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Giant calcifying epithelial odontogenic tumor after I-125 seed implantation: A case report

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ABSTRACT

Calcifying Epithelial Odontogenic Tumor (CEOT), also known as Pindborg tumor, is a rare odontogenic benign tumor. It was first reported by Thoma and Goldman in 1946 and defined as an independent tumor by Pindborg in 1957. Herein, we reported a CEOT case involving most of the mandible after I-125 implantation in a 53-year-old man. We cooperated with governmental and hospital departments to resect the tumors, reconstruct the mandible with a fibular flap graft, and properly dispose of the radioactive particles.

Calcifying Epithelial Odontogenic Tumor (CEOT) was first proposed in 1932 by the German pathologist Heinz under the term "odontogenes Psammocarcinom". This German-language paper included one radiograph, two gross images and three photomicrographs of pericoronal CEOT [1]. In 1934, Thoma described CEOT as "adamantinoma" which was included in the initial edition of his textbook "Oral Pathology" in 1941 and retained in the 4th edition in 1954. During 1953–1958, Pindborg described three cases and introduced the concept of CEOT at the 11th Scandinavian Congress of Pathology and Bacteriology. This transaction was followed by the first of many English-language reports on the topic [2]. In 1963, Shafer used the term "Pindborg tumor". In 1971, CEOT was included in the World Health Organization (WHO) classification of odontogenic tumors [3].

CEOT is rare in the clinic, accounting for only 1% of all odontogenic tumors. CEOT can be divided into intraosseous (central) and extraosseous (peripheral) types. The intraosseous type is more common, comprising more than 90% of the cases, while extraosseous lesions account for less than 5% of the cases [4]. Additionally, CEOT lesions mainly occur at the mandible, the average age of the patients is 38.1, and the incidence frequency has an almost normal distribution. The intraosseous and extraosseous types have the same average onset age and the maxilla and mandible distribution. There is no gender difference in CEOT, but some studies have shown that the incidence of extraosseous CEOT is higher in women but with a smaller average size [5]. Clinically, CEOT is characterized by gradually swelled painless mass. The X-ray film of the intraosseous type has irregular radial light transmission area of the jaw, including light transmission masses of different sizes, some with buried teeth and sometimes cortical bone perforation. The extraosseous type can be shown as a sessile, painless, rigid, and slow-growing mass on the surface of the alveolar process in the anterior

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tooth area. In 2017, Chrcanovic and Gomez showed that the number of CEOT cases published worldwide did not exceed 400. About 50% of 264 central-type lesion cases presented cortical bone perforation, and about 40% of 24 peripheral-type lesion cases had born erosion [5]. Many scholars have contributed to the history and epidemiological data of CEOT.

CEOT can also cause facial deformities, tooth loosening, and displacement in the diseased area. If it occurs at the maxilla, patients will have symptoms such as nasal congestion, nosebleed, and headache, and maxillary tumors tend to grow rapidly and unrestricted [6]. The radiological findings of CEOT are varied and are related to the tumor's size, location, and the number of mineralized products. Moreover, CEOT can be single-room, multi-room, or non-room types. The single-chamber type is common in the clinic, which becomes mixed transmission-transmission during maturation and expansion [7]. Most CEOT masses include teeth, and mandibular first molars are common [8]. Herein, we reported a case of giant CEOT treated after I-125 implantation at the Department of Oral and Maxillofacial Surgery of our hospital in February 2022 and reviewed the literature.

1. Case report

A 53-year-old male (form Hebei Province, China; Mongoloid) was presented to the Department of Oral and Maxillofacial Surgery, complaining of a painless tumor in the left posterior mandible for 20 years. During this period, the tumor gradually increased in size with mild tenderness and was repeatedly infected without spontaneous pain. In November 2020, 80 iodine 125 (I-125) seeds were implanted into the left mandible in a private hospital, but no significant change occurred in the tumor after implantation. One month ago, a biopsy was conducted under local anesthesia in our hospital, and the tumor tissue pathology showed odontogenic calcified epithelioma. The previous history of membranous glomerulonephritis was of one year.

1.1. Clinical examination

The extraoral examination showed that the left and right sides of the maxillofacial region were asymmetrical. The left mandible was about 10 cm in diameter, rigid, had mild tenderness, and was immobile (Fig. 1). The bilateral temporomandibular joint was normal, the opening was slightly limited, the degree of mouth opening was two fingers, and no palpable cervical lymph nodes were detected. The intraoral examination revealed a dentition defect of the left mandible and a firm ulcer-like lesion uplifting from the tooth #45

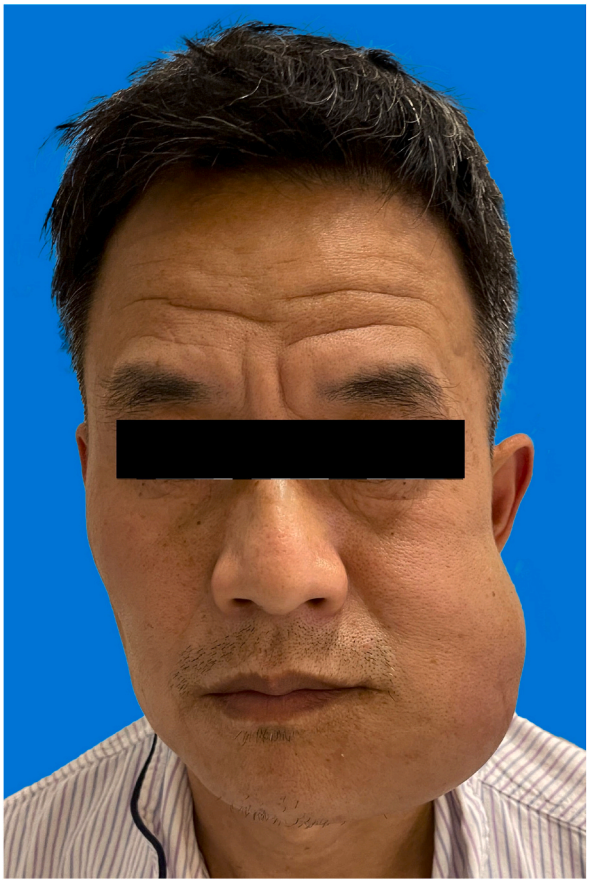

Fig. 1. The tumor on the patient's left mandible is approximately 10 cm in diameter, rigid, had mild tenderness.

buccal vestibular groove to the pterygomandibular fold. On the Cone Beam Computer Tomography (CBCT), high-density multilocular calcification was observed in the left mandible, as well as radioactive particles in the center of the tumor (Fig. 2). (We have obtained the consent from the patient for the publication of his case and images).

1.2. Treatment

Since the scope of the tumor in the patient was large, we consider extended resection of the tumor from the tooth #45 distal to the left condylar neck, and the left mandible should be removed as much as possible to reduce the risk of regional recurrence. Postoperative defects caused by tumor resection can lead to maxillofacial deformities and dysfunction. Before the operation, the compound guide plate for osteotomy and reduction of jaw and fibula was designed by digital technology (Fig. 3). According to the guide plate, segmental jaw resection and free fibula flap transplantation could be performed during the operation to reconstruct the mandible. Antibiotics were used before and after the operation to prevent infection, and albumin was infused for systemic support.

After extraction of tooth #45, we placed the prefabricated osteotomy guide plate in tooth #45 distal and left condylar neck as designed before the operation to resect the mandible. Then, we pulled the truncated mandible outward, cut the mucoperiosteum along the lingual attachment gingiva, returned to the retromolar area, extended the incision laterally, and finally connected it with the left buccal incision. Next, we cut off the muscle connected to the bone segment and the left inferior alveolar neurovascular bundle. At this point, the segmental resection of the mandible could be completed (Figs. 4, 5). The reconstruction titanium plate in the fibula segment was fixed with the nail hole of the fixed osteotomy guide plate (Fig. 6). The peroneal artery was anastomosed with the right facial artery. Due to the insufficient length of the peroneal artery concomitant vein, part of the right external jugular vein was cut off during the operation. The peroneal artery concomitant vein was anastomosed with a free right external jugular vein as a bridging vessel, and the bridged right external jugular vein was finally anastomosed with the right internal jugular vein branch. The I-125 particles belonged to long half-life radioactive sources ($T_{1/2}$: 60 d). The particles extracted from the tumor during the operation were first temporarily stored in the radioactive source bank of the Department of Nuclear Medicine for sealed preservation, then handed over to professional institutions for recovery of radioactive waste sources.

1.3. Result

Postoperative head CT showed that the titanium plate was well connected to the mandible (Fig. 7). The postoperative histopathological analysis showed that the tumor was a CEOT, had partial degeneration and necrosis, local microabscess, the tumor invaded

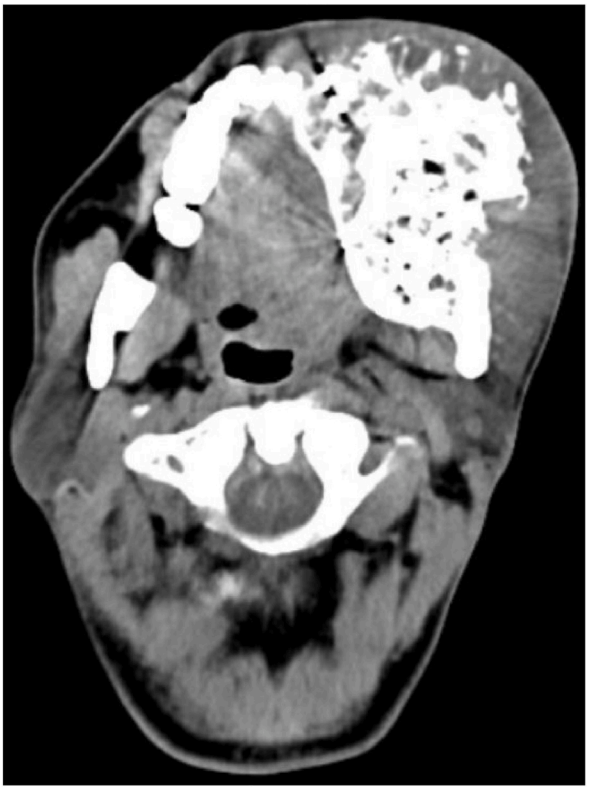

Fig. 2. From the CBCT, high-density multilocular calcification and radioactive particles can be observed in the tumor.

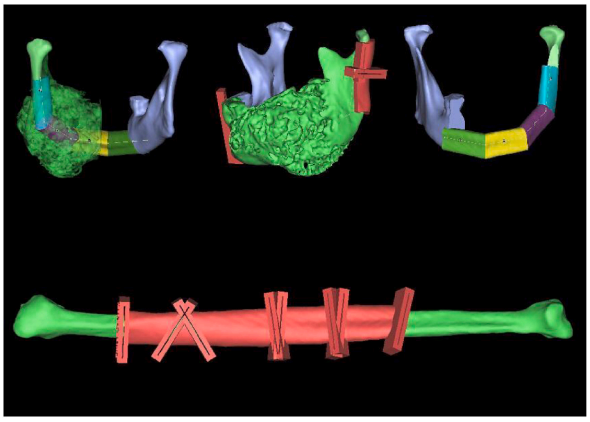

Fig. 3. The compound guide plate was designed by digital technology before the operation.

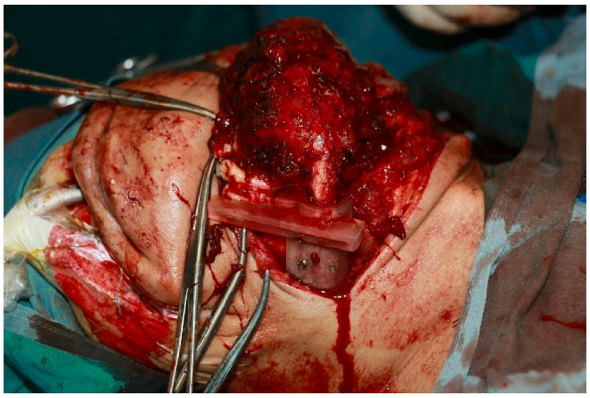

Fig. 4. Performed the segmental resection of the mandible based on the preoperative design.

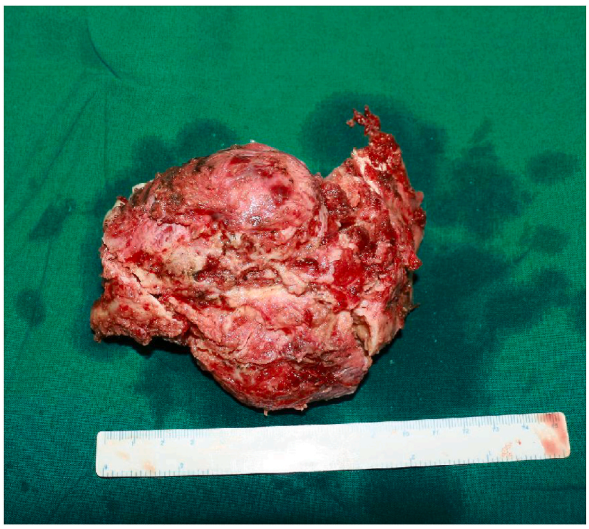

Fig. 5. The resected tumor and partial mandible bone.

the bone and surrounding tissue, and had some concentric calcification (Fig. 8), we also performed Congo red staining to highlight the focus of amyloid-like material with an apple-green birefringence (Fig. 9). Six months after the operation, the patient's facial appearance and mandibular movement returned to normal, and the transplanted fibula flap survived well. The patient had no bilateral

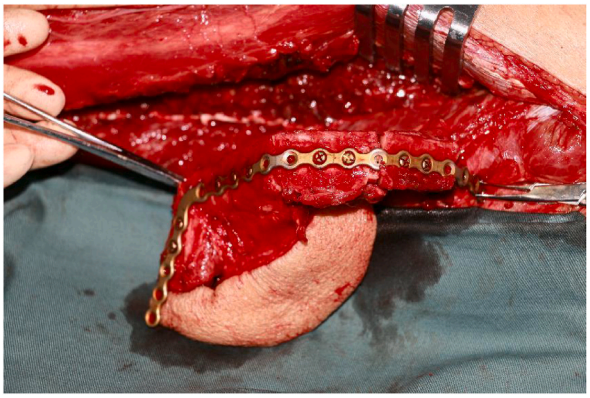

Fig. 6. The reconstruction titanium plate in the fibula segment was fixed with the nail hole of the fixed osteotomy guide plate.

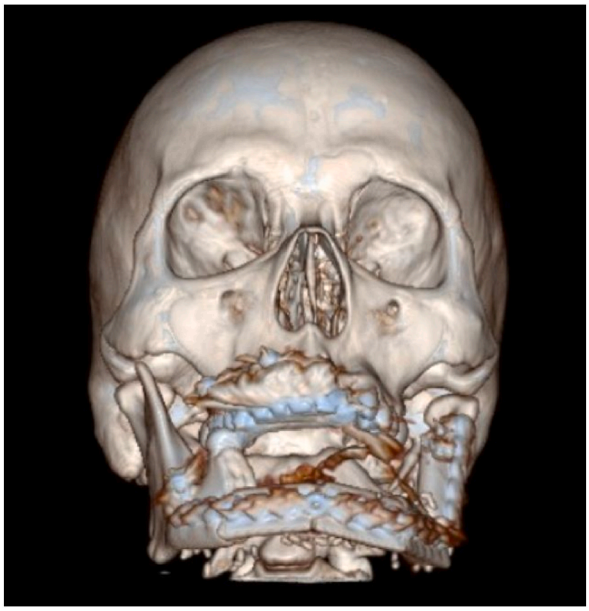

Fig. 7. Postoperative head CT showed that the titanium plate was well connected to the mandible.

temporomandibular joint pain in the occlusal and movement states and completed the restoration of the mandibular denture (Fig. 10, Fig. 11).

2. Discussion

In the case presented above, the CEOT involved most of the mandibular body and left mandibular ramus. The histopathological analyses of the lesions showed that the nucleolus of the tumor cell was large and clear, and the cell morphology was diverse, confirming the diagnosis of CEOT. However, the following neoplasms should be considered in the differential diagnosis [3,9]:

- Clear cell odontogenic carcinoma (calcification and amyloid are relatively rare);
- Primary or metastatic squamous cell carcinoma (pleomorphism and clear intercellular bridges were detected);
- Mucoepidermoid carcinoma (usually manifested as cystic changes with visible glandular tubular structures);
- Salivary gland tumors (histological examination showing salivary gland structures).

At the time of the patient's visit, 80 I-125 particles had been implanted in a private hospital one and a half years ago. The implantation of I-125 seeds can destroy DNA by radiating low-energy gamma rays, comprehending a therapeutic tool for some malignant tumors [10]. However, this is not the routine treatment for CEOT. No evidence has shown that implantation of I-125 particles effectively treats CEOT, without a reported precedent. According to the patient, no significant changes occurred in size, but the tumor

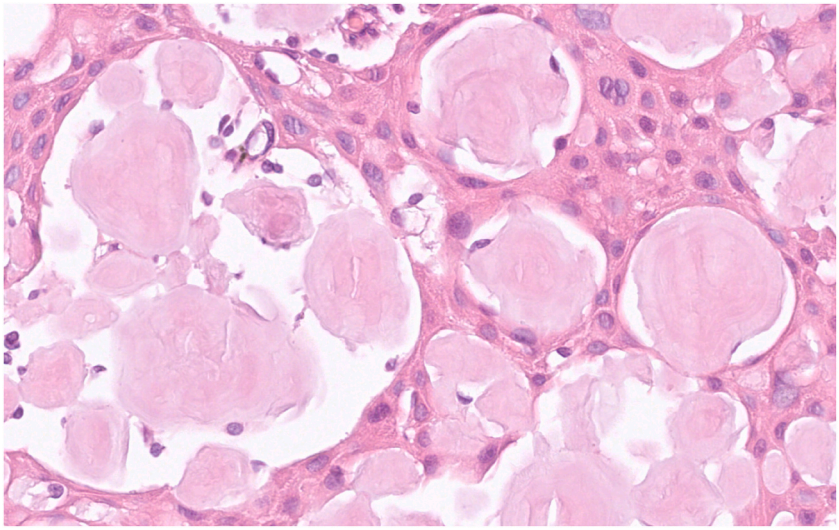

Fig. 8. Postoperative histopathological showed that the tumor had many characteristics of CEOT.

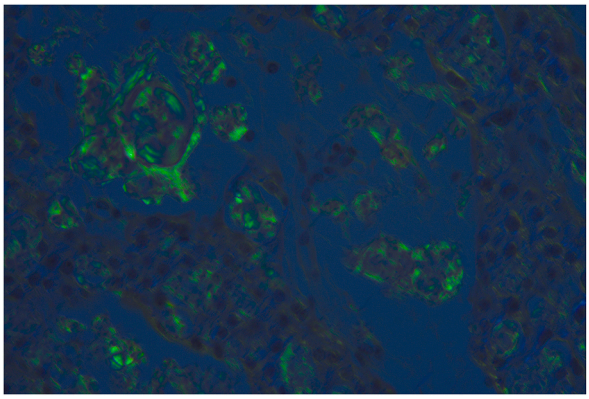

Fig. 9. After Congo red staining, the focus of amyloid-like material with an apple-green birefringence can be observed.

was repeatedly infected after the implantation. Although the implantation might also be related to the patient's reluctance to undergo surgical treatment at the time, we suggest that the implantation was not appropriate. Because of the radioactive I-125 in the tumor, we actively communicated with the local government and environmental protection department and closely cooperated with the oncology and nuclear medicine departments in our hospital to complete the operation.

The tissue origin of CEOT remains controversial. Pindborg believed it came from the retracted enamel epithelium of the embedded teeth. However, the tumor cells are similar to those in the middle layer of the enamel organ. Hence, most scholars believe it comes from the middle layer cells of the enamel organ [11]. Nevertheless, given the distribution of the tumor in the jaw, some scholars think CEOT comes from the residual epithelium of the dental plate [4].

Histologically, CEOT has unique morphological characteristics, including loose clusters or floating tumor cells. The histological hallmarks of "classic" CEOT are sheets of polyhedral epithelial cells with distinct cell borders, prominent intercellular bridges, nuclear pleomorphism, and few mitoses [12]. Mitosis and nuclear polymorphisms are rare [13,14]. The matrix was myxoid or myxoid with calcified islands with malnutrition; some showed concentric or sandy calcification. Amyloid deposition is another CEOT feature, but the source of this homogeneous material is still controversial. El-Labban believes that the amyloid protein in CEOT is derived from the degradation of the dense layer material secreted by tumor epithelial cells [15]. Moreover, PAGE performed a CEOT ultrastructural study and showed that amyloid is a protein product of enamel organs, completely different from endocrine-related or systemic amyloid. The Congo red staining showed amyloid green birefringence in the CEOT, which has been considered helpful in distinguishing CEOT from other lesions [16].

In addition to the classic type of CEOT, some histological variants have been reported, including the Langerhans cell-rich variant of CEOT, clear cell variant of CEOT (CCCEOT), CEOT with cementum-like components, and cystic or microcystic variant of CEOT [9, 17–19]. However, combined CEOT-adenomatoid odontogenic tumor is not considered to be a variant of CEOT [12]. The Langerhans cell-rich variant of CEOT is often observed in the anterior maxilla and is characterized by small nests or strands of neoplastic

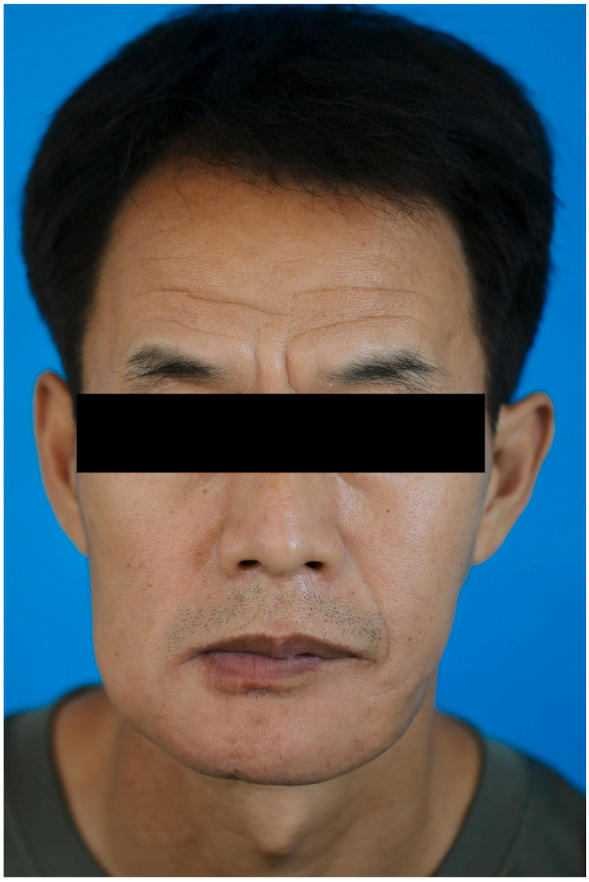

Fig. 10. Six months after the operation, the patient's facial appearance and mandibular movement returned to normal, and the transplanted fibula flap survived well.

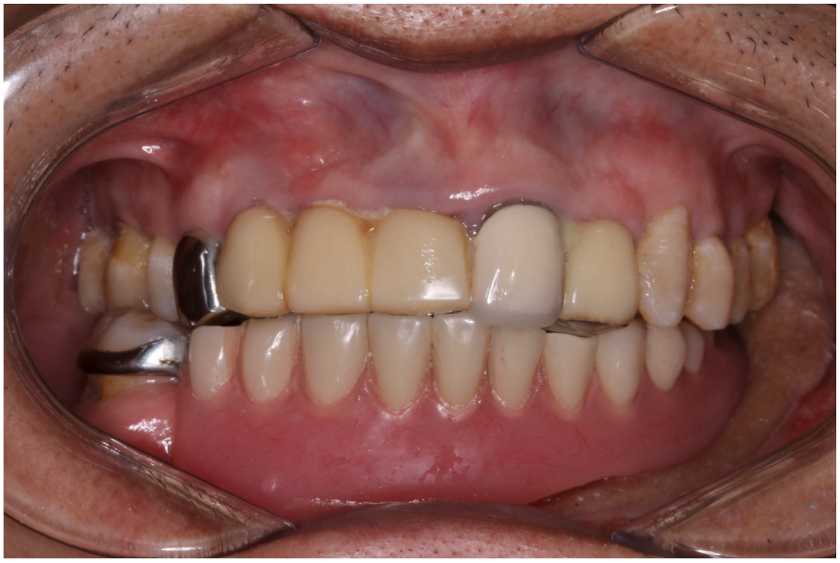

Fig. 11. The restoration of the mandibular denture is completed.

odontogenic epithelial cells scattered in the stroma of non-calcified amyloid globules and fibrous connective tissue, with clear cytoplasm scattered within the epithelium. Compared with the classical type of CEOT, the Langerhans cell-rich variant has fewer epithelial cells, smaller size, less intercellular bridges, and a spherical amyloid substance without calcification. The incompatibility between the Langerhans cell-rich variant and the classical type of CEOT in clinical, radiological, and histological aspects has led to speculation as to whether it is a variant. Some suggest that the Langerhans cell-rich variant of CEOT and amyloid rich variant of the central odontogenic fibroma are the same disease entity [20]. In approximately 8% of CEOT cases, clear cells appear completely absent of calcification [21,22]. Some scholars have described this as a characteristic of cytodifferentiation [23,24], while other believe that the absence of calcification may indicate a less differentiated of the tumor [18]. CEOT with cementum-like components is characterized by a large number of acellular, basophilic particles, cement-like material, and a small amount of calcified components with a morphology similar to bone. Very discrete intracellular calcifications are detectable at high magnification [9]. Currently, all reported cystic or microcystic variant of CEOT exhibited a mixed appearance of radiolucent and radiopaque regions. Those located in the posterior maxillary region is associated with unerupted teeth, and showing the extension of maxillary sinus. Those located in the tooth-bearing regions of the body of the mandible may exhibit root displacement or resorption, or even extend into the ramus. Besides, all cases of cystic CEOT showed significant cortical bone expansion with a mean maximum diameter of 3.3 cm [19]. The discussion of different histological variations has no significant impact on the prognosis and treatment of CEOT [19]. However, further research on different histological variations can improve our understanding of CEOT and help prevent confusion with other tumors.

Due to the clinical, radiological, and histological differences in tumors, CEOT treatment varies between patients [25], but local resection is still the primary method. Some scholars have proposed that extended resection should be adopted when the cortical bone is involved [26]. As for the reconstruction of the mandible, the consensus on the best treatment is to use a free fibula flap with blood vessels to reconstruct the defective mandible currently. Through digital-aided design before operation can improve the accuracy of the reconstruction and shorten the operation time [27]. Additionally, little bone resorption occurs after fibula osteogenesis, and the height of bone reconstruction provides suitable conditions for removable denture and implant denture [28]. However, there is still about a 15% probability of recurrence after CEOT treatment. It is speculated that most recurrence is caused by excessive conservatism or improper treatment [29]. Rare malignant transformation and metastasis cases have also been reported, mainly in cervical lymph nodes and lungs [30–32]. The recurrence rate of patients who underwent resection is low [8]. Besides, due to the slow growth of the tumor, postoperative follow-ups of 5 to 10 years or more are recommended [7,13]. Finally, we will continue the follow-up with the patient and observe if recurrence occurs.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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