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Contents

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REVIEW

- 1535 Intracranial pressure monitoring: Gold standard and recent innovations
Nag DS, Sahu S, Swain A, Kant S
- 1554 Role of the brain-gut axis in gastrointestinal cancer
Di YZ, Han BS, Di JM, Liu WY, Tang Q

MINIREVIEWS

- 1571 Cholestatic liver diseases: An era of emerging therapies
Samant H, Manatsathit W, Dies D, Shokouh-Amiri H, Zibari G, Boktor M, Alexander JS

ORIGINAL ARTICLE**Basic Study**

- 1582 Neural metabolic activity in idiopathic tinnitus patients after repetitive transcranial magnetic stimulation
Kan Y, Wang W, Zhang SX, Ma H, Wang ZC, Yang JG

Retrospective Study

- 1591 Neuroendoscopic and microscopic transsphenoidal approach for resection of nonfunctional pituitary adenomas
Ding ZQ, Zhang SF, Wang QH
- 1599 Safety and efficacy of transjugular intrahepatic portosystemic shunt combined with palliative treatment in patients with hepatocellular carcinoma
Luo SH, Chu JG, Huang H, Yao KC
- 1611 Leveraging machine learning techniques for predicting pancreatic neuroendocrine tumor grades using biochemical and tumor markers
Zhou RQ, Ji HC, Liu Q, Zhu CY, Liu R

Clinical Trials Study

- 1623 Development and validation of a model to determine risk of refractory benign esophageal strictures
Lu Q, Lei TT, Wang YL, Yan HL, Lin B, Zhu LL, Ma HS, Yang JL

SYSTEMATIC REVIEWS

- 1634 Hydatid cyst of the colon: A systematic review of the literature
Lataú-Córdoba MÁ, Ruiz-Blanco S, Sanchez M, Santiago-Boyero C, Soto-García P, Sun W, Ramia JM

CASE REPORT

- 1643 Colon cancer arising from colonic diverticulum: A case report
Kayano H, Ueda Y, Machida T, Hiraiwa S, Zakoji H, Tajiri T, Mukai M, Nomura E
- 1652 Endoscopic submucosal dissection as excisional biopsy for anorectal malignant melanoma: A case report
Manabe S, Boku Y, Takeda M, Usui F, Hirata I, Takahashi S
- 1660 Gastrointestinal infection-related disseminated intravascular coagulation mimicking Shiga toxin-mediated hemolytic uremic syndrome - implications of classical clinical indexes in making the diagnosis: A case report and literature review
Li XY, Mai YF, Huang J, Pai P
- 1671 A complicated case of innominate and right common arterial aneurysms due to Takayasu's arteritis
Wang WD, Sun R, Zhou MX, Liu XR, Zheng YH, Chen YX
- 1677 Multimodality-imaging manifestations of primary renal-allograft synovial sarcoma: First case report and literature review
Xu RF, He EH, Yi ZX, Lin J, Zhang YN, Qian LX
- 1686 Chronic progression of recurrent orthokeratinized odontogenic cyst into squamous cell carcinoma: A case report
Wu RY, Shao Z, Wu TF
- 1696 Gastric adenocarcinoma of fundic gland type after *Helicobacter pylori* eradication: A case report
Yu YN, Yin XY, Sun Q, Liu H, Zhang Q, Chen YQ, Zhao QX, Tian ZB
- 1703 Synchronous multiple primary gastrointestinal cancers with *CDH1* mutations: A case report
Hu MN, Lv W, Hu RY, Si YF, Lu XW, Deng YJ, Deng H
- 1711 Primary hepatoid adenocarcinoma of the lung in Yungui Plateau, China: A case report
Shi YF, Lu JG, Yang QM, Duan J, Lei YM, Zhao W, Liu YQ
- 1717 Liver failure associated with benzbromarone: A case report and review of the literature
Zhang MY, Niu JQ, Wen XY, Jin QL
- 1726 Giant low-grade appendiceal mucinous neoplasm: A case report
Yang JM, Zhang WH, Yang DD, Jiang H, Yu L, Gao F

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Chronic progression of recurrent orthokeratinized odontogenic cyst into squamous cell carcinoma: A case report

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Abstract

BACKGROUND

Orthokeratinized odontogenic cyst (OOC) is a benign odontogenic cyst. It is a variant of the common odontogenic keratocyst (OKC). This case report describes a rare malignant transformation of OOC, with the aim of raising awareness of the malignant potential of OOC and distinguishing it from OKC.

CASE SUMMARY

In August 2018, a 52-year-old man was referred to the Department of Oral Maxillofacial and Head-Neck Oncology of Wuhan University. The patient presented with severe pain in the left mandible for 2 mo, and had a 5-year history of osteomyelitis and mandibular cyst with three recurrences. His latest diagnosis by pathological examination was OOC of the left mandible with mild-to-moderate local proliferation. However, the cyst showed malignant potential by radiographic examination. We performed partial mandibulectomy and sent the lesion tissue for pathological examination. As expected, the cyst had deteriorated to moderately differentiated squamous cell carcinoma. During postoperative follow-up, the patient went for chemotherapy in September 2018 and successfully completed four cycles.

CONCLUSION

Surgeons should be more aware of OOC, which is usually benign but can become malignant.

Key words: Orthokeratinized odontogenic cyst; Cancerization; Cancer recurrence;

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Core tip: Orthokeratinized odontogenic cyst (OOC) is a benign odontogenic cyst that rarely undergoes malignant transformation. In order to highlight the malignant potential of OOC, especially in patients with a history of recurrence and inflammation, we describe a rare case of recurrent OOC that transformed into squamous cell carcinoma after the patient underwent curettage twice.

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INTRODUCTION

Orthokeratinized odontogenic cyst (OOC) has recently been described as a new odontogenic cyst, distinct from odontogenic keratocyst (OKC), by the World Health Organization (WHO). OKC is a benign odontogenic cyst that has the possibility of recurrence and malignant transformation. OOC is milder than OKC, with lower recurrence and more favorable prognosis. A variety of studies have shown that OOC is different from OKC when it comes to clinical features, histological features and immunohistochemistry. After obtaining informed consent from the patient, we reported a rare case of recurrent OOC that transformed into squamous cell carcinoma (SCC) after undergoing curettage twice, and distinguished OOC from OKC.

Clinical features

OOC commonly affects men aged 30–40 years^[1], and affects the mandible more often than the maxilla^[2], especially the mandible angle and ramus. Sometimes OOC is accompanied by impacted teeth; similar to a dentigerous cyst. If the lesion is large and extensive, the bone involved can expand^[3]. OKC is believed to be the first clinical manifestation of nevoid basal cell carcinoma syndrome (NBCCS)^[4], but OOC does not seem to be associated with NBCCS^[5]. OKC can occur at several sites simultaneously, but multiple OOC is rarely reported^[5].

Radiographic features

In imaging examinations, the lesion often shows well-defined boundaries, with or without unerupted teeth. The teeth may or may not be absorbed. Only if the cyst undergoes malignant transformation, the boundaries can be unclear.

Histologic features

OOC has a thick “onion skin-like” uniform orthokeratinized squamous epithelial lining of 4–8 cell layers, while OKC has a thin parakeratotic epithelial lining. The basal cells of OOC lack polarity and nuclear hyperchromatism, while OKC commonly displays prominent palisaded and hyperchromatic basal cells with polarity. In addition, OKC often has a corrugated surface layer of parakeratin^[6]. Light microscopy shows small daughter cysts in OKC but not in OOC, which might be related to the high recurrence rate of OKC.

Immunohistochemistry

Immunohistochemically, there are many differences between OOC and OKC. The most prominent is that OOC has less proliferative potential, which might be due to lower p63 expression. According to Sarvaiya *et al*^[3], p63 is a p53 tumor suppressor gene family member, and it is essential for terminal differentiation of epithelial stem cells and their maintenance. Varsha *et al*^[7] also found that the high level of p63 can be correlated with the aggressive behavior of OKC. In consequence, treatment of OKC might also be more aggressive. OOC has been shown to have fewer Ki67-positive proliferating cells compared with OKC, which reveals that OOC has less proliferative and malignant potential. Modi *et al*^[8] found that compared with radicular and dentigerous cysts, Ki67-positive cells were more common. Moreover, Aragaki *et al*^[9]

revealed that GLI2 (a downstream effector of Hedgehog signaling) is significantly expressed in OKC and basal cell carcinoma. Expression of keratin 17, mammalian target of rapamycin, and BCL2 is more evident in OKC than OOC. These findings support the view that OOC and OKC are separate entities.

Treatment and prognosis

There are two widely accepted methods to treat OKC and OOC: Resection or enucleation with peripheral ostectomy and decompression.

OOC used to be considered a benign variant of OKC that was unlikely to recur, and MacDonald-Jankowski found that the recurrence rate of OOC was 4%, which was less than that of OKC. It is widely believed that OKC has more malignant potential than OOC.

CASE PRESENTATION

In August 2018, a 52-year-old man was referred to the Department of Oral Maxillofacial and Head-Neck Oncology at our hospital. The patient presented with severe pain in the left mandible for 2 mo. His left mandible gradually became swollen with severe pain. He denied a family history. Oral examination revealed a 6 cm × 3 cm firm and ill-defined mass on the left mandible angle and ramus. Other physical examination results were normal. Laboratory examinations such as routine blood tests, routine urine tests and urinary sediment examination, routine fecal tests, serum tumor marker measurement, and blood biochemistry revealed no obvious anomalies. There was a cystic lesion in cone beam computed tomography (CBCT); the left mandibular angle and ramus bone density decreased irregularly; and the lesion boundaries were unclear (Figure 1-4). Combined with history and CBCT images, we considered that the OOC could be cancerous. Therefore, we performed partial mandibulectomy. The diseased tissue was obtained for pathological examination and showed pleomorphic nests of squamous cells infiltrating muscles and nerves. The results revealed moderately differentiated squamous cell carcinoma (SCC) (Figure 5). We recommended the patient for subsequent chemotherapy. Central type oral SCC can sometimes be mistaken for odontogenic SCC. However, we believe that the SCC came from OOC for the following reasons: (1) The SCC arose from the primary lesion site; (2) The central type oral SCC was rarely keratinized; and (3) Combined with clinical and radiographic features, this case conformed more to odontogenic SCC. Therefore, we were sure that the SCC arose from OOC. Besides, the patient had a 5-year history of osteomyelitis and mandibular cyst with three recurrences.

On the first visit in January 2013, his left tempus and parotid region were painful and swollen for about 1 year, and pus was leaking out of the fistula. CBCT showed that tooth 37 was lost and the root zone of 37 and the left mandible ramus had a lower density, and the mesial tissue of the lesion area formed new bone (Figure 6-9). Abscess drainage and curettage of mandibular osteomyelitis was performed, and we diagnosed osteomyelitis and mandibular cyst of the left mandible by pathological examination (Figure 10). After surgery, a fistula appeared in the left cheek with exudation of pale yellow pus, but the patient refused further treatment.

The second visit (first recurrence) was in January 2015, and the patient was diagnosed with osteomyelitis of the left mandible and fistula of the parotidomasseterica region by clinical examination. Further treatment was recommended, but the patient refused. After this recurrence, the disease deteriorated. In February 2017, the patient was admitted to our hospital again (second recurrence), but was sent to Wuhan General Hospital of Guangzhou Military Region because of sudden precordial pain with pus leaking into the thorax. After the pain alleviated and other complications were cured, he was admitted to our hospital in June 2017. CBCT showed that the left mandibular angle and ramus density decreased and the cyst had clear boundaries (Figure 11-14). Cyst curettage was performed and the pathological diagnosis was OOC of the left mandible. The cyst component had an orthokeratinized lining (Figure 15A), and the cystic epithelium showed local mild-to-moderate proliferation (Figure 15B).

FINAL DIAGNOSIS

The final diagnosis was moderately differentiated SCC.

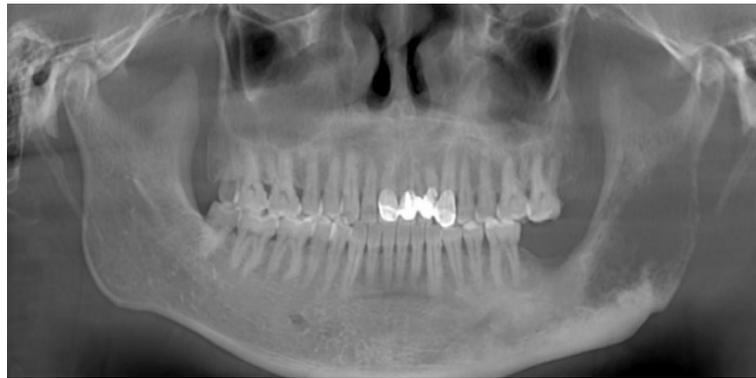


Figure 1 Orthopantomogram showed a lesion in the left mandibular gonial area and ramus with decreased density, which measured 14 mm × 32 mm × 60 mm (anterior/posterior × left/right × cranial/caudal) (August 2018, third recurrence).

TREATMENT

The patient was treated twice with curettage, partial mandibulectomy, and chemotherapy.

OUTCOME AND FOLLOW-UP

After surgery, the patient experienced pain in the surgical area. Therefore, he attended another hospital for chemotherapy in September 2018. Positron emission tomography-CT showed recurrence of the left mandibular SCC. The patient successfully underwent four cycles of chemotherapy.

DISCUSSION

This case showed low patient compliance, which might lead to missed diagnosis of cancerization. Multiple molecular factors and inflammation-cancer chain involved mechanism, and more unknown factors might play crucial roles in malignant transformation. Examination of known factors, such as p63 and Ki67 expression, although not performed in this case, might provide meaningful indications for early intervention.

Surgeons should be alert to recurrent OOC, which might change with time. Furthermore, this patient was diagnosed by pathological examination in 2017 with OOC of the left mandible with mild-to-moderate local proliferation, which was a sign of risk. On the whole, we should be more vigilant about OOC, especially recurrent and proliferative OOC.

The naming and classification of OKC and OOC have been controversial. In the 1950s, odontogenic cyst with keratin formation was designated as OKC for the first time. Afterwards, researchers found that many other cysts also form keratin; therefore, they were called keratocysts. OKC was used to describe a specific cyst in the 1992 classification. In 2005, there was a controversy between cyst and neoplasm, which involved OKC. The WHO working group recommended that OKC should be replaced by keratocystic odontogenic tumor (KCOT) for the following reasons: (1) Aggressive behavior; (2) Occurrence of a solid variant; (3) Possibility of recurrence; and (4) Mutations of the *PTCH* gene^[10]. However, some researchers debated whether gene mutations could be found in other non-neoplastic diseases such as fibrous dysplasia. In other words, the genetic variation that influences OKC can also influence other types of cysts that are not defined as neoplasms^[10]. There is also controversy about the aggressive behavior of OKC. Therefore, in 2017, the WHO working group renamed KCOT as OKC^[6]. As for OOC, it was found and described as a type of OKC in 1981^[11]. However, because of its different clinical and histological behavior, OOC was accepted as a separate entity in the 2017 classification.

OOC used to be considered as a variant of OKC and unlikely to recur, but there are rare reports about its malignant transformation^[3]. The systematic review by MacDonald-Jankowski^[12] in 2010 showed that only 4% of OOC recurred and the average age at first presentation was 35 years. Although OOC was generally believed to have benign clinical behavior, we have found two case reports of malignant OOCs.



Figure 2 Axial plane view showing cystic lesion with irregular boundaries in the mandible (August 2018, third recurrence).

The first one was a report of OOC with 8 mo of chronic inflammation, which turned into SCC^[13]. Kamarthi *et al*^[14] reported a case of OOC that turned into verrucous carcinoma after 1 year of painful swelling of the left maxillary alveolus. Beyond that, OOC is not associated with NBCCS, and differs in many aspects from other odontogenic cysts, especially dentigerous cyst and OKC. Therefore, oral and maxillo-facial surgeons should distinguish OOC from other types of odontogenic cysts and be more alert to the malignant potential of OOC with a history of recurrence and inflammation and encourage patients to have frequent visits after treatment.

CONCLUSION

This case report discussed the chronic progression of recurrent OOC into SCC. It revealed that OOC can also be cancerous. Surgeons should perform long-term follow-up and examination of OOC cases.



Figure 3 Coronal plane view showing the mandibular cortex was invaded by the cystic lesion (August 2018, third recurrence).



Figure 4 Sagittal plane view showing the left mandible was significantly damaged and teeth 37 and 38 were lost (August 2018, third recurrence).

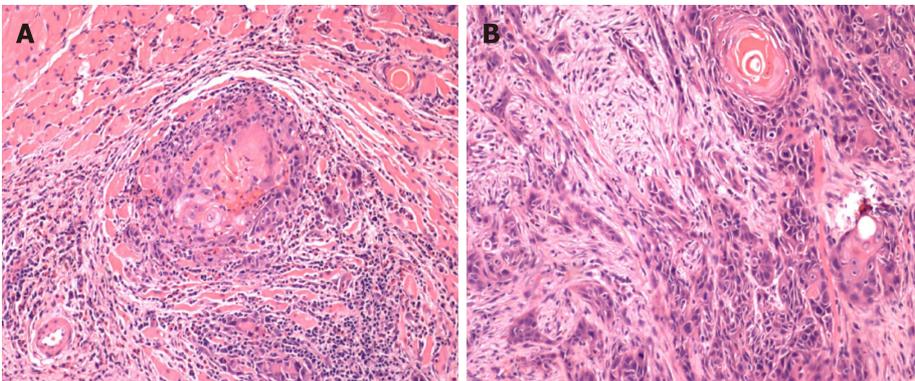


Figure 5 Pathological examination of disease tissue. A: Moderately differentiated SCC, pleomorphic nests of squamous cells infiltrated the tissue; B: Mass of squamous cells penetrated the vascular wall. August 2018, third recurrence.

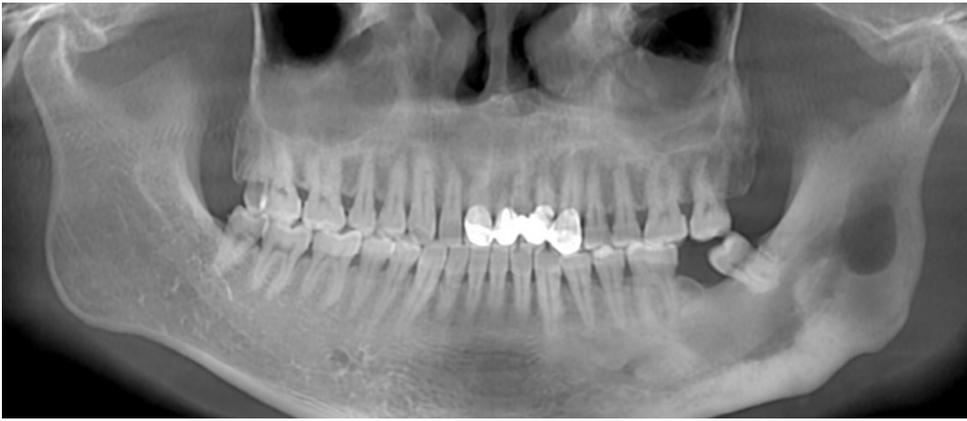


Figure 6 Orthopantomogram from cone beam computed tomography of the left mandibular angle and ramus: the cyst boundary was clear, and tooth 37 was lost (January 2013, first visit).

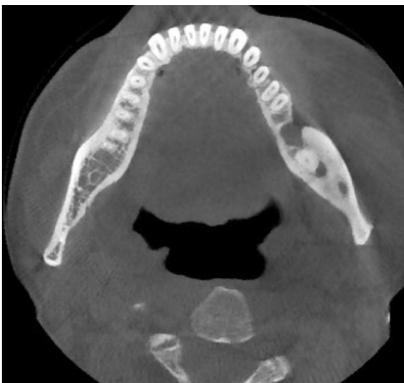


Figure 7 Axial plane of cone beam computed tomography showing the cyst lesion limited in the region of lost tooth 37 with clear margin (January 2013, first visit).



Figure 8 Coronal plane of cone beam computed tomography showing the cortical bone around the cyst incrassates but not damaged (January 2013, first visit).



Figure 9 Sagittal plane of cone beam computed tomography showing a cystic lesion with clear boundaries (January 2013, first visit).

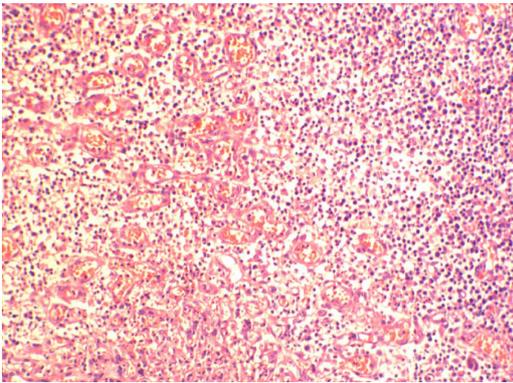


Figure 10 Pathological examination of the lesion tissue consisting of granulation and inflammatory cells (January 2013, first visit).



Figure 11 Orthopantomogram showing the cystic lesion in the left mandible angle and ramus, with area of decreased density measuring 15 mm × 25 mm × 41 mm (anterior/posterior × left/right × cranial/caudal) (February 2017, second recurrence).



Figure 12 Axial plane view of cone beam computed tomography showing that the cystic lesion was larger than in the previous image (February 2017, second recurrence).



Figure 13 Coronal plane view of cone beam computed tomography showing a regular-shaped cyst with clear boundaries (February 2017, second recurrence).



Figure 14 Sagittal plane of cone beam computed tomography showing a cyst involving the previous positions of teeth 37 and 38 (February 2017, second recurrence).

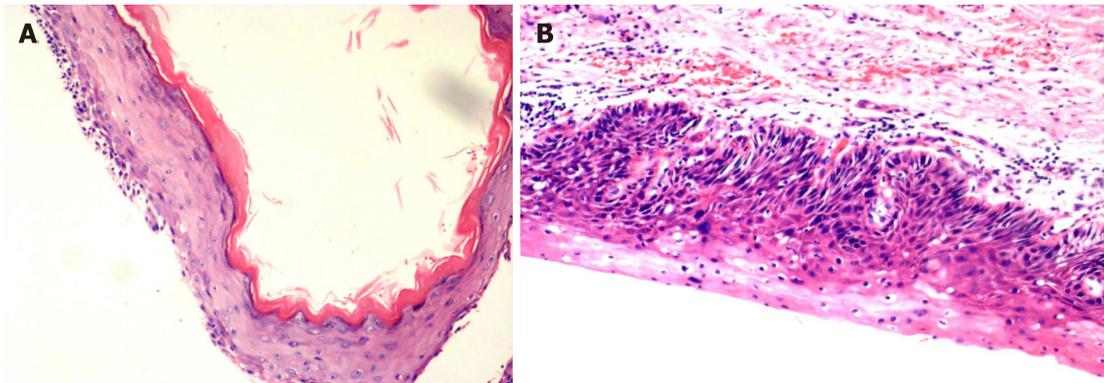


Figure 15 Pathological examination of the disease tissue showing a cyst with thick “onion-like skin” uniform orthokeratinized squamous epithelial lining (A) or mild-to-moderate epithelial dysplasia of the local lesion (B) (February 2017, second recurrence).

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