were reported by only three patients (14.2%), who complained of nasal discharge, obstruction or epistaxis. Lastly, one of our patients had no nasal or ocular signs and symptoms, and was found to have ISSD only on cross-sectional imaging that was done for evaluation of tonic-clonic seizures. Overall, the average duration between the onset of symptoms and diagnosis of ISSD in our cohort was around 6.8 months.

All 21 patients underwent cross-sectional imaging in the form of computed tomography, which showed varying degrees of sphenoid sinus opacification on one side only in 57.2% (n=12) of patients, and on both the sides in the rest of them (n=9). A selected few cases with

neurological signs and symptoms had also got additional magnetic resonance imaging (n=12). Some of the radiological images with typical findings of ISSD based on their etiopathology are demonstrated in Figure 1-3. Each of these patients had undergone endoscopic surgery, diagnostic or therapeutic, under general either anaesthesia. As per the operative notes, during the surgical exploration of the sphenoid sinus by endoscopic sinusotomy, the operating team had found mild to moderate inflammatory changes of the sinus mucosa in most of the patients, suggestive of chronic sinusitis. However, four patients had distinctly unhealthy, friable or necrotic tissue (three of whom with fungal debris), suggestive of invasive fungal infection, two patients had proliferative lesions suggestive of neoplasm, and one patient was found to have frank mucocele of the sphenoid sinus. The tissue retrieved from the sinus wall was sent for histopathology in all cases and for microbiological assessment in selected patients.

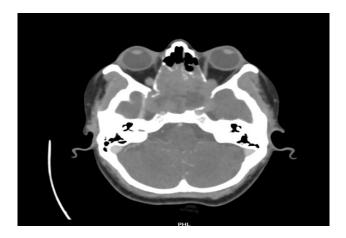


Figure 1: Contrast enhanced CT scan image of a case of invasive fungal sphenoid sinusitis showing ill-defined heterogenously contrast enhancing lesion in bilateral sphenoid sinuses with extensive bony destruction.



Figure 2: Contrast enhanced CT scan image of a case of chronic inflammatory sinusitis showing homogenous soft tissue density in bilateral sphenoid sinuses with surrounding bony sclerosis.

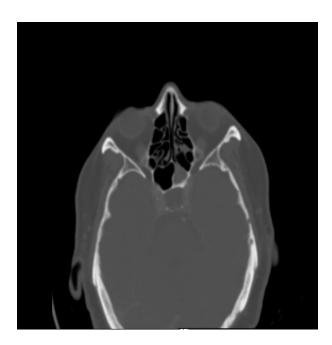


Figure 3: Non-contrast CT scan image of a case of allergic fungal rhinosinusitis showing soft tissue density within the left sphenoid sinus with no bone erosion.

Based on the final pathological report and microbiological corroboration, the actual diagnosis of ISSD was invasive fungal sinusitis in nine cases, caused by aspergillus infection in seven and mucormycosis in the remaining two. All these groups of patients were given appropriate antifungal therapy for the duration of 6 weeks to 12 weeks, along with the medical management of underlying conditions. Chronic non-specific sinusitis was the final diagnosis in seven other cases, managed by a short course of antibiotics, antihistamines and steroid nasal spray. Three of the other cases had allergic fungal rhinosinusitis limited to the sphenoid sinus, without any invasive changes in the mucosa, and were managed by

oral, intranasal steroids, antihistamines, and alkaline nasal douching. Biopsy report from one patient was that of non-keratinizing squamous cell carcinoma. Since this elderly patient had a prior history of breast malignancy, she underwent positron emission testing for estimating the disease extent and for staging. Although there was no other focus of the disease in the functional imaging, the local disease was advanced with extension into bilateral cavernous sinuses. As per the decision made by a multidisciplinary tumour board, the patient received subsequent palliative radiotherapy to the local site and succumbed to the disease two years after being diagnosed with primary malignant disease of the sphenoid sinus. Lastly, histopathology of the sinus mucosa in a patient who had undergone drainage of sphenoid mucocele was consistent with the same. With respect to the therapeutic outcome in our cohort of ISSD, the results of combination therapy with endoscopic surgery and appropriate medical treatment was effective in relieving the symptoms in a majority of the affected patients. Two of our patients had recurrence of the sphenoid sinus disease within 3 months of the initial diagnosis, requiring revision surgery while three of the patients showed no symptomatic recovery. All patients with recurrent or residual disease were that of invasive fungal sinusitis. In other words, except for patient with malignancy, 15 of patients were disease-free at time of last follow-up, which was done at an average of 1 year after initial diagnosis.

When the clinical and radiological characteristics in our cohort were analyzed as per the cause for ISSD, it was found out that the invasive fungal infection had a shorter clinical course and relatively higher rates of cranial nerve involvement. Other findings of this comparison between the subgroups of ISSD are summarized in Table 1. Lastly, in our cohort, the most prominent radiological characteristics of fungal sinusitis were heterogeneous densities inside the sinus, and bone erosion was present in invasive fungal disease but not in allergic fungal sinusitis.

Table 1: Analysis of clinical and radiological characteristics as per the cause of isolated sphenoid sinus disease.

Variables		Invasive fungal sinusitis, (n=9)	Chronic non-specific sinusitis, (n=7)	Allergic fungal sinusitis, (n=3)	
Demographics					
Average age (years)		60	53.7	50.6	
Gender	Male	4	4	1	
	Female	5	3	2	
Comorbidities	Diabetes mellitus	6	4	2	
	Hypertension	2	1	1	
Symptoms					
Average duration (days)		58.2	300	260	
Headache		4	6	2	
Nasal symptoms		-	-	2	
Decreased vision		6	3	-	
Diplopia		5	-	-	
Facial/orbital pain		4	1	-	
Proptosis		3	1	-	
Others		-	-	1 (seizures)	

Continued.

Variables		Invasive fungal sinusitis, (n=9)	Chronic non-specific sinusitis, (n=7)	Allergic fungal sinusitis, (n=3)		
Radiological characteristics						
Soft tissue	Homogenous	2	6	-		
density	Heterogeneous	7	1	3		
Bone erosion	Present	8	5	-		
	Absent	1	2	3		
Contrast enhancing	Yes	2	-	-		
	No	7	5	-		

DISCUSSION

ISSD is an uncommon entity in clinical practice. As per the previously published case series, the average number of newly diagnosed cases of ISSD is between 5 to 10 cases/year.^{3,6} Interestingly, the mean age of the affected individuals in several of the previous reports is around 54-55 years, which is identical to the mean age of patients included in the current study.^{7,8} Even for gender predilection, our cohort was in line with the literature that reports female preponderance for ISSD than males.^{3,8,9}

So far as the clinical manifestations of the isolated sphenoid sinus is concerned, headache remains to be the most common clinical symptom (50 to 82%), followed by ocular manifestations.^{4,7-13} Headache related to ISSD is localized to the vertex, mainly on the affected side, but could be diffuse and bilateral if the condition affects sinuses on both sides.^{4,8,12} In other words, in a patient with an unexplained chronic headache around the vertex, one should evaluate further to rule out an ISSD. 12 Among the ocular symptoms, vision loss predominates, followed diplopia. 7,10,11 Unlike the evident sinonasal symptomology in ethmoid or maxillary sinus diseases, nasal symptoms are hardly ever present in ISSDs. 9 The symptom complex of ISSD in the present study is at par with the literature reported trends. Moreover, the average time lapse between the onset of symptoms and the diagnosis of ISSD in our study is comparable with previous studies.^{5,8}As per a report, in about one-fourth of the patients with sphenoid sinus disease, the diagnosis can be delayed until the disease complicates, which was reflected in our study as well.⁵ This delay in diagnosis is attributable to subtle, slowly progressive and non-specific symptoms as well as to the non-suspecting treating team.^{1,5} High index of suspicion among otolaryngologists and neurologists dealing with such patients is essential to make an early diagnosis. 10,14

Computed tomography is the investigation of choice in patients who are suspected of having ISSD. 10,15 It has been reported that nearly 22% of ISSD are detected incidentally on computed tomography. While the boundaries of the sphenoid sinus and the surrounding bony landmarks can be readily appreciated on computed tomography, the nature of soft tissue density inside the lumen of this sinus also helps in identifying the probable underlying pathology. Like it has been shown in our subjects, fungal disease tends to demonstrate heterogeneous soft tissue density as opposed to the

homogenous lesions in non-specific sphenoiditis. Also, the presence of bone erosion in computed tomography points towards invasive fungal infection or neoplastic aetiology. On the other hand, in selected few cases, particularly in those with neurological deficits, with or without intracranial or intra-orbital extension of the disease, magnetic resonance imaging could be complementary to computed tomography and provide better soft tissue delineation and could aid in therapeutic planning. ^{10,15-17}

The pathological spectrum of ISSD is broad. ¹⁰As seen in our cases, inflammatory lesions like fungal sinusitis, either invasive or non-invasive, and non-specific sphenoiditis are the most common pathologies underlying the ISSD, amounting to up to 75% of the cases. 4,7,10-12 The other frequent diagnoses in sphenoid sinus include mucocele, cerebrospinal fluid leak, and sphenochoanal polyps.^{3,6,10,11}However, unlike the inflammatory conditions, which are primarily idiopathic, isolated mucoceles of the sphenoid sinus or cerebrospinal fluid leaks are mostly secondary to prior insults like exposure to radiation or trauma. 15 As such, neoplasms are rare in ISSD, and if present, they are more likely to be benign than malignant.³ The commonly reported benign neoplasms of the sphenoid sinus include fibrous dysplasia and inverted papilloma, whereas malignant tumours are primarily squamous cell carcinoma. 1,3,6,7,10,11 In the subgroup analysis, on comparing the various clinicradiological features of ISSD as per the underlying pathology, it was noted that the average age of invasive fungal sinusitis patients was more than the other classes; however, they had a relatively shorter duration of clinical manifestations before being diagnosed to have the ISSD. This shorter time-lapse in this sub-group is probably because of more cranial nerve involvement compared to the other pathologies, which might have prompted early consultation, and probably, more active evaluation by the treating clinician. Contrastingly, chronic non-specific sinusitis and non-invasive allergic fungal sinusitis exhibited a more indolent course with long-standing symptomology. Interestingly, nearly 60 to 70% of the patients had diabetes mellitus in all three classes of pathology, causing ISSD.

As for the definitive treatment of ISSD, almost all of the cases would require at least a diagnostic sphenoidotomy under general anaesthesia. In the literature, previous studies have implicated surgical intervention in 80-100% of ISSD.^{1,3,6,8-12,14} On the other hand, a selected few

uncomplicated case of acute or chronic sphenoiditis can be successfully managed by conservative management with antibiotics and antihistamines.^{4,10,13,18}

Like in our surgical cohort, the procedure of choice for surgery in all these published reports of ISSD is endoscopic sphenoidotomy and disease clearance. 1,3,6,8-^{12,14} Endoscopic surgery suffices even in complicated cases, although the prognosis with respect to functional recovery of neurological deficit may be variable. 1,6,11,18,19 The common symptoms of ISSD like headache and diplopia (due to cranial nerve III. IV and VI) are more likely to improve after endoscopic sphenoidotomy compared to the unpredictable recovery of the visual disturbances. 11,12,18,19 Nevertheless, to clear the disease completely, and thus to achieve the optimal therapeutic success by endoscopic approach, it is imperative to have preoperative planning of surgical procedure and techniques.³ As such, the pneumatization of the sphenoid sinus is known to vary between individuals, and the surgeon should assess its status by analyzing the preoperative computed tomography and plan the surgical technique accordingly.²⁰ Also, the actual surgical intervention is also guided by the nature of the disease, wherein the purpose of endoscopic sphenoidotomy in neoplastic disease is mostly for diagnostic or palliation, as opposed to the additional therapeutic clearance of the infection in inflammatory conditions.^{3,10}As seen in one of our patients, the malignant disease necessitated radiotherapy for control of the disease. 10 With regards to prognosis after endoscopic surgery, except for the malignant neoplasms, most of the other causes of ISSD do reasonably well, without any recurrence for years.^{3,15}

Although ISSD is a relatively rare clinical entity, more extensive prospective studies with a larger sample size is required to understand it's pathophysiology and management. Prolonged follow up to assess disease resolution/recurrence and long-term complications is also required.

CONCLUSION

ISSD is an uncommon entity in clinical practice with vague non-specific symptoms that can progress to involve vital structures in the vicinity. Prompt diagnosis and swift surgical treatment is of utmost importance so as to avoid life threatening complication. Therefore, a fair index of suspicion must be borne in clinician's minds when they come across such cases.

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Ethical approval: The study was approved by the

Institutional Ethics Committee

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