

Maxillary sinus aspergilloma of odontogenic origin: Report of 2 cases with cone-beam computed tomographic findings and review of the literature

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ABSTRACT

Aspergilloma of the maxillary sinus is considered rare in immunocompetent patients, but a considerable increase has recently been seen in the incidence of reported cases. Dental procedures involving the antral region are thought to predispose individuals to this form of aspergillosis. Because aspergilloma shares similar clinical features with other sinus pathologies, its diagnosis may be delayed. Thus, an early diagnosis confirmed by a histopathological examination plays a crucial role in the adequate management of aspergilloma. This article provides a concise review of the reported cases of aspergilloma associated with dental procedures and reports 2 new cases of aspergilloma in middle-aged female patients, with a presentation of their cone-beam computed tomographic findings. (*Imaging Sci Dent* 2018; 48: 139-45)

KEY WORDS: Fungi; Maxillary Sinus; Aspergillus; Cone-Beam Computed Tomography

Nature harbors different classes of fungi, some of which are pathogenic for humans. *Aspergillus* is a genus of fungi belonging to the Ascomycota phylum. Despite the enormous diversity among species of *Aspergillus*, only a few thermotolerant groups are capable of causing an opportunistic infection, known as aspergillosis, in human beings.¹⁻³ Aspergilloma is the most common subtype of aspergillosis; it is defined as noninvasive chronic fungal sinusitis, and is predominantly seen in the maxillary antrum of immunocompetent hosts.⁴ Aspergilloma is usually asymptomatic and it may take several years for symptoms to occur.⁵ It usually affects a unilateral sinus cavity and is detected incidentally, with the characteristic appearance of an area with iron-like density resembling a foreign body in a homogeneously clouded maxillary sinus on radiographic examination.^{4,6} In symptomatic cases, the clinical manifestation of aspergilloma is often nonspecific and includes purulent or blood-stained nasal discharge, chronic sinus pain, nasal con-

gestion, impaired sense of smell, headache, and orbital pain.⁷ Complete removal of the lesion via the Caldwell-Luc or endoscopic surgical techniques, with the establishment of natural sinus drainage, is sufficient for the management of aspergilloma, and leads to a low recurrence rate.^{4,7,8}

The aim of this paper is to discuss the etiology and management of maxillary sinus aspergilloma of odontogenic origin, to present 2 new cases, and to review the previously reported cases. For this purpose, a systematic search of the literature on maxillary sinus aspergilloma of odontogenic origin was carried out on PubMed/MEDLINE and Google Scholar through 2017. The search was performed using the keywords ‘aspergillosis,’ ‘*aspergillus*,’ ‘aspergilloma,’ ‘fungus ball,’ ‘mycetoma,’ ‘maxillary sinus,’ ‘odontogenic,’ and ‘dental’ and combinations thereof.

Case Reports

Case 1

A 54-year-old woman was referred to our clinic because of a radiopacity in the left maxillary sinus that was noticed on a routine dental examination by a general practitioner. She had undergone endoscopic sinus surgery due to this

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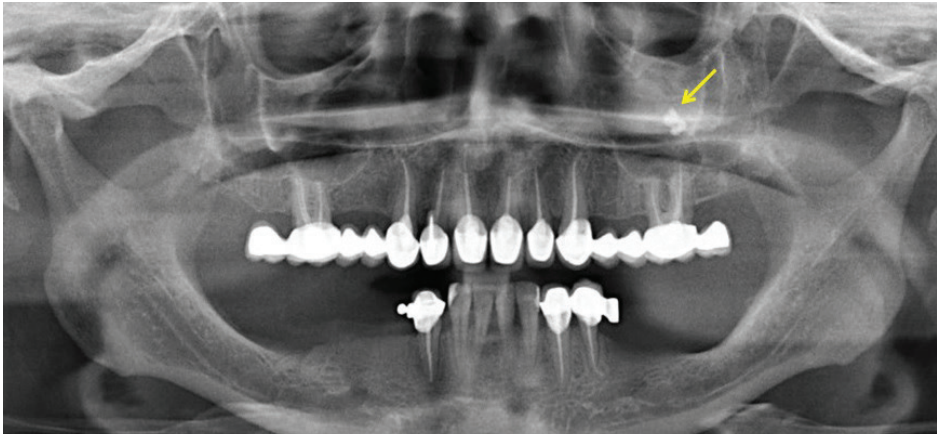


Fig. 1. Panoramic radiograph shows a radiopaque mass in the left maxillary sinus.

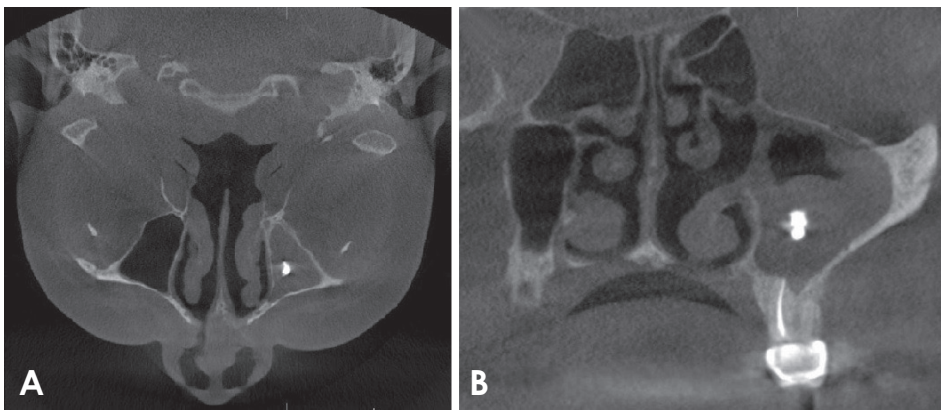


Fig. 2. A. An axial cone-beam computed tomographic (CBCT) image shows an iron-like opacity in the central area of the left maxillary sinus. B. CBCT image on the coronal plane shows the lesion in the maxillary sinus and the sinusitis caused by the aspergilloma.

radiopacity 3 years ago. The patient's general health was unremarkable. She had a history of a nasal obstruction that occurred after root canal treatment of the left maxillary first molar tooth several years previously. Upon clinical examination, no pathology was observed. Panoramic radiography showed a small radiopacity that resembled a foreign body in the maxillary antrum (Fig. 1). Cone-beam computed tomography (CBCT) revealed an iron-like opacity in the central area of the left maxillary sinus (Fig. 2). No evidence of bone destruction was seen on the sinus walls. Under local anesthesia and sedation, extraction of the left maxillary first molar and the Caldwell-Luc procedure were planned. During the operation, a thick gray-brown, paste-like material that resembled root-canal sealer was observed in the sinus. The palatal root of the left maxillary first molar seemed to have perforated the floor of the sinus. Complete curettage and irrigation were performed. An antibiotic was prescribed after the operation to prevent bacterial superinfection. The specimen was sent for a histological examination, which revealed matted fungal hyphae that were evident on hematoxylin and eosin staining. The acute-branched septate hyphae were similar to *Aspergillus* and

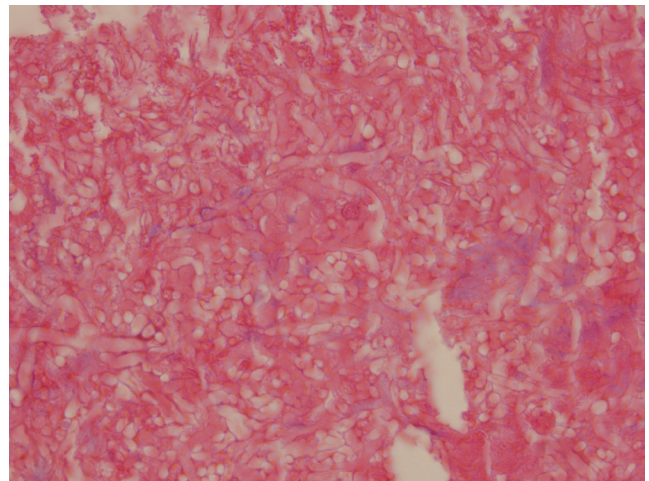


Fig. 3. Histopathologic finding shows a tangled mass of hyphae (H&E staining, original magnification $\times 100$).

showed no tissue invasion. The histopathologic diagnosis was aspergillosis (Fig. 3).

The patient had an uneventful postoperative recovery. One year after surgery, she had no clinical and radiographic evidence of disease (Fig. 4).

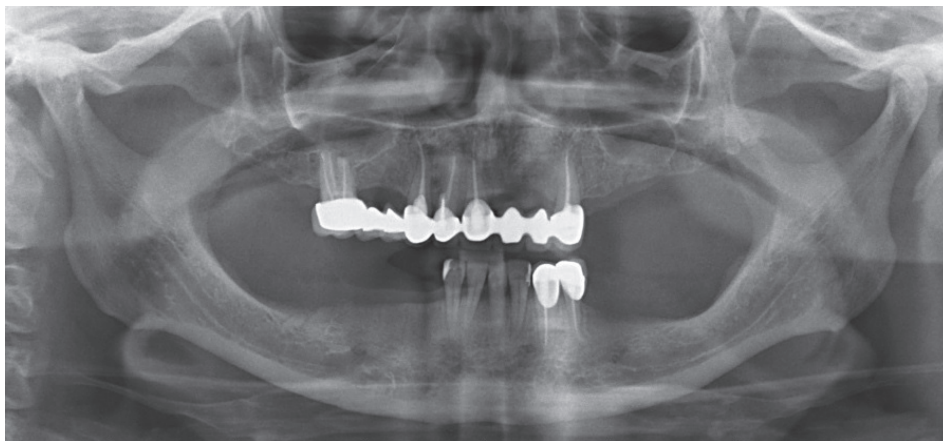


Fig. 4. Postoperative panoramic radiograph of the lesion at 1-year follow-up.



Fig. 5. Panoramic radiograph shows increased radiopacity in the left maxillary sinus and the root of the left maxillary first molar.

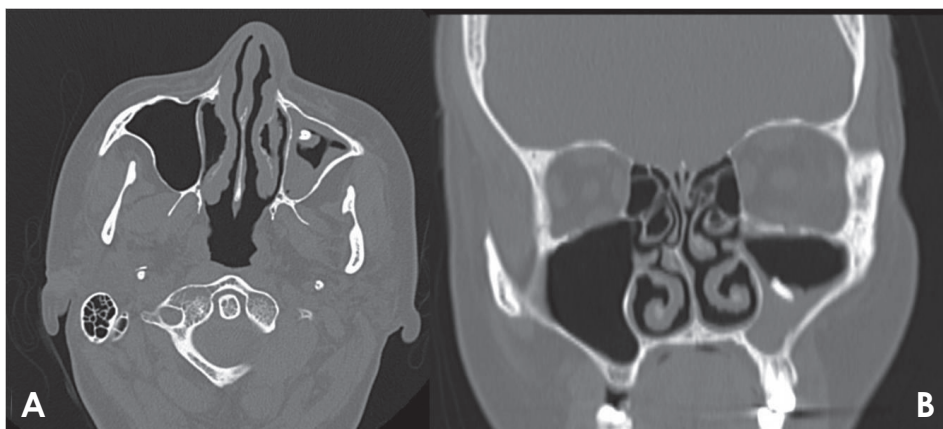


Fig. 6. A. An axial cone-beam computed tomographic (CBCT) image shows an iron-like opacity surrounded by dense tissue and mucosal thickening in the sinus walls. B. CBCT image on the coronal plane shows the lesion in the left maxillary sinus.

Case 2

A 41-year-old woman was referred to our clinic with a complaint of occasional left-sided pain in her upper face. Her medical history included Raynaud syndrome and asthma. Upon clinical examination, no pathology was observed. A panoramic radiographic examination showed a radiopaque area at the level of the left maxillary sinus

(Fig. 5). Her left first molar tooth had been extracted 13 years ago and the left first premolar and second molar teeth had undergone endodontic treatment. CBCT showed a piece of the root of the left first molar tooth in the sinus cavity and mucosal thickening in the sinus walls (Fig. 6). A Caldwell-Luc procedure was performed on the left maxillary sinus under local anesthesia and sedation. A

full-thickness mucoperiosteal flap was raised. A bony window was made using a trephine bur and the root of the left first molar tooth with granulation tissue was removed. The sinus mucosa seemed healthy. The bony window was replaced and sutured with 4-0 Vicryl stitches to the bone. Closure of the flap was performed with 3-0 silk stitches. An antibiotic and analgesic were prescribed after the operation. Cured granulation tissue around the piece of the root was submitted for a histological examination, the results of which were compatible with aspergilloma (Fig. 7). The patient was followed periodically for 1 year. At 1-year check-up, she was completely asymptomatic (Fig. 8).

Discussion

Fungal infection of the maxillary sinus is relatively rare in healthy individuals, but because of the globally uncontrolled consumption of chemotherapeutics that cause pa-

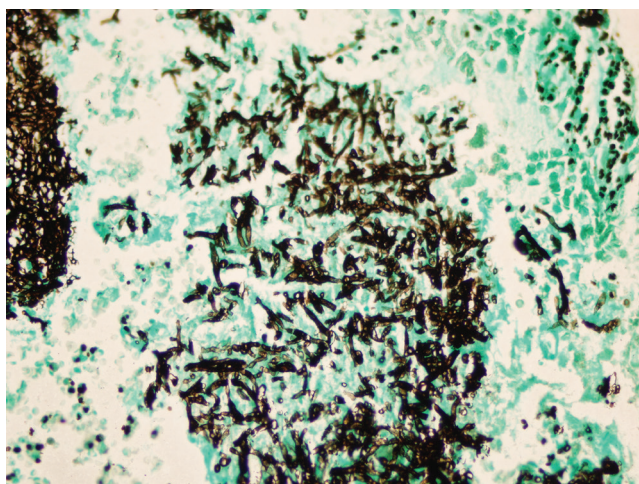


Fig. 7. Histopathologic finding shows the characteristic septate hyphae (Grocott-Gomori methenamine silver stain, $\times 400$).

tients to be vulnerable to fungal infections and as a result of improvements in diagnostic imaging techniques, the detection of this infection among healthy subjects seems to be increasing.^{4,7} It has been reported that more than 10% of patients who had chronic sinusitis were found to have aspergilloma, predominantly in the maxillary sinus.^{5,8} The main aspects of the pathophysiology of aspergilloma of the maxillary sinus are still debated, although contamination of the maxillary sinus with *Aspergillus* has been suggested to occur through various pathways.³ Because *Aspergillus* species do not have the ability to penetrate intact mucus membranes, *Aspergillus* is usually considered to cause infections in maxillary sinus as a result of the inhalation of the airborne spores of *Aspergillus* that are ubiquitous in the environment.^{1,3} According to the aerogenic theory, the accumulation of fungal spores in the maxillary sinus may become pathogenic under relatively anaerobic conditions.⁹ However, unlike the other paranasal sinuses, *Aspergillus* spores may also be transmitted to the maxillary sinus through an iatrogenic pathway associated with dental procedures.^{1,10}

Recently, an increasing number of researchers have suggested that because of the close relationship between the antral teeth and sinus floor, dentogenic factors increase the risk of aspergilloma of the maxillary sinus.^{9,11} Tomazic et al.⁹ suggested that if a dentogenic factor is present, the risk of developing an aspergilloma is 2.7-fold higher than in unaffected sinuses. Dental procedures are thought to be able to cause massive fungal inoculation of the maxillary antrum as a result of perforation of the sinus membrane.⁸ Additionally, dental materials that contain heavy metals (e.g., zinc), such as root canal sealer, gutta-percha, silver cones, and amalgam, may penetrate into the sinus during dental procedures and provide favorable conditions for the growth of *Aspergillus* species.^{4,11} Although eugenol in dental mate-

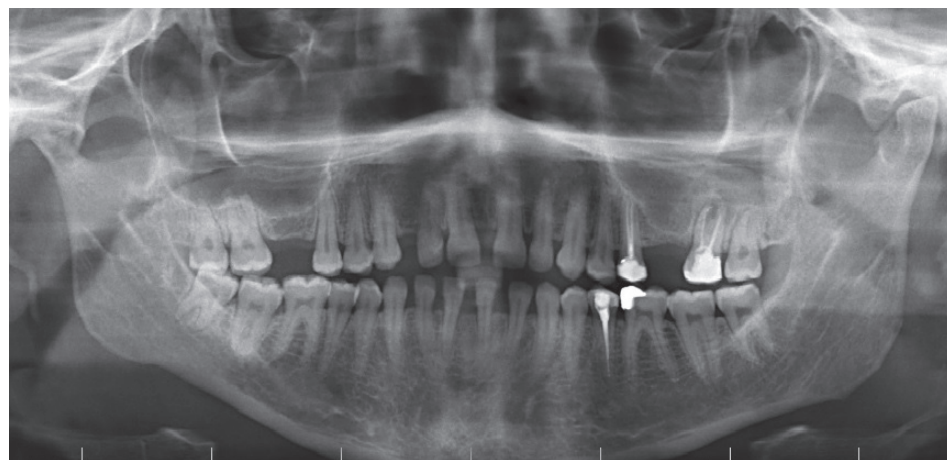


Fig. 8. Postoperative panoramic radiograph of the sinus at 1-year follow-up.

Table 1. Published cases of aspergilloma of odontogenic origin in the literature

Author Year	Age-Sex	Systemic status	Site	Symptoms	Etiology	FBS	DOS	Imaging modality	Surgical approach	Antifungal therapy	Follow-up
Axelsson et al. 1978 ¹⁸	36-F	NC	L	P, NO, R	Extraction-NA	-	6Y	NA	CL	-	3Y
Kawana et al. 1987 ¹⁹	47-M	NC	L	S, P, F, ND	Extraction-26	Root	22Y	W	CL	-	NA
De Foer et al. 1990 ¹⁰	31-F	NA	L		Imp. surgery-25	Implant	6M	NA	CL	-	9Y
De Foer et al. 1990 ¹⁰	31-F	NA	R	P	Extraction-16	-	3M	NA	CL	-	6Y
De Foer et al. 1990 ¹⁰	30-M	B	L	-	RCT-26	Sealer	10M	NA	CL	-	4Y
De Foer et al. 1990 ¹⁰	35-F	NA	L	S, P	RCT-25,27	Sealer	NA	NA	CL	-	1Y
De Foer et al. 1990 ¹⁰	35-F	NA	L	-	RCT-26	Sealer	12M	NA	CL	-	7Y
De Foer et al. 1990 ¹⁰	56-M	NC	R	NO, R	Extraction-13	Root	1M	NA	CL	-	5M
Kobayashi 1995 ²⁰	22-F	NA	R	-	RCT-15,16	Gutta		PAN	CL	-	8Y
Falworth et al. 1996 ¹	41-F	NA	L	P	RCT-24	Sealer	6M	OM, PAN	CL	-	1Y
Ogata et al. 1997 ¹⁷	58-M	NA	L	PD	Extraction-NA	Antrolith	NA	CT	CL	Amphotericin B	6M
Khongkhunthian et al. 2001 ⁴	25-F	NC	R	-	RCT-16	Sealer	NA	PAN, W	A	-	NA
Khongkhunthian et al. 2001 ⁴	25-F	NA	L	P, S	RCT-14	Sealer	2Y	PAN, W	A	-	NA
Horre et al. 2002 ²¹	28-F	NC	R	P	RCT-16	ZOE	10Y	PAN, W	NA	Antifungal	NA
Martins et al. 2004 ²²	30-F	NC	L	S, NO, PD	RCT-27	Sealer	NA	W	CL	Itraconazole	12M
Majaz et al. 2004 ¹¹	22-NA	NA	L	S, P	RCT-26	Sealer	1Y	PAN	ESS	-	4M
Giardino et al. 2005 ¹⁵	60-M	NC	R	NA	RCT-15	Sealer	2Y	PAN, CT	CL	-	1Y
Burnham et al. 2009 ⁸	46-M	NA	R	P, NO, ND	Extraction-17	Amalgam	2Y	CT, OM	FESS	-	6M
Sohn et al. 2009 ⁷	48-M	NC	R	-	Bone grafting	Graft	6M	CT, PAN	CL	-	15M
Bosi et al. 2010 ²³	78-F	NA	L	P	RCT-26	Sealer	6M	CT	ESS	-	NA
Sato et al. 2010 ⁶	50-M	NC	L	S	Imp surgery-Zygomatic	Implant	12M	CT	SE	-	12M
Fanucci et al. 2013 ¹⁴	54-F	NA	L	Sin, P, R	RCT-26	Sealer	2Y	PAN, CT	CL	-	NA
Guivarc'h et al. 2015 ¹²	64-NA	PR, D	R	Sin	RCT-16	Sealer	NA	CT	CL	-	6M
Urs et al. 2015 ³	35-F	NC	L	P, S	Extraction-25	Root	1M	CECT	NA	Itraconazole	6M
Vinciguerra et al. 2016 ¹⁶	34-M	NC	B	-	RCT-15,16,25,26	Sealer	-	PAN, CT	ESS	-	12M
Harada et al. 2017 ⁵	59-F	NC	L	NO, ND, P, S	Imp. surgery-NA	Implant	4Y	PAN, CT	CL	-	12M
Cansiz et al. 2017 ²⁴	32-F	NC	L	NO, ND	SARPE	-	2W	CT	FESS	-	3M
Present case 1 2017	54-F	NC	L	NO	RCT-26	-	6Y	PAN, CBCT	CL	-	12M
Present case 2 2017	41-F	A, RF	L	P	Extraction-26	Root	13Y	PAN, CBCT	CL	-	12M

NA: not available M: male F: female NC: non-contributory, B: Behçet, D: diabetes, PR: psoriatic rheumatism, A: asthma, RF: Raynaud phenomenon, R: right, L: left, S: swelling, P: pain, F: fever, ND: nasal discharge, NO: nasal obstruction, PD: purulent discharge, R: rhinorrhea, NB: numbness, Sin: sinusitis, RCT: root canal treatment, FBS: foreign body in maxillary sinus, M: month, Y: year, DOS: duration of symptoms occur, CL: Caldwell-Luc, LR: lateral rhinoscopy, A: antroscopy, ESS: endoscopic sinus surgery, FESS: functional endoscopic sinus surgery, SE: sinusotomy, SARPE: surgically assisted rapid palatal expansion

rials has a fungicidal effect, it loses its inhibitory function when it penetrates into the sinus, enabling heavy metals to promote fungal growth.¹² Furthermore, dental procedures that perforate the sinus membrane can cause mucociliary paralysis and mucosal hyperemia, resulting in epithelial dysfunction in the maxillary sinus.⁶ Due to disturbances in mucociliary action, the natural sinus drainage deteriorates and an anaerobic environment associated with local tissue hypoxia occurs.⁸

Among the published cases of aspergilloma associated with dental procedures, the predominant etiologic factor is root canal treatment, but aspergilloma associated with dental implants, extraction, or grafting procedures has also been reported.^{4,5,7,10} In the studies of Tomazic et al.⁹ and Legent et al.,¹³ it was reported that 84% and 96% of patients with aspergilloma had undergone previous root canal therapy, respectively. Similarly, several cases of aspergilloma in the literature have been detected in sinuses that had been perforated by a previous dental procedure, while the contralateral side remained unaffected (Table 1).^{1,3-8,10-12,14-24} Root canal treatment and the displaced root were considered to be etiologic factors for the occurrence of aspergilloma in our cases.

From a clinical point of view, aspergilloma is usually underestimated because the infection only becomes symptomatic after a long period of fungal contamination.⁵ It was reported that in 29% of patients, aspergilloma was diagnosed 1 year after the onset of symptoms because of the noninvasive character and slow progression of the lesion.¹⁴ Giardino et al.¹⁵ reported a case of aspergilloma that arose 2 years after root canal therapy. In another case, Sohn et al.⁷ reported a case of *Aspergillus* 1 year after the patient had undergone sinus bone grafting. However, in some cases, the time of onset of the infection was shorter.⁶ In our cases, the fungal infections were detected 6 and 13 years after the dental procedures, respectively. Thus, it is critical to ensure adequate follow-up after dental treatment involving the maxillary sinus.

Panoramic radiographic examinations are a straightforward way to evaluate the maxillary sinus bilaterally for the diagnosis of aspergilloma.¹⁴ Maxillary sinus aspergilloma is usually seen unilaterally, and bilateral lesions are very rare.^{1,4} However, a case of bilateral maxillary-ethmoidal sinus aspergilloma that occurred after bilateral endodontic treatment was reported by Vinciguerra et al.¹⁶ The pathognomonic iron-like density could be seen incidentally on panoramic radiography or on the Waters view.^{4,7} This characteristic appearance is due to high levels of calcium phosphate in the intracellular milieu of the necrotiz-

ing *Aspergillus* cells, and in some cases may result from accumulation of the heavy metals that were pushed into the sinus with the dental materials.^{7,8,10} A more precise examination with computed tomography (CT) may be necessary to exclude other sinus diseases, such as antrolith, osteoma, mucocele, B cell lymphoma, squamous cell carcinoma, adenoid cystic carcinoma, and inflammatory myofibroblastic tumors, from the differential diagnosis.¹⁴ The extent of the lesion, bone involvement, and erosion can also be evaluated using CBCT, which requires a lower radiation dose, is cost-effective, and is not time-consuming.¹⁴ Magnetic resonance imaging (MRI) can also be helpful, as decreased signal intensity on T2-weighted MRI has been described as characteristic of aspergilloma, and MRI can also help clinicians to differentiate aspergilloma from inflammatory or neoplastic changes.^{1,10}

The treatment of aspergilloma primarily consists of surgical removal of the lesion. Both the Caldwell-Luc and endoscopic techniques can be used.^{4,8} In most of the reported cases, the Caldwell-Luc procedure was used successfully for the management of aspergilloma.^{5,10,12,14,17} Systemic antifungal therapy is not generally required. However, if symptoms persist for a long time after surgery, an oral antimycotic drug may be required as an additional therapy.⁷ Nonetheless, clinicians should be careful about using these drugs because of severe adverse effects, such as nephrotoxicity.⁶ Since bacterial superinfection can cause acute sinusitis attacks, an appropriate antibiotic therapy is recommended in order to avoid bacterial coinfections.¹

Different types of dental procedures that involve the maxillary sinus may facilitate the occurrence of fungal sinusitis, which shares similar features with other infections of the sinus. Clinicians should be aware of the possibility of fungal etiology, especially in cases resistant to treatment, and should follow the patient periodically if sinus perforation occurs during a procedure to minimize toxicity, costs, and other complications because of an inappropriate treatment strategy. Although the management of aspergilloma is much simpler than the management of the invasive form of aspergillosis, delays can occur in management because the likelihood of fungal origin may be underestimated. Thus, diagnostic tools, especially imaging modalities, play a crucial role in detecting aspergilloma, which is usually an incidental finding. CBCT can provide useful information to clinicians about the location and the extent of the lesion.

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