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CASE REPORT

Intraosseous verrucous carcinoma arising from an infected dentigerous cyst—A case report

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Intraosseous verrucous carcinoma (IOVC) arising from an odontogenic cyst is extremely rare. We report a case of intraosseous verrucous carcinoma in a 74-year-old male who presented with a left mandibular swelling with recurrent pus discharge from gingiva of tooth #35. Panoramic radiography revealed an impacted tooth #34 and a large well-defined, radiolucent lesion surrounding the crown of tooth #34. The clinical diagnosis was an infected dentigerous cyst. Surgical excision of the cyst together with extraction of tooth #34 was performed. Histopathological examination showed proliferation of hyperparakeratotic stratified squamous cyst lining epithelium and down-growth of broad and bulbous epithelial ridges with pushing border invasion into the fibrous cystic wall. A verrucous carcinoma arising from an infected dentigerous cyst was diagnosed. There was no recurrence of the tumor 5 months after surgery.

Introduction

Primary intraosseous squamous cell carcinoma (PIOSCC) is a rare entity of oral cavity. It is defined as a central jaw bone carcinoma derived from odontogenic epithelia. There are three subcategories of PIOSCC: (1) a solid tumor that invades marrow spaces and induces osseous resorption, (2) squamous cancer arising from the epithelial lining of an odontogenic cyst, and (3) a squamous cell carcinoma in association with other benign epithelial odontogenic tumors.[1]

The incidence of PIOSCC is estimated to be 1—2% of all oral cancers.[2] The most common type of PIOSCC is a well-

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to moderately differentiated squamous cell carcinoma,[2] and most are arising from residual/radicular cyst.[2,3] Primary intraosseous verrucous carcinoma (PIOVC) arising from an odontogenic cyst, which belongs to a subtype of PIOSCC, is extremely rare. Only three cases have been reported in the English literature up to date.[4–6] In this article, we report a PIOVC arising from an infected dentigerous cyst in the left anterior and premolar region of the mandible of a 74-year-old male patient. Comparison of patients' demographic data, treatment, and prognosis with three previously reported cases are also presented and discussed.

Case report

A 74-year-old male patient complained of a swelling with mild pain at teeth #34 and #35 area for 6 months. He noticed it because of pus discharge from the lingual gingiva of tooth #35. He visited a local dental clinic, where antibiotics and analgesics were prescribed for the patient without a definite diagnosis. The symptoms subsided after medication but the swelling persisted. He ignored it until biting pain and severe mobility of tooth #35 developed 2 months ago. He did not seek treatment and took some medicines bought from a local pharmacy. Although he felt better after medication, the swelling was still present. On August 12, 2011, pus discharge recurred and increased in amount than that of the previous episode. He visited the Department of Dentistry, Oral Medicine Center, Chung Shan Medical University Hospital and asked for treatment.

Extraoral examination showed no significant facial asymmetry or cervical lymphadenopathy. Intraoral examination revealed a swelling at the lingual side of the left lower canine and premolar area. Mobility grade II (tooth mobility more than 1 mm) of tooth #35 was noted. The mandibular occlusal radiograph revealed a prominent lingual cortical plate expansion from tooth #33 to #35 (Fig. 1A). Panoramic radiography demonstrated an impacted tooth #34 with a large well-defined, radiolucent lesion surrounding the crown of tooth #34. The radiolucent lesion extended from the periapical area of tooth #31 to the mesial aspect of tooth #36 (Fig. 1B). It measured approximately 3.5 × 1.9 cm in diameter. Under the clinical impression of an infected dentigerous cyst, operation was suggested but delayed because the patient had hypertension and cardiovascular disease that was currently treated

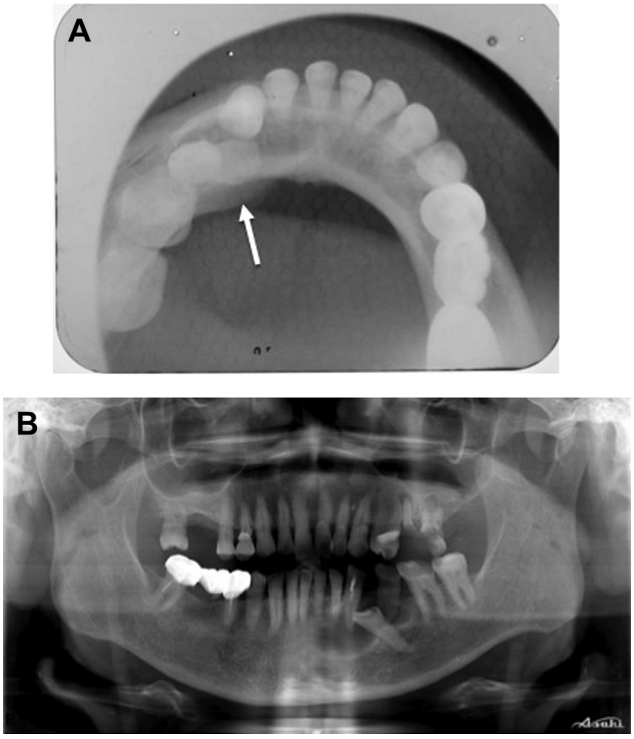

Figure 1 Radiographic images of the patient. (A) Mandibular occlusal radiograph revealing a prominent lingual cortical plate expansion from tooth #33 to #35 (arrow). (B) Panoramic radiograph demonstrating an impacted tooth #34 and a large well-defined, radiolucent lesion surrounding the crown of tooth #34. The radiolucent lesion measured approximately 3.5 × 1.9 cm in diameter and extended from the periapical area of tooth #31 to the mesial aspect of tooth #36.

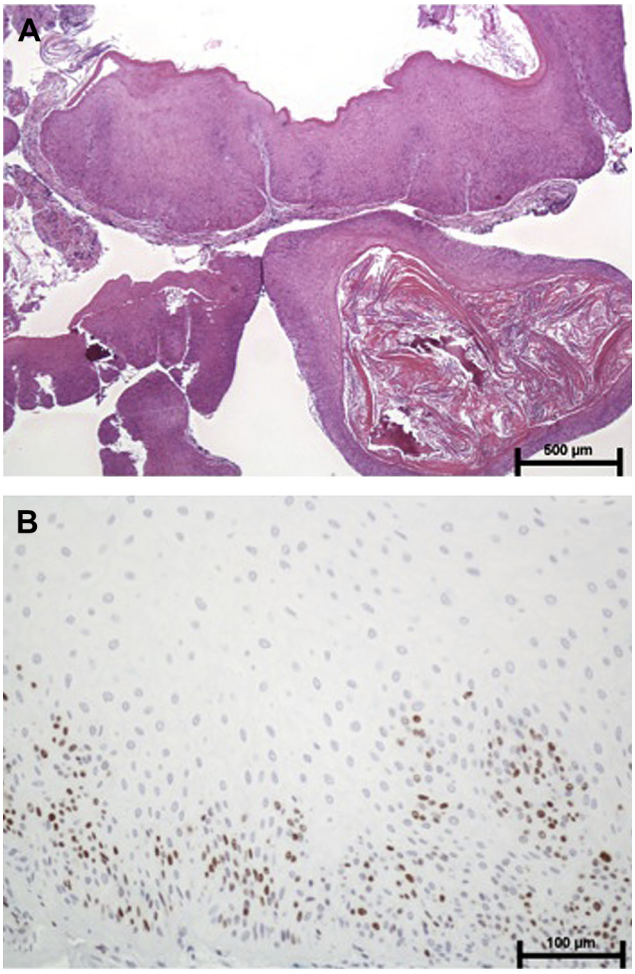

Figure 2 Histopathologic microphotographs of the incisional biopsy specimen. (A) Low-power view showing hyperparakeratotic and acanthotic stratified squamous cyst lining epithelium. Epithelial dysplasia with broad rete ridges was also seen (H&E, original magnification, 40×). (B) Immunohistochemical staining of Ki-67 demonstrating numerous positive nuclear staining at the lower one-third layer of the lining epithelium (original magnification, 200×).

with aspirin. He was arranged for extraction of tooth #35 on August 19, 2011. Incisional biopsy of the cyst wall was performed, and the histopathological diagnosis was "an odontogenic cyst with dysplasia of the lining epithelium" (Fig. 2A). Immunohistochemical staining of Ki-67 demonstrated numerous positive nuclear staining at the lower one-third layer of the lining epithelium, suggestive of a relatively high proliferation activity of the lining epithelial cells (Fig. 2B). Root canal therapy for tooth #33 was finished on September 16, 2011, and the patient was admitted for surgical excision of the cyst on October 13, 2011.

The patient's medical history included a colon cancer which was treated by surgery 39 years ago, a duodenal ulcer-induced peritonitis that was treated with surgery 6 years ago, and an abdominal fistula which was treated with surgery 3 years ago. Recently, he had hypertension and diabetes mellitus that were well controlled by medication. The patient had an areca quid chewing habit for 15 years, but had quit the habit 12 years ago. He also had been smoking cigarettes for 50 years.

Routine blood and chest X-ray examinations showed no abnormal findings. After general anesthesia, the cystic lesion together with the impacted tooth #34 was surgically removed. The specimen was subsequently sent for histopathological examination. Grossly, the surgical specimen exhibited a cystic lesion that was attached to the cervical area of the crown of an impacted tooth #34. On cutting, the inner surface of the cyst revealed prominent grayish-white verrucous projections (Fig. 3). Microscopically, it showed proliferation of hyperparakeratotic stratified squamous cyst lining epithelium and down-growth of broad and bulbous epithelial ridges with pushing-border invasion into the fibrous cystic wall. There was also a moderate chronic inflammatory cell infiltrate in the fibrous cystic wall. Transition of an odontogenic lining epithelium to a verrucous hyperplastic epithelium could be seen (Fig. 4A). Mild dysplasia, focal dyskeratosis, and atypical squamous cells with prominent nuclear and cellular pleomorphism were present. Increased mitotic figures in the basal and parabasal epithelial cells were also seen (Fig. 4B). A verrucous carcinoma (VC) arising from an infected dentigerous cyst was diagnosed. The clinical stage of the VC was stage IV because of bone involvement.[7]

The patient had an uneventful recovery after surgery. Post-operation computed tomography scan and whole-body fluorodeoxyglucose positron emission tomography scan

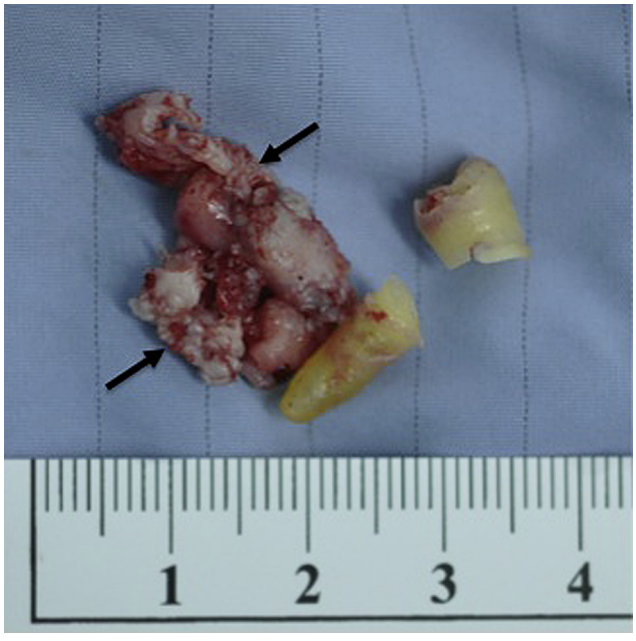

Figure 3 Gross photograph of the surgical specimen exhibiting a cystic lesion attached to the cervical area of the crown of an impacted tooth #34. On cutting, the inner surface of the cyst revealed prominent grayish-white verrucous projections (arrows).

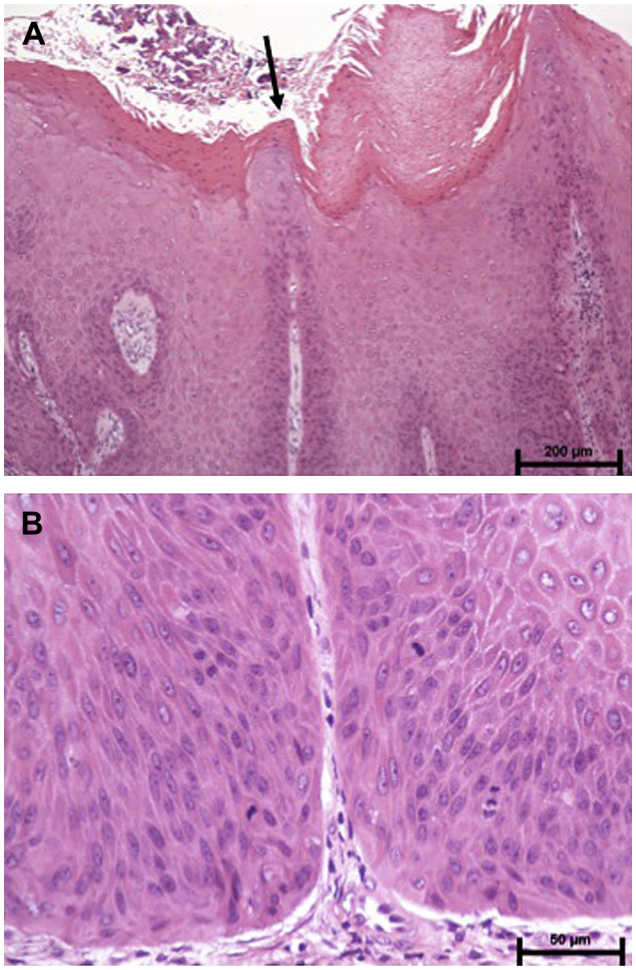

Figure 4 Histopathologic microphotographs of the surgical specimen. (A) Low-power view showing proliferation of hyperparakeratotic stratified squamous cyst lining epithelium and down-growth of broad and bulbous epithelial ridges with pushing-border invasion into the fibrous cystic wall. There was a moderate chronic inflammatory cell infiltrate in the fibrous cystic wall as well. Transition of an odontogenic lining epithelium (left to the arrow) to a verrucous hyperplastic epithelium (right to the arrow) could be seen (H&E, original magnification, 100×). (B) High-power view showing nuclear and cellular pleomorphism and increased mitotic figures in the basal and parabasal epithelial cells (H&E, original magnification, 400×).

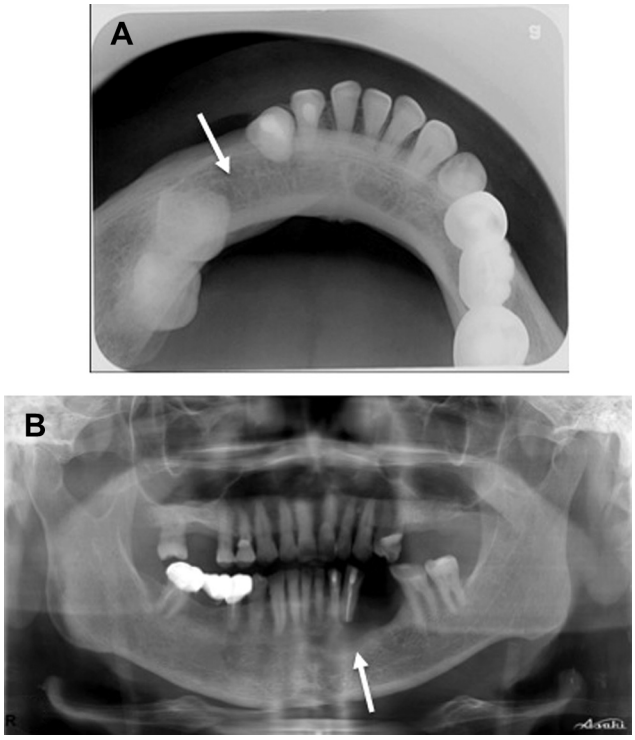

Figure 5 (A) Mandibular occlusal and (B) panoramic radiographs taken 5 months after surgery, showing a well-healed surgical bone defect (arrows).

were taken 2 months after surgery. Positron emission tomography image showed no residual tumor and regional or distant metastasis of the tumor. The computed tomography image was also unremarkable. Mandibular occlusal and panoramic radiographies showed a well-healed surgical bone defect and no recurrence of the tumor 5 months after surgery (Fig. 5A and B).

Discussion

PIOVC arising from an odontogenic cyst is extremely rare. Bodner et al[2] reviewed the literature from 1938 to 2010 and found only three cases of PIOVC arising from an odontogenic cyst. Data on age, sex, size, location, and symptoms and signs of the three reported cases and the present case are listed in Table 1. The age of the three patients ranged from 56 to 74 years, while in one patient the age was not given. There were three male and one female patients, and both jaws were equally affected. Clinically, PIOVC was reported as a swelling or a mass with or without abscesses. The size of the lesion varied from 2.0 to 3.5 cm in greatest diameter.

The definite diagnosis of PIOSCC may sometimes be difficult. Suei et al[8] proposed three criteria for the diagnosis of PIOSCC: (1) it should be distinguished from SCC of the surface oral epithelium; (2) it should be ruled out as another odontogenic carcinoma; and (3) it is not a metastatic tumor from distant primary site. Woolgar et al[7] suggested a useful criterion in which a transition between the normal cyst lining epithelium and the SCC may be present in histologic sections. Our present case fulfilled both of their criteria and would be the fourth of such a case.

The pathogenesis of PIOSCC is still unknown. The mechanisms of malignant transformation of lining epithelium in odontogenic cysts are not clear. It is still controversial that long-standing chronic inflammation appears to be a predisposing factor for malignant transformation of the cyst lining epithelium.[3,7,9] Molecular investigations revealed that genetic alterations may be involved in part of the pathogenesis.[10]

VC is a low-grade variant of squamous cell carcinoma (SCC)[11] that may arise from potentially malignant disorders, such as oral leukoplakia, oral erythroleukoplakia, or oral verrucous hyperplasia.[12] There is a significant correlation between areca quid chewing and the development of SCC and leukoplakia.[13–16] The main etiologies that cause oral SCC in Taiwan are areca quid chewing, cigarette smoking, and alcohol consumption. There are 2 million people who habitually chew areca quids[17]; approximately 80% of all oral cancer deaths are associated with this habit.[18] Of the three previously reported cases, only one patient presented by Enriquez et al[4] had a long history of cigarette smoking. In our case, the patient had an areca quid chewing habit for 15 years but had quit the habit 12 years ago. He also smoked for 50 years. Further studies are needed to elucidate whether the areca quid or tobacco carcinogens in the bloodstream may circulate to the chronic inflammatory site to induce a PIOSCC or a PIOVC.

The treatment, follow-up period, and prognosis of the four PIOVC cases are shown in Table 2. The treatment of choice for a VC is surgical excision without radical neck dissection because metastasis of VC is extremely rare.[11] In three of the four cases, surgical excision was the treatment modality, whereas one patient received enucleation of the lesion. All patients did not accept any form of neck dissection. There is no recurrence or metastasis of tumor observed in the follow-up period ranging from 5 to 48 months.

Table 1 Age, sex, size, location, and symptoms and signs of the four patients with an intraosseous verrucous carcinoma arising from an odontogenic cyst.

Authors (year of publication)	Age (y)	Sex	Size (mm)	Location	Symptoms and signs
Enriquez et al (1980)	56	Male	20 × 20	Right mandible	A draining mass
Pomatto et al (2001)	Young woman	Female	[a]	Left maxilla	Recurrent abscesses
Mohtasham et al (2008)	58	Male	35 × 25	Right maxilla	Exophytic polypoid mass
Peng et al	74	Male	35 × 19	Left mandible	Swelling and recurrent pus discharge

[a] From tooth #26 to the posterior wall of the maxillary tuberosity.

Table 2 Treatment, follow-up period and prognosis of the four patients with an intraosseous verrucous carcinoma arising from an odontogenic cyst.

Authors (year of publication)	Treatment	Follow-up period (mo)	Prognosis
Enriquez et al (1980)	Surgical excision (*en bloc* resection)	48	No recurrence or metastasis
Pomatto et al (2001)	Surgical excision	8	No recurrence or metastasis
Mohtasham et al (2008)	Enucleation	20	No recurrence or metastasis
Peng et al	Surgical excision	5	No recurrence or metastasis

We reported a case of PIOVC arising from an infected dentigerous cyst in a 74-year-old male patient. The tumor was treated by surgical excision. After a 5-month follow-up, radiographic images showed a well-healed surgical bone defect. No recurrence or metastasis of the tumor was found. Although the pathogenesis of PIOSCC or PIOVC is still unknown, we suggest that it may arise from the lining epithelium of an odontogenic cyst after long-term stimulation from a chronic inflammatory process induced by repeated infections. Because of the excellent prognosis of VC following surgical resection, it is mandatory to correlate the clinical and histopathological findings when establishing a diagnosis.

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