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CASE REPORT - INFECTION

Nocardial clival osteomyelitis secondary to sphenoid sinusitis: an atypical skull base infection

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Abstract

Clival osteomyelitis is a life-threatening complication of untreated malignant otitis externa or paranasal sinus infection. Although various pathogens have been implicated, to our knowledge, primary nocardial clival osteomyelitis has never been reported. We describe a 74-year-old woman who presented with headaches, abducens and hypoglossal nerve palsies, facial numbness, photophobia, and neck stiffness. Imaging revealed a heterogeneous mass within the sphenoid sinus with clival extension. The lesion was extirpated via a binostril endoscopic endonasal transsphenoidal approach. Histopathological and microbiological examination revealed a nocardial source. Clival osteomyelitis associated with sphenoid sinusitis should be included in the differential diagnosis of progressive skull base lesions in the setting of an underlying infection. Early recognition and intervention with antibiotics and surgical debridement is essential in the management of this rare entity.

Keywords Osteomyelitis · Skull base · Clivus · Sphenoid sinus · Sinusitis · Nocardia · Infection

Introduction

Clival osteomyelitis is a rare skull base infection that is associated with high morbidity and mortality rates. The disease generally presents after inadequate treatment of a malignant otitis externa, or less commonly a paranasal sinus infection that directly extends into the nearby skull base [4, 10]. Patients typically present with headaches and cranial nerve palsies [11]. *Pseudomonas aeruginosa* and *Staphylococcus* spp. are the most commonly implicated pathogens; however, other microorganisms have been reported in the literature [4, 11].

Nocardia is a gram-positive, rod-shaped bacterium that primarily affects the lungs of immunocompromised patients but is disseminated to other organs in approximately half of patients [8, 20, 26]. Numerous cases of nocardial osteomyelitic infections occurring both intracranially and extracranially have been described in the literature; however, despite the description of two *Nocardia* spp. sphenoid sinusitis cases previously [7, 8], to the best of our knowledge, no cases of nocardial clival osteomyelitis secondary to sphenoid sinusitis have been published. Herein, we report a case of nocardial clival osteomyelitis secondary to sphenoid sinusitis in an immunocompetent patient and review the associated literature.

Case report

Clinical presentation

A 74-year-old woman with a past medical history of rheumatic fever presented to an outside institution with a 2-week history of headaches, dizziness, and diplopia secondary to a left abducens nerve palsy. Magnetic resonance imaging (MRI)

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revealed a heterogeneous sphenoid sinus mass (Fig. 1a, b). The patient was evaluated by an otolaryngologist, and an endoscopic endonasal biopsy was obtained. The otolaryngologist noted yellow fluid at the time of biopsy that was sent for culture. Histopathological examination of the biopsy specimen revealed the presence of inflammation and fibrosis but no signs of malignancy. Blood cultures obtained during this initial hospitalization were negative. The patient was discharged on trimethoprim-sulfamethoxazole, but 10 days later, the nasal biopsy and culture grew *Nocardia abscessus*. Antibiotic coverage was broadened to also include imipenem. Notably, the patient did not fully complete therapy because of medication-induced nausea.

A week later, the patient returned to the outside facility because of worsening headaches, left hand and facial numbness, and new left hypoglossal nerve palsy in addition to her preexisting abducens nerve palsy. A culture of cerebrospinal fluid obtained via lumbar puncture was negative. MRI with gadolinium contrast depicted extension of the sphenoid sinus lesion into the clivus, with evidence of dural enhancement and bony destruction (Fig. 1c, d). The patient was started on meropenem and transferred to our institution for further evaluation and management. On arrival, she began to complain of nausea, photophobia, and neck stiffness. At that time, the results of laboratory studies were unremarkable with the exception of leukocytosis to 22.21/L (normal 4.5–11/L).

The infectious disease specialist consulted recommended reinitiation of imipenem therapy. MRI and MR angiography demonstrated new narrowing of the left internal carotid artery, invasion into the occipital condyles, myositis of the longus colli muscle, and progressive left transverse and sigmoid sinus thrombosis (Fig. 1e–g). Given the progression of her disease process on imaging as well as her worsening confusion, impulsiveness, and agitation despite intravenous antibiotic administration, the patient elected to proceed with surgical debridement of her sphenoid sinus and skull base lesion.

Operation

The patient was positioned supine with her head held in a Mayfield head clamp for endoscopic endonasal transsphenoidal biopsy and debridement using intraoperative neuronavigation. We used a rigid endoscope to lateralize the middle turbinate, and the right posterior ethmoid partitions were removed. Suppurative fluid emanated from the left sphenoid ostium and ultimately from within the right lateral sphenoid recess. A bilateral sphenoidotomy was performed, and the lesion was easily visualized as pinkish brown necrotic-appearing tissue extending into the clivus, with significant bony dehiscence of the sella and clivus to the posterior fossa dura. Fragments of the lesion were obtained for frozen histopathologic analysis. Debridement of the mass was initiated

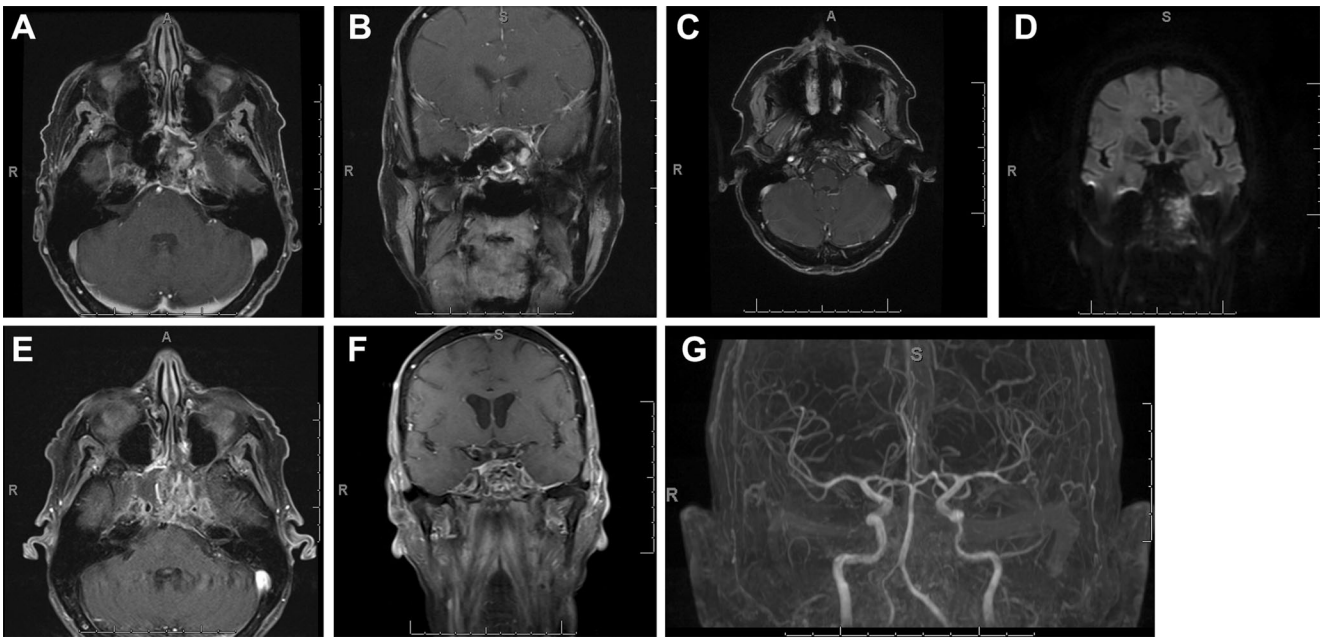

Fig. 1 Preoperative magnetic resonance imaging (MRI) with gadolinium contrast of the brain. **a** Axial and **b** coronal T1-weighted MR images at presentation demonstrating heterogeneously enhancing lesion in the sphenoid sinus involving the right petrous apex and upper clivus, as well as linear enhancement of the petrous and clival dura. **c** T1-weighted axial MR image and **d** coronal diffusion-weighted image performed 1 week after the patient started on antibiotics demonstrating extension of the enhancement and diffusion restriction signal along the left petroclival junction and jugular foramen. **e** Axial T1-weighted and **f** coronal T1-weighted MR images performed 3 weeks after presentation and **g** MR angiography demonstrating worsening of the heterogeneous enhancement with progressive increase in size, involvement of the petrous apex bilaterally, and inferior extension toward the left jugular foramen and hypoglossal canal

using pituitary forceps and ring curettes, with care taken around an exposed dehiscent left internal carotid artery. The lesion consisted of a mixture of mucus, pus, and soft necrotic tissue that had eroded through the clival bone to the petrous apex. Once the mass was sufficiently debulked and the clival dura exposed, the field was copiously irrigated. Meticulous hemostasis was achieved, and a finger cot nonabsorbable nasal pack was placed after remedialization of the middle turbinates.

Histopathological findings

Gross examination of the resected lesion revealed an aggregate of tan–red soft pliable tissue and bone. Histopathologic examination of the resected specimen demonstrated filamentous bacteria (by Modified Gomori Methenamine Silver Nitrate Stain) with bone involvement that was morphologically compatible with *Nocardia* spp. (Fig. 2). Microbiological cultures confirmed the presence of *Nocardia abscessus*, *Nocardia exalbida*, and *Nocardia gamkensis* organisms.

Postoperative course and follow-up

Postoperatively, the patient remained at her neurologic baseline. Based on her culture sensitivity and susceptibility report, she was placed on imipenem, linezolid, and trimethoprim-sulfamethoxazole. Her leukocytosis improved to 15.21/L. Her antibiotic regimen was then further tailored based on culture-derived susceptibilities to ceftriaxone, trimethoprim-sulfamethoxazole, and linezolid for 12 months. The patient was discharged home on postoperative day 18. At her last follow-up appointment 12 months after surgery, the patient was doing well, with significant improvements in her symptoms, including complete recovery of her diplopia and almost full recovery of her left tongue deviation. MRI depicted progressive decrease in contrast enhancement and reduced T1 hypointensity involving the clivus, occipital condyles, and jugular tubercles, indicating significant improvement of her infection (Fig. 3).

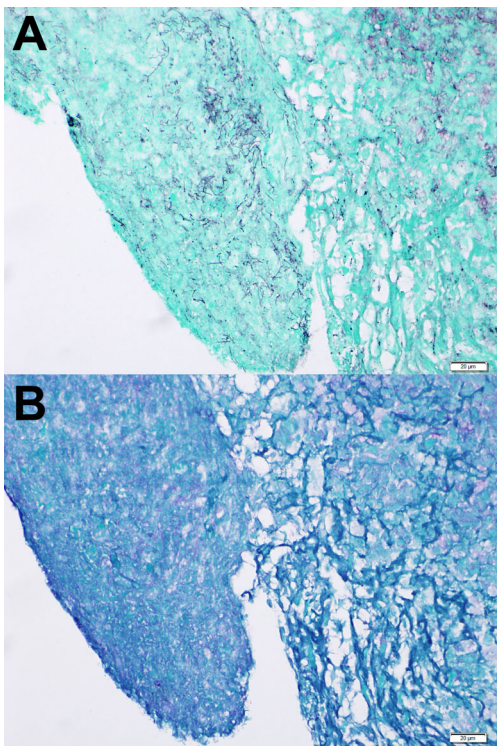

Fig. 2 Histochemical staining of the surgical specimen. **a** Modified Gomori Methenamine Silver Nitrate (GMS) staining demonstrating branching filamentous bacteria and **b** periodic acid–Schiff (PAS) staining that is partially acid-fast positive with bone involvement. These findings are morphologically compatible with *Nocardia* infection

Discussion

Clival osteomyelitis is a rare and serious infection of the skull base that is associated with high morbidity and mortality rates. In the majority of cases, the cause of clival osteomyelitis is direct extension of the infection from an untreated malignant otitis externa [4, 10]. Less frequently, direct extension from an adjacent infected sinus can lead to clival osteomyelitis [4, 10]. Isolated sphenoid sinusitis is the least common site of sinus infections, accounting for less than 3% of sinusitis cases [9]. Most patients present with headaches and cranial nerve deficits [11]. The abducens nerve is the most commonly involved cranial nerve in clival osteomyelitis, followed by the lower cranial nerves (IX, X, XI, XII). Other reported presentations include facial pain, fever, and nasal discharge or congestion [11].

Various pathogens have been implicated in the development of clival osteomyelitis. As expected, *Pseudomonas* and *Staphylococcus* infections account for the majority of cases [4, 11]. However, various other microorganisms have also been reported in the development of skull base osteomyelitis, including *Streptococcus* spp., *Mycobacterium*, *Aspergillus*, mucormycetes, among others [1, 3, 11, 13].

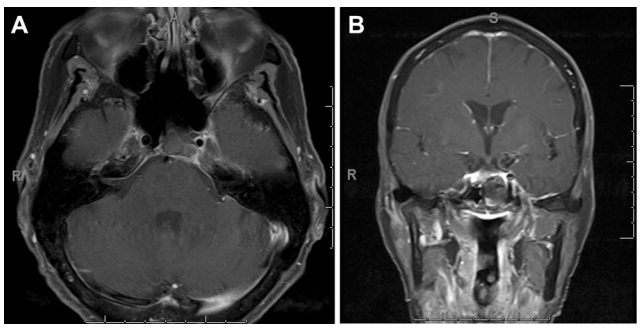

Fig. 3 Follow-up **a** axial and **b** coronal MRI with gadolinium of the brain 8 months postoperatively demonstrating marked improvement of the enhancement with residual postoperative changes

Table 1 Reported cases of nocardial paranasal sinusitis

Study	Age (years) /sex	Clinical presentation	Immune status	Location	Extension	Lesion biopsy/ aspiration	Operation	Medical treatment	*Nocardia* spp.	Outcome
Katz and Fauci [12]	39/F	Fever, rigors, diaphoresis, and night sweats	Competent	Left maxillary sinus	–	+	Left nasal-antral window	Sulfadazine and sodium bicarbonate	*Nocardia asteroides*	Complete recovery
Roberts et al. [22]	35/M	Headache, increasing lacrimation, nausea, proptosis and ptosis of the left eye, impairment of horizontal gaze in the left eye, and diplopia on upward gaze	Compromised (cadaveric renal transplant recipient)	Sphenoid sinus	Extension into the adjacent nasoethmoidal region, pituitary fossa, and suprasellar cistern	+	Bilateral sphenoidal sinusotomies	Sulfadimidine, amikacin, cotrimoxazole, imipenem, roxithromycin	*Nocardia asteroides*	Complete left external ophthalmoplegia and decreased visual acuity in the left eye that completely resolved at his 2-year follow--up, and bitemporal hemianopia compatible with cavernous sinus thrombophlebitis
Unzaga et al. [25]	42/F	Recurrent maxillary sinusitis and iridocyclitis	Competent	Left maxillary sinus	–	+	–	Trimethoprim-sulfamethoxazole switched to erythromycin	*Nocardia nova*	Complete recovery
Chawla et al. [6]	43/M	Nose block, watery non-foul smelling nasal discharge, snoring, and mouth breathing	Competent (diabetic)	Left maxillary sinus	–	+	Septoplasty and functional endoscopic sinus surgery with left spur removal	Trimethoprim-sulfamethoxazole	*Nocardia nova*	Patient improved gradually over time
Giordano et al. [9]	72/F	Headache and left trigeminal neuralgia	Competent (diabetic with a history of breast adenocarcinoma)	Sphenoid sinus	Osteolysis of the greater wing of the left sphenoid bone and the base of the pterygoid processes and a deep abscess of the infratemporal fossa within the pterygoid muscles with meningeal involvement over the left temporal lobe	–	Left endoscopic sphenoidotomy	Trimethoprim-sulfamethoxazole and folic acid	*Nocardia nova*	Complete recovery
Present case	74/F	Headache, left hand and facial numbness, nausea, photophobia, neck stiffness, and left hypoglossal and abducens nerves palsy	Competent	Sphenoid sinus	Extension into the clivus	+	Binarial endoscopic endonasal transsphenoidal biopsy and debridement	Ceftriaxone, trimethoprim--sulfamethoxazole, and linezolid	*Nocardia abscessus*, *Nocardia exalbida*, and *Nocardia gamkensis*	Patient improved gradually over time

Nocardia is a gram-positive, catalase-positive, acid-fast, rod-shaped aerobic actinomycete with filamentous hyphae-like branching on direct microscopy [8, 20, 26]. It primarily affects immunocompromised hosts in the form of pneumonia after inhalation of the spores or direct inoculation of the skin. In 50% of cases, the infection can disseminate into other organs and cause debilitating symptoms [8, 20, 26]. Nocardial spread into the brain—causing abscesses—and into bones—leading to osteomyelitis—has been well described in the literature [18, 24]. Isolated nocardial paranasal sinus infection is uncommonly encountered, especially in the sphenoid sinus (Table 1). To the best of our knowledge, only two cases of nocardial sphenoid sinusitis have been reported in the literature [9, 22].

The present case offers a new and significant addition to the literature. First, our case constitutes the third case of nocardial sphenoid sinusitis and apparently the first case of nocardial sphenoid sinusitis with direct extension into the clivus and the development of skull base osteomyelitis. Second, the *Nocardia* spp. in our case have not been reported before in the setting of sphenoid sinusitis. The patient in the current case incurred an infection involving three disparate nocardial species, namely *Nocardia abscessus*, *Nocardia exalbida*, and *Nocardia gamkensis*. The two previously reported cases of sphenoid sinusitis were attributed to *Nocardia asteroides* [22] and *Nocardia nova* [9]. Finally, our case depicts the importance of employing a multidisciplinary team approach to such lesions, as well as the need for early and aggressive surgical debridement to eradicate the infection and exclude other causes. The patient in our case did well with treatment. At her last follow-up, 12 months after surgery, she reported significant improvement in her symptoms with complete recovery of her diplopia and almost full recovery of her left tongue deviation.

Radiological imaging is essential to delineate the lesion and aid in establishing the diagnosis. Computed tomography scans typically show regional destruction of the bony cortex of the clivus [15], whereas on MRI, skull base osteomyelitis demonstrates clival hypointensity on T1-weighted images and hyperintensity on T2-weighted images because of bone marrow infiltration, as seen in our patient [5]. Because of the low specificity of these findings and their similarity to other conditions such as tumors, Paget disease, and inflammatory conditions, nasal biopsy and histopathological and microbiological examination of the lesion are of paramount importance to differentiate among such causes, allowing appropriate treatment of the lesion [5, 11, 15].

The pathophysiology of clival osteomyelitis secondary to sphenoid sinusitis has been suggested as direct bony extension of the infection, propagated thrombophlebitis through the venous system, or hematogenous dissemination [16, 18]. The management of clival osteomyelitis involves a prolonged antibiotic regimen tailored to the pathogen's specific sensitivity profile, as well as surgical debridement to evacuate the infection, identify the microorganism, and rule out other diagnoses [8, 11, 19, 20, 26]. Adjuvant hyperbaric oxygen therapy has been employed in some patients with promising results. It may aid in reversing tissue hypoxia, increasing phagocytosis, and stimulating new blood vessel formation (neomicroangiogenesis) [7, 14, 19, 23].

Despite complete eradication of the infection, cranial neuropathies usually resolve slowly in patients with clival osteomyelitis, as was seen in our patient [5, 10]. Finally, it is worth noting that even after successful medical and surgical intervention, the reported mortality rate of skull base osteomyelitis may be as high as 30%, and it can lead to septic cavernous sinus thrombosis and intracranial extension [2, 7, 17, 21].

Conclusion

Nocardial clival osteomyelitis following sphenoid sinusitis is a rare and potentially life-threatening infection of the skull base. It should be included in the differential diagnosis of progressive skull base lesions in the setting of an underlying infection. Early recognition and intervention with antibiotics and surgical debridement is essential in the management of this rare entity.

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Compliance with ethical standards

Patient consent The patient has consented to the submission of the case report for submission to the journal.

Conflict of interest The authors declare that they have no conflict of interest.

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