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Original Article

Orofacial soft tissues actinomycosis: A retrospective, 10-year single-institution experience

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KEYWORDS
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Abstract *Background/purpose:* Actinomycosis is a rare disease. It can often mimic other infectious or malignant diseases, and it is often misdiagnosed. Therefore, it is necessary to provide clinicians with clinical findings of patients with actinomycosis as many cases as possible. The aim of this study was to analyze the clinical features of actinomycosis of the orofacial soft tissues from the clinical data of the patients at the department in the past 10 years.
Materials and methods: A retrospective study was designed, and the general characteristics of the patients, and the clinical characteristics of actinomycosis, including the initial diagnoses, the treatment methods, and the treatment outcomes, were studied.
Results: Nine patients were included in the study. Initially, they were diagnosed with various diseases and treated by extraoral or intraoral surgical procedure with the administration of antibiotics. All patients were diagnosed with actinomycosis histopathologically, and lesions were cured.
Conclusion: The diagnoses of actinomycosis is often challenging. The histopathologic examination may provide the most valuable information for clinicians than any other examination. In most cases of actinomycosis of the orofacial soft tissues, clinicians should consider the methods of treatment along with the administration of penicillin because it is a chronic disease and usually has a good prognosis.

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Introduction

Actinomycosis is a rare disease, chronic, and slowly progressive granulomatous disease caused by gram-positive anerobic and microaerophilic bacteria (genus *Actinomyces*).[1–3] *Actinomyces* species are commensal in human open cavities, including the mouth, and the most common pathogenic species encountered is *A. israelii*.[2] In addition, coinfection by other organisms is common, and common symptoms include fever, chronic painless or painful soft-tissue swelling, and fistula.[1–3] However, it sometimes develops without these symptoms and is characterized by a wide range of clinical presentations, including nonspecific symptoms.[1–3] In developed countries, the incidence of actinomycosis has declined because of improvements in oral health and susceptibility to a broad range of antibiotics.[1]

Actinomycosis often mimics other infectious or malignant diseases, and it is often misdiagnosed.[1–3] Thus, surgical biopsy may play an important role in its diagnosis.[2] Actinomycosis is usually treated with the long-term administration of penicillin, but patients diagnosed with it may not avoid surgical procedures.[1,2]

Orocervicofacial actinomycosis is the most common form of this disease, and almost 70% of orocervicofacial infections are caused by *A. israelii* and *A. gerencseriae*.[1] Orocervicofacial actinomycosis is usually associated with dental treatment or trauma to the oral cavity, and it occurs in patients with poor oral health.[1] Differential diagnoses of orocervicofacial actinomycosis, abscess by other typical bacteria, cysts, and tuberculosis can be considered.[1] In addition, there is a problem with the differentiation of actinomycosis from malignant diseases because lesions may develop a firm woody character.[1,3] A previous study about medication-related osteonecrosis of the jaw suggested that *Actinomyces* in the resected specimens could not be a predictor of treatment outcome after surgical procedures, although it may be an important factor affecting that disease.[4]

Although there have been some case reports of actinomycosis of orofacial soft tissues, there have not been case series from a single institution. The aim of this study was to analyze the clinical features of actinomycosis of orofacial soft tissues from the clinical data of patients at a single department in the past 10 years. Additionally, some cases with difficult differential diagnoses were presented in this article.

Materials and methods

We designed a retrospective study and analyzed all patients histopathologically diagnosed with actinomycosis of the orofacial soft tissues who received treatment at the Department of Dental and Oral Surgery of University of Fukui Hospital from April 2009 to March 2019. The general characteristics of the patients and the clinical characteristics of actinomycosis, including the initial diagnoses, the treatment methods, and the treatment outcomes, were studied.

This study was approved by the Institutional Research Board (Ethics Committee of the University of Fukui, Faculty of Medical Sciences, No. 20190022). Informed consent was obtained from the patients for publication of this study.

Results

Nine patients (three men and six women) were included in the study (Table 1). The youngest was 28 years old, and the oldest was 81 years old. Their mean age ± standard deviation was 67.9 ± 15.8 years. Eight of these patients were older than 60 years. Regarding the sites affected by *Actinomyces*, two patients required extraoral procedures for the treatment of lesions, and seven patients were affected in the oral cavity. All patients were histopathologically diagnosed with actinomycosis.

Extraoral lesion

The cases requiring the extraoral procedure were found to have subcutaneous indurations in the cheek and the submandibular region. At the first visit, facial and neck skin lesions, including fistula and redness, were not found, and the patients complained of swelling but no pain (Table 2). Laboratory examinations at the first visit of two patients who required extraoral procedures did not show elevated total white blood cell counts (mean, 7100/μL; range: 5600–8600/μL) but had slightly elevated serum C-reactive protein levels (mean, 0.62 mg/dL; range: 0.28–0.97 mg/dL). Therefore, tumors such as minor salivary gland tumors or metastatic tumors were suspected at the initial diagnosis in these patients (Table 3). The treatment details of these patients are described below (Table 4).

In the patient with the cheek lesion (Fig. 1A), enhanced CT showed a moderately enhancing soft-tissue mass but no abnormal bone destruction in that region (Fig. 1B). On the MRI, a T1-weighted image showed a low signal intensity,

Table 1 The general characteristics of patients.

	Cases (n)	(%)
Gender		
Men	3	33.3
Women	6	66.7
Age		
20–29 years	1	11.1
30–39 years	0	0
40–49 years	0	0
50–59 years	0	0
60–69 years	2	22.2
70–79 years	5	55.6
80–89 years	1	11.1
Location of actinomycosis		
Extraoral lesion	2	22.2
Cheek	1	11.1
Submandibular region	1	11.1
Intraoral lesion	7	77.8
Maxillary alveolar region	2	22.2
Mandibular alveolar region	3	33.3
Buccal	1	11.1
Tongue	1	11.1

Table 2 The subjective symptoms.

	Cases (n)	(%)
Subjective symptoms		
Extraoral lesion	2	100
Swelling	2	100
Intraoral lesion	7	100
Gingival swelling	4	57.1
Buccal swelling	1	14.3
Sore tongue	1	14.3
No symptoms	1	14.3

Table 3 The initial diagnoses.

Initial diagnoses	Cases (n)	(%)
Extraoral lesion	2	100
Tumor	2	100
Intraoral lesion	7	100
Tumor	2	28.6
Leukoplakia	2	28.6
Epulis	2	28.6
Gingival enlargement	1	14.3

Table 4 Treatment methods and outcomes.

Treatment methods	Outcomes	Cases (n)	(%)
Extraoral lesion		2	100
Surgical procedures		2	100
Biopsy		1	50.0
Excision		1	50.0
Antibiotics		2	100
CAM → CEZ → AMPC		1	50.0
CTRX → ABPC → AMPC		1	50.0
	Cured	2	100
Intraoral lesion		7	100
Surgical procedures		7	100
Biopsy		4	57.1
Excision		3	42.9
Drainage		1	14.3
Antibiotics		6	85.7
ABPC → AMPC		2	28.6
AMPC		1	14.3
CTRX		1	14.3
CEZ → CFDN		1	14.3
CFDN		1	14.3
	Cured	7	100

CAM = clarithromycin, CEZ = cefazolin sodium, AMPC = amoxicillin hydrate.
CTRX = ceftriaxone sodium hydrate, ABPC = ampicillin, CFDN = cefdinir.

and a T2-weighted image showed a high signal intensity of that lesion. Enhanced MRI revealed a moderately enhancing soft-tissue mass. ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography (FDG PET/CT) of the cheek lesion showed abnormally increased FDG uptake (Fig. 1C). Because adhesion between the lesion and the buccal mucosa was suspected by palpation, the lesion was excised with a facial skin incision performed under general anesthesia (Fig. 1D–F). The administration of penicillin was started before surgery. The findings of an intraoperative pathologic assessment suggested that it was not malignant. *Actinomyces* species were detected by histopathological examination (Fig. 2). The postoperative course was uneventful, and there was no recurrence 4 months after surgery.

Intraoral lesion

Five of seven patients affected in the oral cavity were found to have alveolar lesions, while others were found to have tongue lesions and buccal lesions. Patients complained of gingival or buccal swelling or a sore tongue (Table 2). At initial diagnosis, two patients were suspected to have leukoplakia, two of them with epulis, two patients with gingival tumors and enlargement, and one patient with a buccal tumor (Table 3). One of the two patients suspected to have epulis was pregnant, and thus, the so-called "pregnancy epulis" was suspected. Treatment for the particular two cases who required intraoral procedures are described below (Table 4).

In the nonpregnant patient suspected of having epulis (Fig. 3A), enhanced CT showed the lesion that was slightly hyperintense with strong peripheral contrast enhancement with a diameter of 30 mm without abnormal bone destruction of the right maxilla (Fig. 3B). On the MRI, a T1-weighted image showed a low signal intensity, and a T2-weighted image showed high signal intensity of that lesion (Fig. 3C). Enhanced MRI revealed a moderately enhancing soft-tissue mass. The lesion was excised under general anesthesia with an intraoperative pathological assessment. The findings of this intraoperative assessment suggested that it was not malignant. *Actinomyces* species were detected by histopathological examination. The postoperative course was uneventful, and there was no recurrence 14 months after surgery.

Discussion

Diagnosing actinomycosis in orofacial soft tissues is often challenging. The problem is to differentiate actinomycosis from malignant diseases because in both, firm woody lesions may develop, and they may be slowly progressive without nonspecific symptoms including pain.[1,2] Some previous articles reported cases of actinomycosis mimicking facial tumors, such as desmoid tumor, cutaneous tumor.[3,5] Raj et al. also reported the case of oral squamous cell carcinoma mimicking facial actinomycosis.[6] In oral soft tissues, lesions associated with *Actinomyces* of the gingiva, the tongue, the buccal, and the tonsil have been reported.[7–9] In this study, four of the cases (44.4%) were suspected to have tumors at initial diagnosis. Additionally, various antibiotics were used based on different initial diagnoses.

CT and MRI did not provide valuable information on the diagnosis of actinomycosis. Park et al.[10] reported the CT findings of seven patients with cervicofacial actinomycosis

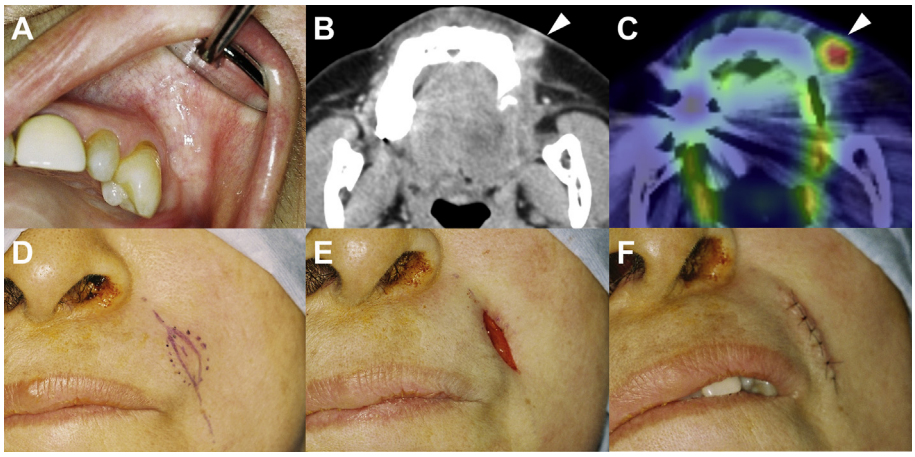

Figure 1 Clinical photographs and imaging examinations of the patient with the cheek lesion. (A) Intraoral photograph before surgery. (B) Computed tomography showed a soft-tissue mass (white arrow). (C) ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography (FDG PET/CT) showed abnormally increased FDG uptake in the cheek lesion (white arrow). (D—F) Intraoperative photographs.

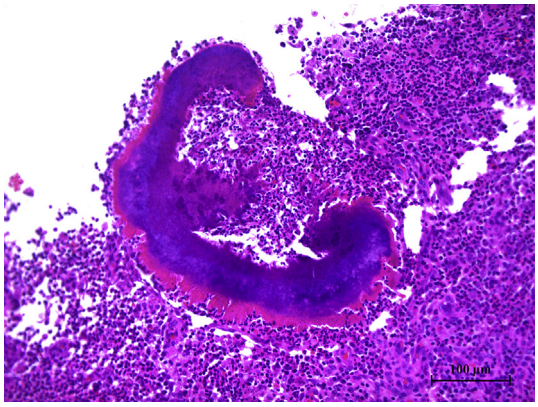

Figure 2 Histopathological examination demonstrated sulphur granules supporting the diagnosis of actinomycosis.

and the MRI findings of two of those patients. Six of seven patients showed moderate contrast enhancement, and only one of them showed mild contrast enhancement.[10] In cases examined using enhanced CT in this study, two of three cases showed moderately enhancing soft-tissue masses. Therefore, it is thought that there is consistency of findings of enhanced CT of the soft-tissue lesions associated with *Actinomyces* to some degree. However, Park et al.[10] reported that five of six patients showed moderate contrast enhancement and were suspected to have malignant diseases based on CT findings. Additionally, they reported that T1-and T2-weighted MRI showed an intermediate signal intensity associated with a moderately enhancing soft-tissue mass, which may be associated with the histological feature of abundant granulation and fibrous tissue in actinomycosis.[10] However, the T1-weighted image showed a low signal intensity, and the T2-weighted image showed a high signal intensity in the case with the cheek lesion. The results of this study suggested that CT and MRI may not be a useful imaging modalities for the differential diagnosis of actinomycosis in facial and oral soft tissues.

There have been a few reports about FDG PET/CT for actinomycosis. In a recent article regarding 28 patients with actinomycosis reported by Bonnefond et al.,[2] although the most frequent initial diagnoses suspected were malignant diseases and infections, imaging examination was performed in 82% of the patients, and only one patient was examined using FDG PET/CT. Deswysen et al.[11] reported a case of actinomycosis mimicking esophageal malignant disease, and FDG PET/CT showed abnormally increased FDG uptake in the esophageal region in that case. In this study, excluding the pregnant patient, eight patients underwent imaging examinations for differential diagnosis. Two of

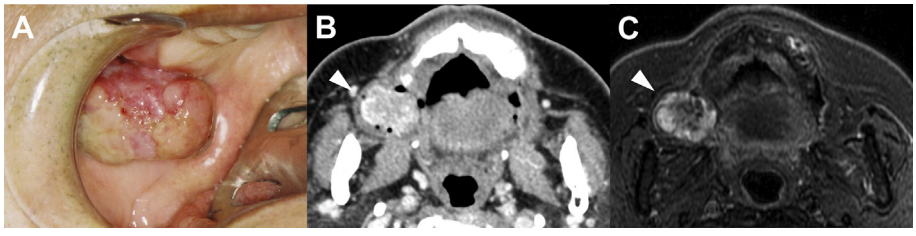

Figure 3 Clinical photograph and imaging examinations of the nonpregnant patient suspected of having epulis. (A) Intraoral photograph. (B) Computed tomography showed the lesion (white arrow). (C) T2-weighted magnetic resonance imaging showed high signal intensity in the lesion area (white arrow).

eight patients were examined using FDG PET/CT, and they showed abnormally increased FDG uptake in the lesions. Although the usefulness of FDG PET/CT is well known, it may be one of the factors confusing clinicians with regard to the diagnosis of actinomycosis because infection, inflammation, and malignant disease cause abnormally increased FDG uptake.

In histopathological examination, Gram positive filamentous organisms and sulphur granules that are colonies of organisms strongly support the diagnosis of actinomycosis.[1] These colonies appear as round or oval basophilic masses with eosinophilic terminal on staining with hematoxylin-eosin.[1] On the other hand, direct isolation of the organism is important for diagnosis in microbiologic examination.[1] In this study, *Actinomyces* were detected only on histopathological examination in two of two cases with both microbiologic and histopathologic examination. These results suggest that surgical procedures, including biopsy with histopathological examination, may provide more valuable information for clinicians than microbiological examinations. However, Bonnefond et al.[2] reported actinomycosis in various organs, and 50% of those patients were diagnosed by microbiological examinations, 42% by histopathological examination, and 7% by both methods. The detection rate of *Actinomyces* by microbiological and histopathological examinations may change depending on the organ. If possible, clinicians should perform both microbiological and histopathological examinations. Compared to the inner organs, biopsies are relatively easy to perform in orofacial soft tissues. Thus, biopsy should be considered for firm woody lesions.

In conclusion, the diagnosis of actinomycosis in orofacial soft tissues is often challenging. If actinomycosis is suspected, histopathological examination may provide more valuable information for clinicians than any other examination. In most cases of actinomycosis of the orofacial soft tissues, clinicians should consider the methods of treatment combined with the administration of penicillin because it is a chronic disease and usually has a good prognosis.

Declaration of Competing Interest

The authors declare that no conflicts of interest related to this study.

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None.

References

1. Wong VK, Turmezei TD, Weston VC. *Actinomycosis*. *BMJ* 2011; 343:d6099.
2. Bonnefond S, Catroux M, Melenotte C, et al. Clinical features of actinomycosis: a retrospective, multicenter study of 28 cases of miscellaneous presentations. *Medicine (Baltim)* 2016;95:e3923.
3. Pant R, Marshall TL, Crosher RF. Facial actinomycosis mimicking a desmoid tumour: case report. *Br J Oral Maxillofac Surg* 2008;46:391—3.
4. Matsuda S, Yoshimura H, Sano K. Risk factors and treatments for medication-related osteonecrosis of the jaw: a 10-year single-institution experience. *J Oral Maxillofac Surg Med Pathol* 2018;30:10—6.
5. Özkan A, Topkara A, Özcan RH. Facial actinomycosis mimicking a cutaneous tumor. *Wounds* 2017;29:10—3.
6. Raj KA, Vinay K, Saikia UN, Kumaran MS. Oral squamous cell carcinoma mimicking cervico-facial actinomycosis: a rare presentation and review of literature. *J Cutan Med Surg* 2015;19:346—8.
7. Kuyama K, Fukui K, Ochiai E, et al. Pyogenic granuloma associated with *Actinomyces israelii*. *J Dent Sci* 2018;13:285—8.
8. Kurtaran H, Ugur KS, Ark N, Vuran O, Gunduz M. Tongue abscess with actinomycosis. *J Craniofac Surg* 2011;22:1107—9.
9. Samant S, Sandoe J, High A, Makura ZG. Actinomycosis mimicking a tonsillar neoplasm in an elderly diabetic patient. *Br J Oral Maxillofac Surg* 2009;47:417—8.
10. Park JK, Lee HK, Ha HK, Choi HY, Choi CG. Cervicofacial actinomycosis: CT and MR imaging findings in seven patients. *AJNR Am J Neuroradiol* 2003;24:331—5.
11. Deswysen Y, Van Ginderachter L, Dano H, Belkhir L. Mimicking oesophageal cancer: oesophageal actinomycosis. *Lancet Infect Dis* 2019;19:558.