sinusitis

MDPI

Systematic Review

The Association of Sinusitis with Central Skull Base Osteomyelitis: A Systematic Review

Owen Tsung Wen Ho [1,2] and Alex Chengyao Tham [2,3,4,*]

[1] MOH Holdings, Singapore 139691, Singapore
[2] Tan Tock Seng Hospital, Singapore 308433, Singapore
[3] Yong Loo Lin School of Medicine, National University of Singapore, Singapore 117597, Singapore
[4] Lee Kong Chian School of Medicine, Nanyang Technological University, Singapore 308232, Singapore
* Correspondence: alexcytham@gmail.com

Abstract: We aim to provide an updated and comprehensive review of the current literature on the clinical profile and treatment options of CSBO caused by sinusitis. Three databases, Pubmed, Embase and Scopus, were searched from inception until 2 October 2022. Titles and abstracts were used for the first stage of study selection; subsequently, full texts were screened for final inclusion. Nine studies were included, with eight case reports and one case series. Patients ranged between 33 and 75 years old, with four females and four males total in the case reports. In the case series, there were 14 patients with a mean age of 62 years old. Patients with CSBO secondary to sinusitis often present with non-specific symptoms which may mimic other pathologies of the head and neck. A high index of suspicion for CSBO is important in the presence of an unremitting headache or cranial nerve palsy. Treatment options include culture-directed long-term antibiotics and surgery. The role of surgery in these patients, however, needs to be investigated more thoroughly. We believe that more large-cohort observational studies assessing the association between sinusitis and CSBO should be performed to further analyze and evaluate this topic.

Keywords: sinusitis; skull base osteomyelitis; rhinology

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1. Introduction

Skull base osteomyelitis, commonly defined as an inflammatory process of the bones of the skull base secondary to pus-forming organisms, is a complex and dangerous disease with potential for multiple complications [1,2]. It is commonly caused by infections arising from the head and neck region, including the ear, sinuses, nose and teeth. Multiple studies have described the role of malignant otitis externa and other otogenic infections in causing skull base osteomyelitis, especially that of the temporal bone [3,4]. In recent years, a new clinical entity known as central or atypical skull base osteomyelitis has been described in a few studies, in which it is often described as skull base osteomyelitis not primarily due to an otogenic source affecting the sphenoid, occipital and clival bones of the skull base [5–7]. Diagnosis of central skull base osteomyelitis (CSBO) is often challenging, as patients usually present late in the course of disease with non-specific symptoms such as headache and cranial nerve neuropathies, which may also mimic a malignancy [8,9].

Various reports have described CSBO arising from underlying sinusitis [10–12]. A majority of these studies found that the underlying diagnosis of CSBO was often only diagnosed late into the course of disease, and that patients were initially treated for what was presumed to be just sinusitis [13,14]. Sinusitis, which is often referred to as inflammation of the paranasal sinus mucosa, is a common disease affecting up to 12.5% of adults in the United States [15,16]. Given its prevalence in our population, there could be a substantial proportion of patients who may be at risk of developing CSBO in the future. However, the underlying characteristics and pathophysiological mechanisms are still not clear in terms of how sinusitis may lead to CSBO. Thus, we aim to provide an updated and comprehensive

review of the current literature on the clinical profile and treatment options of CSBO caused by sinusitis.

2. Materials and Methods

Our review was performed as recommended by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. This review was previously registered on PROSPERO (CRD 42022364505).

Three databases—Pubmed, Embase and Scopus—were searched from inception until 2 October 2022. The following free text search strategy was used: ("central" OR "clival" OR "clivus" OR "petroclival" OR "atypical" OR "non oto*" OR "sphenoid" OR "occipital") AND ("skull base" OR "Skull Base"[Mesh]) AND ("osteomyelitis" OR "Osteomyelitis"[Mesh]) AND ("Sinusitis"[Mesh] OR "sinonasal inflammation" OR "sinusitis" OR "chronic sinusitis" OR "acute sinusitis" OR "rhinosinusitis" OR "chronic rhinosinusitis" OR "acute rhinosinusitis" OR "sinus inflammation" OR "sinus infection" OR "sinusitides").

Relevant articles were independently reviewed by OTWH and ACYT. Titles and abstracts were used for the first stage of study selection; subsequently, full texts were screened for final inclusion. Case reports, case series, observational studies, cross-sectional studies, as well as any interventional trials were included; ideas, editorials, conference abstracts and perspectives, records not published as full-length articles in peer reviewed journals, as well as non-English publications without available translations, were excluded. Study populations included were individuals 18 years and older, with diagnoses of sinusitis, compared against those without a diagnosis of sinusitis. Relevant outcomes reported included demographics, clinical presentation, risk factors, pathophysiology, treatment, morbidity and mortality of patients with CSBO.

OTWH and ACYT extracted the following data into a standardized extraction template: title and year of publication, first author, study design, setting, country, ethnicity, sample size, percentage of males, and mean/median age, as well as relevant interventions, exposures and outcomes, covariates, statistical methods and key findings.

Our included studies consisted of case reports and case series. The Joanna Briggs Institute (JBI) Critical Appraisal Checklist for Case reports and Case series was used to evaluate the methodological quality and determine the risk of bias in the included studies [17].

3. Results

The study selection process is summarized in Figure 1. Our systematic search retrieved 82 results. A total of 37 duplicates were removed. Title and abstract screening excluded a further 21 articles. Full text screening included 24 articles, with nine studies included in this systematic review. 12 articles were excluded after full text screening as the underlying cause of the CSBO was not due to sinusitis.

3.1. Baseline Characteristics

Nine studies were included in this systematic review, with the study details summarized in Tables 1 and 2. Six studies were conducted in the United States of America [10,11,13,14,18,19], and one study each in India [12], Italy [20] and the United Kingdom [21]. Among the studies, eight were case reports [10–14,18,19,21], and one was a case series [20]. The age of the patients ranged between 33 and 75 years old, with four females and four males total in the included case reports. In the case series, there were 14 patients with a mean age of 62 years old [20].

3.2. Comorbidities

Eight patients had a history of diabetes mellitus [12,14,20], two patients had hypertension [14,21] and one patient had hyperlipidemia [21]. Four patients had received various surgeries in the head and neck region in the past [11,14,20,21]. Six patients had a previous history of rhinosinusitis or chronic sinusitis [11,20]. In the case series, five patients had

received chemotherapy or immunosuppressive therapy in the past, four patients had a bone marrow or organ transplant, three patients had hematological cancers and one patient had human immunodeficiency virus. Two patients in the case reports were considered to be immunocompromised due to their underlying diabetes mellitus [12,14].

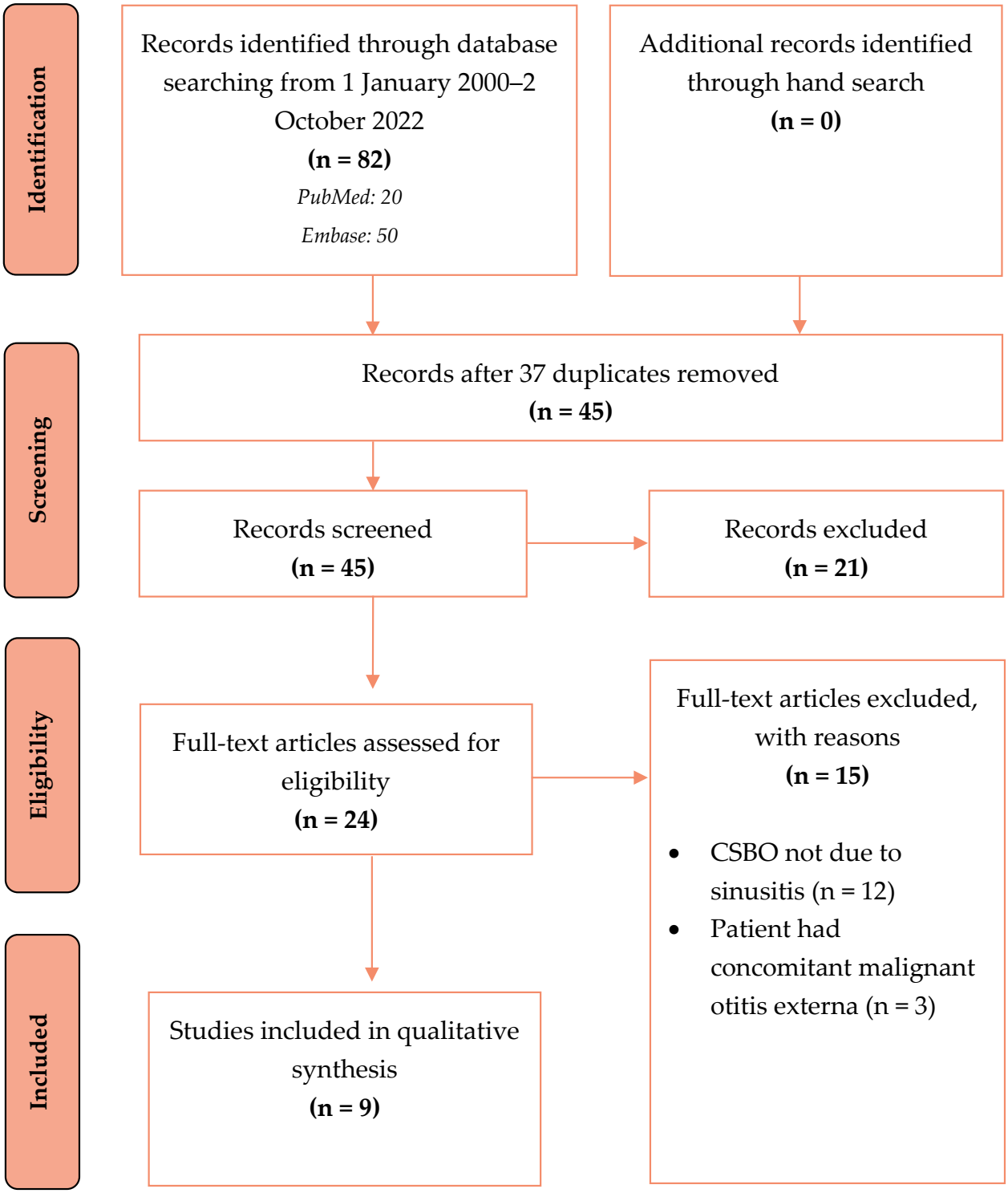

Figure 1. PRISMA Flow Diagram.

Table 1. Characteristics of included studies.

First Author & Year Published	Study Design	Sample Size	Setting/Country	Age (Years)	Gender	Comorbidities	Immunocompromised	Sinus Involved
Abou-Al-Shaar 2019	Case report	1	United States of America	74	Female	Rheumatic fever	No	Sphenoid sinusitis
Gupta 2017	Case report	1	United States of America	50	Male	NIL	No	Acute sinusitis
Hoistad 1999	Case report	1	United States of America	38	Female	NIL	No	Ethmoid and sphenoid sinusitis
Kayode-Ajala 2022	Case report	1	United States of America	36	Male	Type 1 Diabetes Mellitus, hypertension, previous tonsillectomy and adenoidectomy	Yes	NIL
Prendiville 2000	Case report	1	United States of America	48	Female	Chronic sinusitis, previous bilateral maxillary antrostomies	No	Sphenoid sinusitis
Radhakrishnan 2020	Case report	1	India	59	Female	Diabetes mellitus, thymoma, myasthenia gravis	Yes	NIL
Schreiber 2021	Case series	14	Italy	62 (mean)	NIL	Diabetes mellitus (6), human immunodeficiency virus (1), haematological cancer (3), bone marrow or organ transplant (4), chemotherapy or immunosuppressive therapy (5), rhinosinusitis (5), surgery at craniocervical region (1)	Yes - Human immunodeficiency virus (1) - Haematological cancer (3) - Bone marrow/organ transplant (4) - Chemotherapy/ immunosuppressive therapy (5)	NIL
Shellman 2021	Case report	1	United Kingdom	75	Male	Hypertension, hyperlipidemia, atrial fibrillation, previous functional endoscopic sinus surgery	No	Sphenoid sinusitis
Tomovic 2012	Case report	1	United States of America	33	Male	Previous frontal head trauma	No	Sphenoid sinusitis

Table 2. Clinical presentation and treatment.

First Author & Year Published	Clinical Presentation	Microbiology	Radiological Diagnosis and Findings	Choice and Duration of Antimicrobials *	Surgery	Morbidity and Mortality
Abou-Al-Shaar 2019	Headache (3 weeks), dizziness (2 weeks), facial and hand numbness (1 week), nausea, photophobia, neck stiffness Cranial nerve palsies: abducens (3 weeks), hypoglossal (1 week)	Nocardia abscessus, Nocardia exalbida, Nocardia gamkensis Source: sphenoid sinus and clivus	MRI brain: heterogenous sphenoid sinus mass involving upper clivus and and right petrous apex	12 months of imipenem, linezolid, ceftriaxone	Bilateral endoscopic sphenoidotomy with debridement of sphenoid sinus and skull base lesion	Completye recovery of diplopia and almost full recovery of hypoglossal nerve palsy after 12 months
Gupta 2017	Eye pain and swelling, vision loss, proptosis, chemosis, ptosis, eyelid oedema	Beta haemolytic group C streptococcus, staphylococcus, proteus mirabilis Source: sinuses and bloodstream	CT head, orbit and sinuses: panopacification of sinuses with bony dehiscence in skull base and right superior ophthalmic thrombus	Vancomycin, cefepime, metronidazole	Debridement and drainage of sinuses	NIL
Hoistad 1999	Upper respiratory tract symptoms (3 days), headache (24 h), vomiting, meningism, fever, chills	Coagulase negative staphylococcus Source: clivus	CT head: bilateral ethmoid and sphenoid sinus disease with an air–fluid level involving the clivus	Augmentin for 7 days, Oral Augmentin for 6 weeks	Trans-oral drainage of clivus	Complete recovery after 2 years, with no residual inflammation or intracranial abnormalities seen on CT scan of the sinuses, clivus, basioccipital bone and petrous apices
Kayode-Ajala 2022	Purulent rhinorrhoea, purulent otorrhoea, hearing loss, ear fullness, loss of appetite and weight, night sweats	Group F streptococcus Source: sinus	CT sinus and neck: soft tissue collection within the nasopharynx, maxillary sinus mucosal thick-ening, periosteal reaction and bony destruction of the clivus	Meropenem for 3 weeks; Ceftriaxone and oral metronidazole for 3 weeks	Incision and drainage of retropharyngeal abscess	Repeat CT imaging after 6 weeks of antibiotic treatment showed progressive resolution of clival osteomyelitis, with subsequent resolution of his presenting symptoms
Prendiville 2000	Headache, blurring of vision, post-nasal drip, malaise (5 months) Neck stiffness, nausea, fever, chills (24 h) Cranial nerve palsies: abducens	Cryptococcus Source: sphenoid sinus	CT sinus and head: non-enhancing mass in sphenoid sinus MRI brain: sphenoid sinus mass	Fluconazole, Amphotericin B for 7 days, oral fluconazole for 4 weeks	Bilateral wide sphenoid sinusotomy, takedown of sphenoid keel and intersinus septum	Patient was readmitted 8 weeks after initial discharge for bony invasion of the posterior sphenoid wall, for which she underwent revision endoscopic sinusectomy

Table 2. *Cont.*

First Author & Year Published	Clinical Presentation	Microbiology	Radiological Diagnosis and Findings	Choice and Duration of Antimicrobials *	Surgery	Morbidity and Mortality
Radhakrishnan 2020	Headache (8 months), slurred speech (1 week), thyroid mass, acro-oral vitiligo, hirsutism Cranial nerve palsies: hypoglossal	Aspergillus Source: sphenoid sinus and clivus	CT sinus: sclerotic changes involving the sphenoid body and greater wing, clivus, squamous temporal bone, and petrous apex with soft tissue density and calcification in right sphenoid MRI brain: hypointense lesion involving sphenoid body and clivus	Ceftazidime for 10 days, oral voriconazole for 10 weeks	Endoscopic sphenoidotomy and debridement	Improvement of hypoglossal nerve palsy on subsequent follow-up
Schreiber 2021	Fever, vision loss, diplopia, ptosis, facial paralysis, sensorineural hearing loss, pain	Pseudomonas, Klebsiella, Morganella, Staphylococcus, Aspergillus, Mucormycosis Source: NIL	MRI scans	NIL	NIL	NIL
Shellman 2021	Occipital pain (3 months), dysphagia and dysphonia (2 months), bilateral otalgia (3 months), vocal cord palsy Cranial nerve palsies: hypoglossal (2 months), abducens, spinal accessory	Staphylococcus aureus, Propionibacterium acnes, serratia marcescens Source: nasopharynx	MRI: soft tissue enhancement of the entire clivus extending to soft tissues of the nasopharynx	Meropenem for 22 weeks, Linezolid for 4 weeks	NIL	Complete recovery of cranial nerve palsies 17 months later
Tomovic 2012	Fever, chills, photophobia, headache, nausea, vomiting, altered mental status	Methicillin-resistant staphylococcus aureus Source: sphenoid sinus	CT sinus: bilateral sphenoid sinusitis with lytic lesion of clivus extending to foramen magnum and right hypoglossal canal with hypodensity	Vancomycin for 6 weeks	Endoscopic bilateral sphenoid sinusotomies, left total ethmoidectomy, maxillary antrostomy	Neurological symptoms recovered 1 year later

* All antibiotics were given intravenously unless stated otherwise.

3.3. Microbiology and Source of Infection

Five patients were diagnosed with sphenoid sinusitis [10,11,13,19,21] and one patient had ethmoid sinusitis [10]. Staphylococcus was cultured in five of the studies, Aspergillus in two and Streptococcus in two. Six of the studies obtained the microbiology from the sinuses [11–14,18,19], while three studies derived it from the clivus [10,12,13].

3.4. Clinical Presentation

Cranial nerve palsies were reported in four of the case reports, with three hypoglossal [12,13,21] and three abducens nerve palsies [11,13,21]. Headache was a common symptom stated in six studies [10–13,19,21], while four studies reported fever in their patients [10,11,19,20].

3.5. Radiological Diagnosis and Findings

Four of the case reports utilized computed tomography (CT) scans of the paranasal sinuses, head, neck and orbits to aid their diagnosis of CSBO [10,14,18,19], while two used magnetic resonance imaging (MRI) scans instead [13,21]. The last two case reports stated the use of both CT and MRI scans in their studies [11,12]. Four studies reported radiological findings of sinusitis on imaging [10,14,18,19], while six of the case reports found pathologies involving the clivus [10,12–14,19,21]. In the case series, the authors described the use of MRI images in their analysis of CSBO, and excluded CT scans due to lower accuracy in studying the underlying inflammatory process [20]. They also classified the radiological findings based on the pattern and site of inflammation.

3.6. Treatment and Outcome

In terms of definitive antimicrobial treatments, three studies used intravenous carbapenems [13,14,21], with linezolid [13,21], vancomycin [18,19] and azoles [11,12] being utilized in two studies each. Total duration of antimicrobials ranged between 5 and 22 weeks. Seven of the case reports reported some form of surgical intervention for the patients [10–14,18,19]. Two studies reported an improvement of cranial nerve palsies [12,13], while two studies cited a complete recovery of symptoms [10,21]. None of the studies reported any mortality among the patients.

4. Discussion

In this review, we define CSBO as osteomyelitis of the skull base arising from infections other than the ear, and in particular we aim to characterize CSBO due to sinusitis. Previous systematic reviews and meta-analyses by Johnson et al. and Ridder et al. were able to give more insight into the clinical profile and treatment strategies of CSBO in general [8,9]. However, they were limited by the small number of patients and studies included in their analysis, as well as the fact that treatment outcomes were unable to be identified accurately as some of the included studies were published midway through the patients' treatment. Moreover, there was little information on CSBO secondary to sinus infections, with Ridder et al. also reporting that majority of the included cases arose from otogenic infections [9].

Frontal bone osteomyelitis has been described as a complication of frontal sinusitis, often due to thrombophlebitis of the diploic veins or direct extension to the frontal bone from the underlying infection [22,23]. In our review, we noticed that most patients had sphenoid sinusitis as a source of infection, and given the close proximity of the sphenoid sinus to the clivus and skull base, we believe that direct spread of the sphenoid sinus infection is most likely the main cause of CSBO in patients with sinusitis. Furthermore, sinusitis involving the other paranasal sinuses such as the maxillary or ethmoid sinuses can also result in CSBO due to the contiguous arrangement of the paranasal sinuses, whereby the infection spreads via the different paranasal sinuses into the cranial fossa and skull base. As such, it is evident that sinusitis involving any of the paranasal sinuses has the potential to cause CSBO.

However, simply having an infection of the paranasal sinuses is likely insufficient to result in a devastating complication like CSBO. We believe that there are certain predisposing factors and comorbidities which can increase the likelihood of the development of CSBO in patients with sinusitis. In our review, diabetes mellitus seems to be a common predisposing factor, which is similar to how diabetes mellitus is associated with the development of malignant otitis externa [24]. Previous studies have postulated that this may be due to the inadequate function of the innate immune system in diabetics, coupled with ischemia and neuropathies caused by the underlying disease [25,26]. Johnson et al. hypothesized that drawing from the above mechanism, any disease disrupting blood flow and oxygen supply through bone could result in osteomyelitis [8]. As such, there is a possibility that many other comorbidities such as previous surgeries, radiotherapy or trauma to the head and neck region, or even sinusitis, could eventually lead to CSBO. We believe that there could also be some form of impairment in the blood flow to and from the skull base caused by the underlying sinusitis, which may contribute to the development of CSBO. The pathophysiology of immunodeficiency leading to skull base osteomyelitis is similar to that in diabetics, with studies citing a decreased immune response in the form of reduced phagocytosis, impaired leukocytic response and dysfunctional intracellular digestion of microbes [1]. It is interesting to note that sinusitis and its resultant inflammation could lead to a dysfunctional immune system, as shown by the upregulation of various cytokines, chemokines, adhesion molecules and matrix metalloproteinases in chronic rhinosinusitis [27,28]. In addition, the loss of protective mechanisms due to underlying sinusitis may lead to a decrease in epithelial integrity and decreased production of anti-inflammatory cytokines. With a drop in function of the local immune system in the skull base caused by the surrounding sinusitis, coupled with the potential for contiguous spread of the sinusitis in the paranasal sinuses, this could possibly provide another explanation of how sinusitis leading to immunodeficiency may result in CSBO.

Furthermore, the underlying pathophysiological mechanisms and biological changes seen in sinusitis may also increase the likelihood of CSBO. The paranasal sinuses are lined by cells that perform mucociliary clearance, whereby the mucus is swept down into the pharynx for clearance [27]. In patients with sinusitis, certain bacteria including Staphylococcus aureus are known to impair this mucociliary clearance, which may promote overgrowth and colonization of pathogenic organisms. This dysfunction compromises the protective capabilities of the nasal mucosa, which may contribute to the formation of biofilms that may propagate ongoing infections and make them harder to treat. The complications of biofilms and their role in preventing eradication of the bacteria on their surfaces have been described in other conditions such as cholesteatomas [29], of which there has also been mention of mediating the local host immune response and perpetuating a state of chronic inflammation. Biofilms in sinusitis have also been shown to be associated with defects in the local host's innate and adaptive immune system, resulting in damaged mucosa and a loss of epithelial integrity in the lining of the paranasal sinuses [30]. As such, with these biological and immunological changes present in the nasal mucosa, there is a possibility that these changes may propagate to the surrounding areas and tissue, including the skull base. Thus, we believe that patients with sinusitis may also be more prone to CSBO due to these changes caused by sinusitis.

Many of the included studies reported headache as a common presenting symptom among the patients with CSBO secondary to sinusitis, along with non-specific symptoms such as fever and chills. Only two studies reported nasal symptoms such as rhinorrhea and post-nasal drip [11,14]. This is congruent with the findings seen in the previous studies aiming to summarize the clinical findings in patients with CSBO, who also cite an unremitting headache as the most common initial presenting complaint [7–9]. As most of the studies reported sphenoid sinusitis as the main source of infection, it is possible that there could be an overlap of symptoms between sphenoid sinusitis and CSBO, given that patients with sphenoid sinusitis also present with headache as the main presenting symptom [31–33]. This could potentially allow for physicians to pick up patients with sphenoid sinusitis

earlier and prevent them from developing CSBO. The other common clinical presentation of CSBO seen would be cranial nerve palsies, with hypoglossal and abducens nerve palsies being the more common ones. As compared to malignant otitis externa, which mainly affects the facial nerve and rarely the abducens nerve [32], patients with CSBO often present with abducens and lower cranial nerve palsies (glossopharyngeal, vagus, spinal accessory, hypoglossal) due to their close proximity to the clivus. Due to the non-specific symptoms that these patients present with, many of the included studies were unable to correctly diagnose CSBO at first presentation. Instead, these patients were either treated for sinusitis or worked up for possible malignancy. Definitive diagnosis was eventually made on further investigations such as imaging, histopathology or microbiology. Therefore, this often poses a diagnostic challenge to many physicians, and the importance of having a high index of suspicion in identifying patients with CSBO cannot be overemphasized.

There was a wide range of organisms found in the included studies, with Staphylococcus being the most common one, and fungal infections by Aspergillus and Cryptococcus also present. In contrast, Pseudomonas aeruginosa is usually the causative organism seen in malignant otitis externa, especially in patients with concomitant diabetes mellitus [3,4]. This difference in microbiology and predominant organism seen in patients with CSBO and those with malignant otitis externa may also give an indication of how sinusitis can cause CSBO. The literature has shown that the most common organism seen in patients with sphenoid sinusitis is Staphylococcus aureus, followed by anaerobes and Haemophilus species [34]. Similarly, our included studies as well as other articles also found Staphylococcus to be the most common organism isolated from patients with CSBO [35], which further reinforces the point that the ongoing infection in the sinuses is most likely the cause of CSBO. The included studies report that definitive antimicrobial therapy is often culture-directed and given intravenously or orally for a certain period of time. Broad spectrum antibiotics such as carbapenems seem to be the preferred choice for Gram-positive organisms such as Staphylococcus, Streptococcus and Norcadia, as well as for infections which are polymicrobial. The duration of antimicrobial treatment varied widely between the studies, but there did not seem to be much correlation between the type of organism and the chosen duration of treatment.

Imaging techniques such as CT and MRI have always been crucial in aiding the diagnosis of skull base osteomyelitis and delineating the extent of infection [1]. CT scans are useful in picking up bony erosions of the skull base but may be insensitive in picking up intracranial extension and bone marrow involvement. As such, MRI imaging is currently the preferred choice of imaging modality by many physicians, as it not only can pick up early disease and better show extent of osteomyelitis, but also is useful in monitoring response to treatment [36]. However, in the case of CSBO, the literature has shown that a combination of both CT and MRI techniques may be useful [37]. CT scans are able to show any underlying invasive sinusitis with cortical erosions and also reveal any extension to the clivus and skull base. The MRI scans can then be used to delineate the extent of soft tissue and bone marrow involvement, as well as any intracranial complications. In the included case reports, both CT and MRI imaging techniques were used to aid the diagnosis of CSBO in the patients. The CT scans generally showed sinusitis changes in the paranasal sinuses as well as bony erosion or destruction in the clivus and skull base. The MRI scans, on the other hand, revealed masses or lesions in the sphenoid sinus, which appeared to involve or extend to the clivus and skull base. In the case series, the authors analyzed the MRI images, as they felt that CT scans were less accurate in displaying the inflammatory processes [20]. In the patients who had CSBO due to invasive fungal rhinosinusitis, the MRI findings correlated with the typical site of development of invasive fungal rhinosinusitis. However, it is also important to note that MRI findings in CSBO are not specific and can also be seen in neoplastic and other non-infectious inflammatory conditions [6]. Although some researchers have found that combining both CT and MRI imaging may help to differentiate between CSBO and malignancy based on the extent of involvement on the scans, they also acknowledge that small or occult tumors are difficult

to distinguish from CSBO based purely on radiological findings [37]. This is even more so for other non-neoplastic and inflammatory diseases including Immunoglobulin G4 (IgG-4) related diseases, as the imaging findings can be nearly identical to that of CSBO. As such, definitive diagnosis would likely still have to be achieved via tissue sampling and histopathological means, which was the case in the included studies.

All but one of the patients in the eight case reports underwent surgery, with debridement and drainage of the sinuses and the suspected skull base lesion being a common procedure among them. In certain studies, surgery was diagnostic rather than therapeutic, to determine the nature of a skull base lesion seen on imaging investigations in order to come to the final diagnosis of CSBO [10,12,13,19]. Ridder et al. stated that the role of surgery was more to rule out a malignancy via biopsy, citing evidence that surgery did not necessarily affect treatment duration with antibiotics or eventual survival [9]. This is similar to what our included studies show, as despite going through similar surgical procedures, the duration of antimicrobial treatment still varied widely. For the studies that reported data on eventual treatment outcomes, there was eventual recovery of symptoms including cranial nerve palsies within one to two years. It is interesting to note that the patient reported in the study by Shellman et al., who did not undergo any form of surgery but had the longest duration of antimicrobial treatment of 22 weeks, had complete recovery of symptoms 17 months later [21]. This may further reinforce the point that surgery is not necessary in the treatment of CSBO. Only one study reported a relapse of CSBO with symptoms such as headache and nausea, of which the patient subsequently underwent revision surgery and a further nine-week duration of antimicrobials [11].

The advantages of this review would be that this is one of the first to analyze the clinical characteristics and treatment strategies of CSBO secondary to sinusitis. Nevertheless, this study should be interpreted in the context of known and potential limitations. Firstly, the majority of our included studies were case reports, with only one study being a case series. As such, there was a lack of observational studies to allow us to establish any cause–effect relationship between sinusitis and CSBO. Furthermore, the data and population characteristics from the various case reports were unique to each study; thus, we are unable to generalize most of the findings from this review to other patients in the world. The retrospective design of the included studies coupled with the risk of publication bias may further decrease the validity of our findings. Moreover, the total number of patients included in the studies is relatively small, which may also prevent our findings from being extrapolated. Despite the above descriptions of the association of sinusitis and CSBO, we must acknowledge that CSBO can also develop in the absence of sinusitis, which also indicates that there are still gaps in the knowledge and literature surrounding this topic.

5. Conclusions

In summary, patients with CSBO secondary to sinusitis often present with non-specific symptoms which may mimic other pathologies of the head and neck. Diabetes mellitus and being in a state of immunodeficiency seem to predispose patients to CSBO as well. Having a high index of suspicion for possible CSBO is important, especially in the presence of an unremitting headache or cranial nerve palsy, as this may be a warning sign of underlying CSBO. Treatment options include culture-directed long-term antibiotics and surgery. The role of surgery in these patients, however, needs to be investigated more thoroughly, as the current literature did not show significant benefits of surgery in patients with CSBO. We believe that more large-cohort observational studies assessing the association between sinusitis and CSBO should be performed to further analyze and evaluate this topic, which may shed light on more effective diagnostic and therapeutic options for this disease.

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