

Received: 2022.05.20

Accepted: 2022.07.19

Available online: 2022.08.05

Published: 2022.09.02

# Hypoproteinemia Associated with a Gigantic Odontogenic Tumor: A Report of 2 Cases

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Statistical Analysis C  
Data Interpretation D  
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**Financial support:** None declared  
**Conflict of interest:** None declared

## Case series

**Patients:** Male, 65-year-old • Female, 60-year-old  
**Final Diagnosis:** Hypoproteinemia  
**Symptoms:** Swelling  
**Medication:** —  
**Clinical Procedure:** —  
**Specialty:** Dentistry

## Objective: Rare coexistence of disease or pathology

**Background:** Hypoproteinemia is caused by a decrease in protein level in the blood. This report describes 2 cases of hypoproteinemia associated with a gigantic odontogenic tumor.

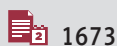
**Case Reports:** Case 1, a 65-year-old man, visited our hospital with the chief concern of swelling in the right mandible, approximately 100 mm in diameter, and ameloblastoma was diagnosed. Abscess drainage was observed in the fistula of the tumors. Total protein and albumin levels were low before surgery. Hemimandibulectomy was performed under general anesthesia. The final pathological diagnosis based on the specimen was ameloblastic carcinoma. After surgery, the total protein and albumin levels improved and remained stable 6 months after the operation. At 21 months after surgery, there were no signs of recurrence.

Case 2, a 60-year-old woman, visited our hospital with a chief concern of swelling in the left mandible, approximately 100 mm in diameter, and ameloblastoma was diagnosed. Abscess drainage was observed in the fistula of the tumors. The patient had a history of hypoproteinemia; preoperative levels of total protein and albumin were low, and edema of the body was observed before surgery. Hemimandibulectomy was performed under general anesthesia. The final pathological diagnosis based on the specimen was ameloblastoma. After surgery, the total protein and albumin levels improved, and remained stable 6 weeks after surgery. There were no signs of recurrence 9 months after surgery.

**Conclusions:** These 2 cases indicate the possibility that hypoproteinemia can be caused by plasma leakage from fistulas associated with gigantic odontogenic tumors.

**Keywords:** Hypoproteinemia • Odontogenic Tumors • Plasma Leakage • Abscess Drainage

**Full-text PDF:** <https://www.amjcaserep.com/abstract/index/idArt/937301>



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## Background

Ameloblastomas are local odontogenic tumors that occur in the mandibular and maxillary regions [1]. Ameloblastoma accounts for almost 1% of tumors found in the maxillofacial field [2]. The most common location of ameloblastoma is posterior to the mandible, followed by anterior to the mandible [3]. The tumor increases in size over time and progresses with almost no symptoms [4]. Therefore, ameloblastoma is usually incidentally detected on X-rays during dental treatment or after changes in facial shape or symptoms caused by infection of the tumor. If left untreated, an ameloblastoma can occasionally become a malignant ameloblastic carcinoma [5]. Gigantic ameloblastoma affecting the whole mandible has been observed in developing countries, such as West African countries [6].

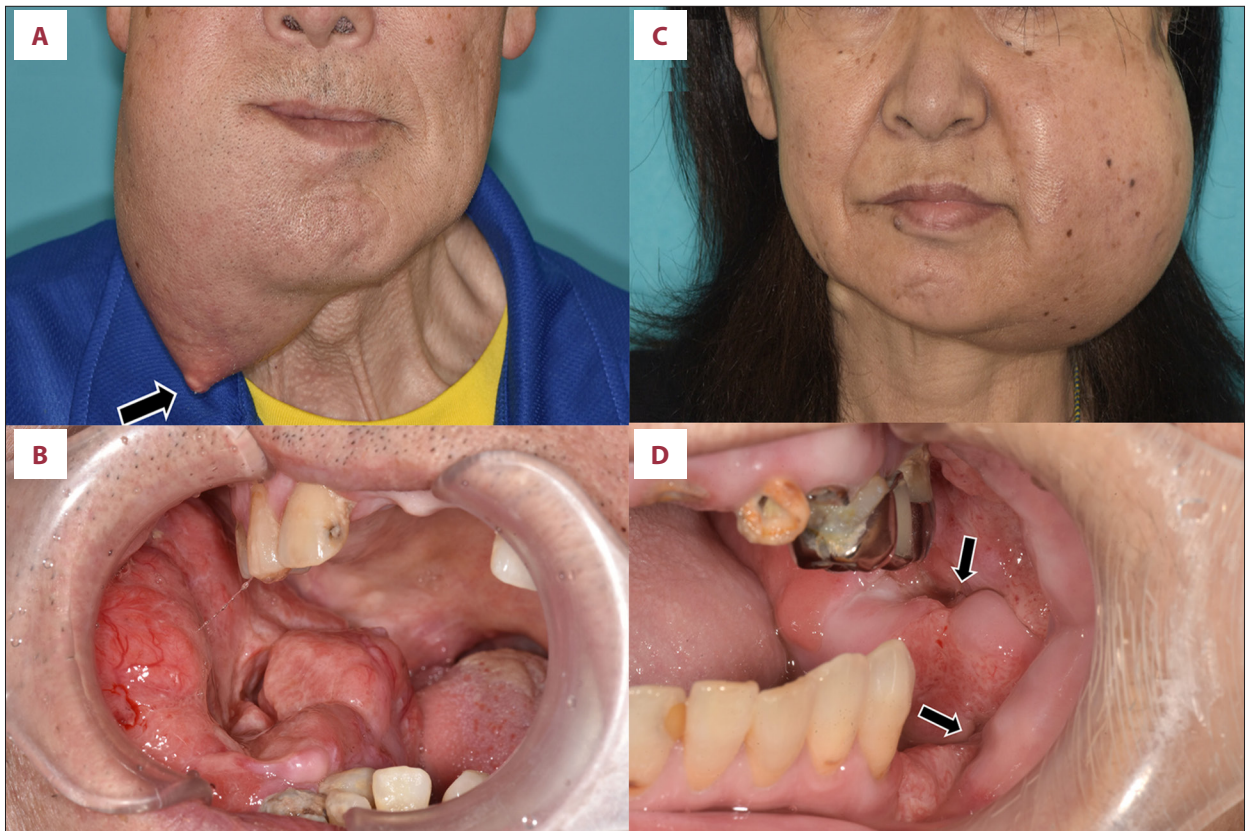
Hypoproteinemia is a condition in which the level of protein present in the blood is lower than normal, and it is related to malnutrition [7], heart disease [8], lung disease [9], kidney disease [10], liver abnormalities [11], and septic shock [12]. Hypoproteinemia causes edema, ascites, pleural effusion, decreased urine output, and decreased blood pressure. Several

research groups have reported gigantic ameloblastoma cases combined with hypoproteinemia [13-15]. These groups have reported leakage of serum protein through the fistulas and edema of the body in these patients, and hypoproteinemia was improved after surgery; the final diagnosis of 1 case was ameloblastic carcinoma. Here, we report 2 cases of hypoproteinemia associated with gigantic ameloblastoma that improved after surgery.

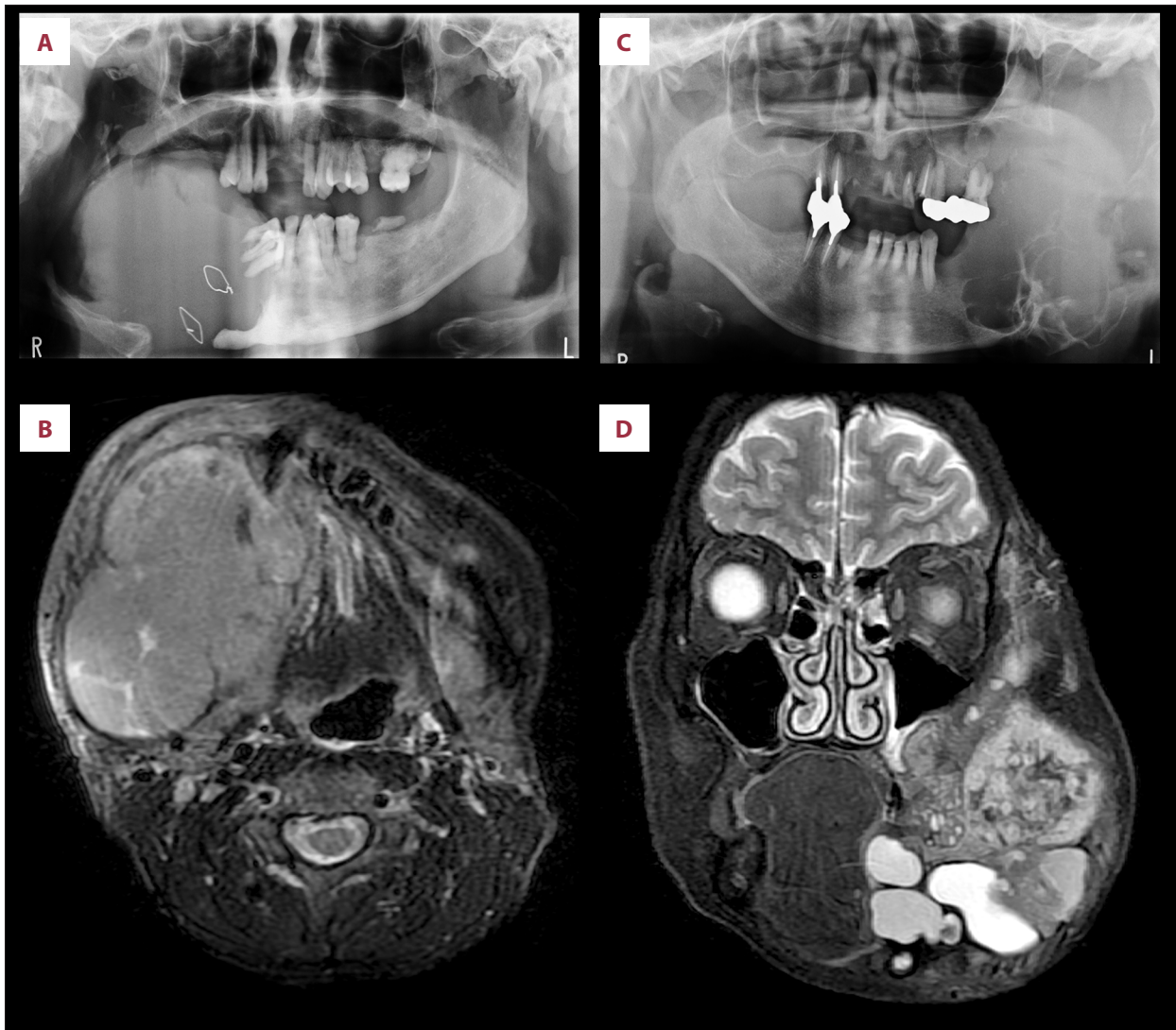
## Case Reports

### Case 1

A 65-year-old man visited our hospital with the chief concern of swelling of the right mandible (Figure 1A). The patient had recognized the swelling approximately 6 months previously. Five decades earlier, he underwent segmental resection of the right mandible with a diagnosis of ameloblastoma. The patient had an unusually large tumor (approximately 100 mm in diameter) in the right mandible. His height and weight were 159.3 cm and 44.0 kg, respectively, and his body



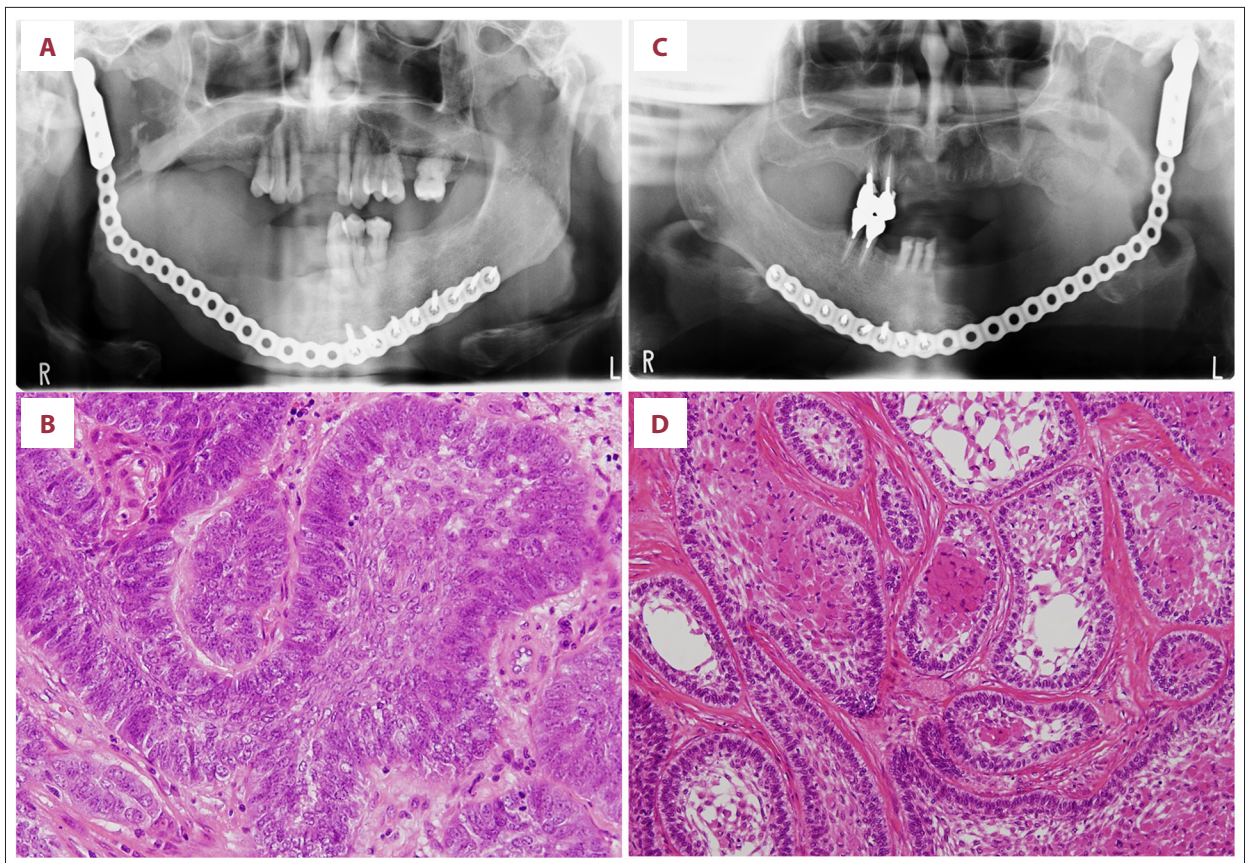
**Figure 1.** (A) Facial photograph of the patient in case 1. Significant swelling is found in the right mandible. An arrow indicates a fistula. (B) Intraoral photograph of the patient in case 1. The lesion growth is observed around the right mandibular gingiva. (C) Facial photograph of the patient in case 2. Significant swelling is found in the left mandible. (D) Intraoral photograph of the patient in case 2. Drainage of abscess is found from some fistulas of the intraoral lesion. Arrows indicate fistulas.



**Figure 2.** (A) Pantomography of the patient in case 1. The right mandible is absorbed by the tumor. There are wires used in past surgery. (B) T2-weighted magnetic resonance imaging (MRI) of the horizontal section of the patient in case 1. It confirms a large mass, including a multicystic region. (C) Pantomography of the patient in case 2. The left mandible is absorbed by the tumor. (D) T2-weighted MRI of the coronal section of the patient in case 2. The tumor expands to the left temporomandibular region from the mandible.

mass index (BMI) was 18.58 kg/m<sup>2</sup>, which was considered normal weight. There was no anamnesis; however, the blood examination showed anemia (hemoglobin level was 9.8 g/dL), and slight hypoproteinemia (total protein: 6.4 g/dL, albumin: 3.2 g/dL). Total cholesterol and lymphocyte count were normal at 160 mg/dL and 1530 cells/mL, respectively. There were no abnormalities in the liver, kidney, or heart. Abscess drainage was confirmed in a fistula on the right submandibular skin (Figure 1B). A swollen lesion was also confirmed in the alveolar and oral vestibular regions of the right mandible. Dental caries and apical periodontitis were also observed. No abscess drainage was observed in the oral cavity. Pantomography, computed tomography (CT), and magnetic resonance imaging (MRI)

confirmed 96.7×76.4×104.1 mm mass, including a multicystic region, that expanded to the condyle from the center of the mandible (Figure 2A, 2B). Based on these findings, the clinical diagnosis was a benign or malignant odontogenic tumor. Biopsy of the oral lesion led to a diagnosis of ameloblastoma. With the patient's consent, we performed hemimandibulectomy and reconstruction of the mandible shape with a titanium plate under general anesthesia (Figure 3A). The operation duration was 5 h 20 min, the total volume of blood loss was 1540 mL, and a transfusion of 4 units of red cell concentrate mannitol adenine phosphate (RC-MAP) was performed during the operation. Pathology confirmed a malignant area at the center of the specimen (Figure 3B), and the final diagnosis



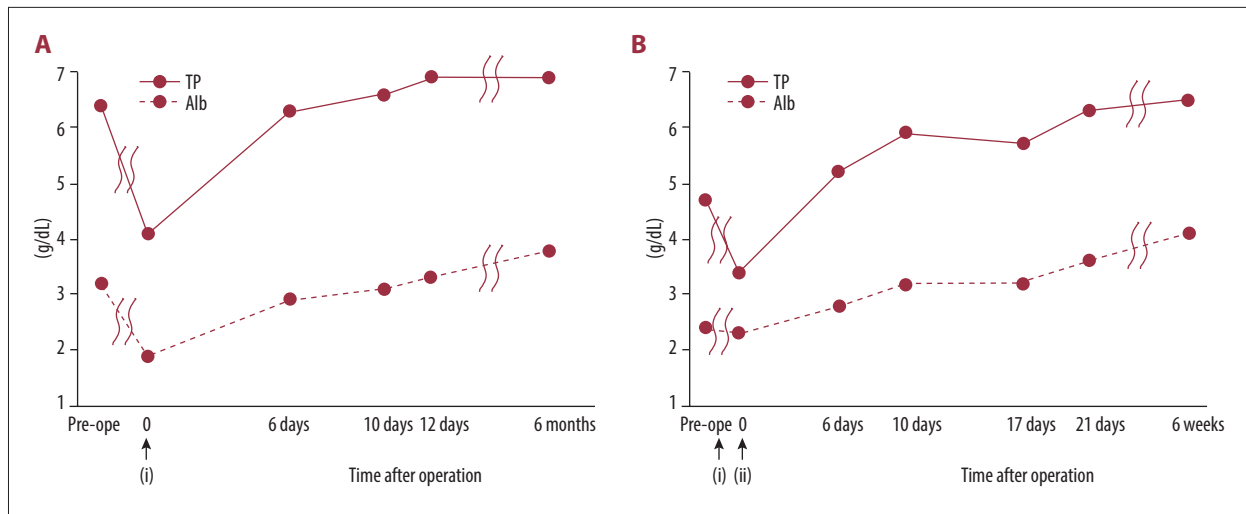
**Figure 3.** (A) Pantomography of the patient in case 1 at 6 months after surgery. The tumor was resected, and the mandibular shape was reconstructed using a titanium plate with the condyle head. (B) Pathological photograph of the patient in case 1. Tumor nests showing densely packed cells rimmed by tall columnar cells with marked pleomorphism ( $\times 200$ , H-E stain). (C) Pantomography of the patient in case 2 at 6 weeks after surgery. The tumor was resected, and the mandibular shape was reconstructed using a titanium plate with the condyle head. (D) Pathological photograph of the patient in case 2. Tumor consisting of various-sized and -shaped follicular parenchyma, dense collagenous stroma, and granular cells in central areas of the tumor nests ( $\times 100$ , H-E stain).

was ameloblastic carcinoma. After distant metastasis was not confirmed by positron emission tomography – CT, the patient was discharged with good progress on day 22 after the operation. The protein and albumin levels were 6.1 g/dL and 3.3 g/dL, respectively, and slight hypoproteinemia remained at discharge, because there was a secondary infection of the wound. However, total protein and albumin levels had increased to 6.9 g/dL and 3.8 g/dL, respectively, at the next examination (at 6 months after the operation) (Figure 4A). Hemoglobin also increased to 10.2 g/dL.

### Case 2

A 60-year-old woman visited our hospital with a chief concern of swelling in the left mandible (Figure 1C). The patient's height and weight were 162.0 cm and 50.2 kg, respectively. The BMI was 19.13 kg/m<sup>2</sup>, which was considered normal weight. The patient had undergone partial resection of the left mandible

with a diagnosis of ameloblastoma approximately 40 years earlier. Subsequently, follow-up was interrupted, and swelling of the left side of face developed over time. The patient had an unusually large tumor (approximately 100 mm in diameter) in the left mandible. The swelling had spread left from the temporomandibular region to the submandibular region. In the oral cavity, the lesion had expanded to the maxilla from the mandible, and the maxilla was compressed and absorbed by the lesion. Abscess drainage was observed in several regions of the oral lesion (Figure 1D). Dental caries and apical periodontitis were also observed. The patient had a history of anemia and edema of the lower extremities due to hypoproteinemia. The laboratory examinations indicated low total protein and albumin levels of 4.7 g/dL and 2.4 g/dL, respectively. Total cholesterol and lymphocyte count were normal at 165 mg/dL and 1740 cells/mL, respectively. The hemoglobin level was also low, at 8.2 g/dL. There were no abnormalities in the liver, kidney, or heart. Pantomography, CT, and MRI



**Figure 4.** The progress records of total protein and albumin levels. (A) Case 1. Total protein and albumin levels increased moderately after their decrease due to surgery and increased 6 months after surgery compared to before surgery. (i): Transfusion of 4 units of red cell concentrate mannitol adenine phosphate (RC-MAP) during surgery. (B) Case 2. Total protein and albumin levels increased after their decrease due to surgery and increased significantly 6 weeks after surgery compared to before surgery. (i): Transfusion of 4 units of RC-MAP and intravenous injection of 2 vials of 5% Albuminar® before surgery. (ii): Transfusion of 10 units of RC-MAP and 6 units of fresh-frozen plasma and intravenous injection of 2 vials of 5% Albuminar® during and after surgery.

confirmed a mass of 80.5×71.2×100.1 mm, including a multicystic region that expanded to the condyle from the center of the mandible (Figure 2C, 2D). Based on these findings, the clinical diagnosis was a benign or malignant odontogenic tumor. Biopsy of the oral lesion led to a diagnosis of ameloblastoma. With the patient's consent, we performed hemimandibulectomy and reconstruction of the mandible shape with a titanium plate under general anesthesia (Figure 3C). We did not perform reconstructive surgery of the maxilla because the maxillary sinus remained even though the maxilla was compressed and absorbed. As marked hypoproteinemia was noted before the operation, 2 vials of 5% Albuminar® (12.5 g/250 ml, 1 vial, CSL Behring K.K., Tokyo, Japan) were intravenously injected 2 days before the operation, and 2 vials were used during the operation. The operation duration was 7 h 23 min and the total bleeding was 1769 mL. There were 4 units of RC-MAP transfused during the 2 days before surgery due to anemia, and 10 units of RC-MAP were used during and after the operation. Six units of fresh-frozen plasma were also transfused, and 2 vials of 5% Albuminar® were intravenously injected after the operation. Pathology confirmed no evidence of malignancy (Figure 3D). The edema of the lower extremities improved, and the patient was discharged with good progress on day 26 after surgery. At 6 weeks after the operation, the total protein and albumin levels had increased to 6.5 g/dL and 4.1 g/dL, respectively (Figure 4B). Hemoglobin also increased to 10.9 g/dL, and the maxilla defect disappeared with the growth of soft tissue.

## Discussion

Ameloblastoma is more commonly found as an odontogenic tumor, and the most common site of occurrence is the angle or ramus of the mandible [3]. Some patients with ameloblastoma affecting the entire mandible have been observed in developing countries, such as West African countries [6]. However, such patients are sometimes found in developed countries, and they usually have poor oral hygiene. Certainly, the patients in this report had few remaining teeth, which had caries, and they did not use dentures. If these patients had undergone a dental check-up in the early stages, or were more interested in good oral health, appropriate treatment could have been administered, and it might have been possible to reduce the invasion and dysfunction caused by surgery.

Several research groups have reported gigantic ameloblastomas with hypoproteinemia [13-15]. In 2 of these reports, the patient had previously been diagnosed with ameloblastoma and had a history of surgery [14,15]. One of the reports was of a patient who refused treatment prematurely [14]. In our report, both case 1 and 2 had a history of treatment with a diagnosis of ameloblastoma in the past, and treatment in case 2 was discontinued. Hypoproteinemia in gigantic ameloblastoma might be due to the cyst wall acting as a semipermeable membrane: numerous feeding vessels can be present in a gigantic ameloblastoma, and it is conceivable that protein permeates through the cyst wall and is transferred into the cystic cavity, thus resulting in an albumin level in the odontogenic cyst fluid that is almost

the same as that of serum. Another reason may be discharge of intracystic liquid from the fistula, resulting in loss of a large amount of plasma [13-15]. Gigantic ameloblastoma is at risk of hemorrhage from ulcerations and can develop anemia [14]. The liquid can discharge from the fistula, and a large amount of plasma component can be lost [13]. In this report, case 1 had a fistula on the tumor. Although the patient had hypoproteinemia, it was slight, and there were no symptoms of edema, possibly because there was only 1 discharge channel, and the degree of protein consumption was low. A postoperative increase in protein level was also confirmed, albeit a small amount. In contrast, case 2 had marked hypoproteinemia compared to case 1, possibly because there were more fistulas and more plasma was lost. Hypoproteinemia remained after the operation due to intraoperative bleeding and consumption at the postoperative wound, but marked improvement was observed approximately 1 month after the operation. Albumin was the only substance administered.

Regarding nutritional status in case 1 and 2, total cholesterol and lymphocyte count were normal, so these patients were

not considered malnourished before surgery. In addition, malnutrition due to an eating disorder associated with a tumor is also possible, but since prostheses such as dentures have not yet been prepared, it is thought that there will be no major changes in eating conditions.

## Conclusions

We presented 2 cases of hypoproteinemia with gigantic ameloblastoma or ameloblastic carcinoma as a final diagnosis, both demonstrating improvements after surgery. This hypoproteinemia was thought to be caused by plasma leakage through the fistulas in gigantic odontogenic tumors.

## Declaration of Figures' Authenticity

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

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