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Case report

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Abstract

Refractory osteomyelitis can lead to recurrent cellulitis and pathological fractures in patients with advanced mandibular osteoradionecrosis (ORN), the optimal treatment for which remains to be established. In addition, difficulties in intake due to trismus and severe pain caused by mandibular ORN may lead to malnutrition and underweight. Therefore, refeeding syndrome (RFS) should be considered when highly invasive surgical procedures are performed. In this report, we discuss the case of an 80-year-old woman with underweight status who had undergone radiotherapy for oropharyngeal malignant melanoma, following which she developed severe pain and a pathological fracture in the right mandible. Given her advanced age and cognitive decline, decision-making regarding the treatment plan was difficult. After repeated consultations with the patient and her family members, the treatment priorities were established as pain control, infection control, and increased mouth opening. A segmental mandibulectomy was performed. After nutritional intake was initiated postoperatively, a marked decrease in serum potassium and phosphorus levels was observed. Because there were no symptoms suggestive of RFS, imminent RFS was considered. Appropriate management in accordance with the National Institute for Health and Care Excellence guidelines prevented progression to RFS. Overall, surgery was successful in achieving the initial treatment objectives, and the patient exhibited a general improvement in quality of life. Careful perioperative management for RFS prevention should be considered necessary when performing surgical procedures for advanced mandibular ORN, especially in older adults.

Keywords: hypophosphatemia, osteoradionecrosis, refeeding syndrome, segmental mandibulectomy, underweight

1. Introduction[1]

Refractory osteomyelitis, which occurs in patients with osteoradionecrosis (ORN) of the jaw and medication-related osteonecrosis of the jaw, can lead to recurrent cellulitis and pathological fractures in advanced stages. In addition, advanced refractory osteomyelitis can lead to trismus and severe pain, feeding problems, chronic malnutrition, and weight loss (Fig. 1). Because refractory osteomyelitis is most common in older adults, decision-making regarding treatment plans is often difficult, especially since the optimal treatment strategy has not been established. Complications after radiation therapy include taste disorders, decreased saliva production, and trismus, which increase the risk of eating disorders [1]. As both irradiation and malnutrition are detrimental to wound healing [2, 3], reconstructive surgery with good blood flow is preferable [4].

Refeeding syndrome (RFS) is a potentially fatal condition that can develop in patients with chronic malnutrition when rapid nutritional supplementation is administered [5]. Although a few reports have discussed cases of RFS in the head and neck region [6, 7], to our knowledge, none have focused on patients with refractory osteomyelitis.

In this report, we discuss a case of ORN in an older patient with a pathological fracture who experienced a good outcome following segmental resection despite difficulties in decision-making.

[1] Abbreviations: ORN: osteoradionecrosis; RFS: refeeding syndrome; AS: aortic stenosis; BMI: body mass index; ADL: activities of daily living; NICE: National Institute for Health and Care Excellence; NST: nutritional support team; PAD: peripheral artery disease

2. Case report

An 80-year-old woman with a history of severe aortic stenosis (AS), hypertension, osteoporosis, dyslipidemia, and coronary artery stenosis presented to our department for the first time with pain in the right mandibular molar region. Eight years before the first visit to our department, she underwent radiotherapy (conventional, 66 Gy/33 Fr.) for malignant melanomas of the oropharynx. Following the diagnosis of ORN, sequestrectomy and saucerization were performed 8 months after the initial visit. Thereafter, although wound dehiscence and mild pain were confirmed, the extent of bone exposure was small, and there were no signs of acute inflammation. Therefore, conservative treatment was recommended. However, 1 year and 4 months after the initial visit, the patient presented with severe pain in the right mandible.

2.1 Physical findings

The patient's height, weight, and body mass index (BMI) were 143 cm, 29 kg, and 14.2 kg/m^2, respectively, and she exhibited independence in activities of daily living (ADL). No abnormal findings were observed in the eyelids or ocular conjunctiva. Chest examination revealed no heart murmurs or abnormal breath sounds. Abdominal examination results were normal, and edema of the extremities was not observed. Although she exhibited mild impaired swallowing function, there were no obvious findings suggestive of aspiration. Cognitive function was moderately impaired (Mini-Mental State Examination: 17/30, disorientation, short-term memory impairment).

2.2 Echocardiographic findings

Echocardiographic examination revealed an ejection fraction of 59.5% and severe AS. No pulmonary congestion was observed.

2.3 Blood test findings

Blood tests revealed mild anemia, as well as low serum levels of sodium and chloride. In addition, the lymphocyte count, serum albumin, and total protein levels were low. The serum potassium and phosphorus levels were within the normal ranges (Table 1).

2.4 Local findings

Local findings included erythema, swelling, severe pain in the right mandible, and paresthesia in the area innervated by the right inferior alveolar nerve. In addition, trismus (approximately 0.5 finger breadth) and thrush (scarring) at the corners of the mouth made it difficult for the patient to ingest food. Pain assessment revealed allodynia. Bone exposure was observed in the mandibular right first and second molar equivalent areas (Fig. 2A).

2.5 Imaging findings

Panoramic X-ray and computed tomography findings revealed bone destruction from the right lower quadrant to the right ramus of the mandible and a pathological fracture at the right mandibular angle (Fig. 2B, C, D).

2.6 List of concerns

The following concerns were raised: 1) pathological fracture of the right mandible with ORN, 2) severe pain, 3) trismus, 4) difficulty in dietary intake, 5) underweight and malnutrition, 6) severe AS, 7) advanced age and cognitive decline, and 8) history of radiation therapy.

2.7 Treatment strategy

Advanced age, severe AS, underweight, and malnutrition raised concerns regarding the patient's ability to tolerate surgery. In such cases, our institutional policy typically includes segmental

mandibulectomy alone, without reconstructive surgery. Additionally, cognitive decline was observed, making it difficult to obtain informed consent. After repeated consultations with the patient and her family members, the treatment priorities were pain control, infection control, and increased mouth opening. Surgical treatment, nerve destruction, and conservative treatment (periodic irrigation for bone exposure area and administration of antibiotics) were presented as treatment plans, and the characteristics of each were repeatedly explained (Table 2). Finally, a surgical treatment plan was developed.

2.7.1 Surgical treatment

Sulbactam/ampicillin was chosen for perioperative antimicrobial treatment and as prophylaxis for infectious endocarditis. Segmental mandibulectomy was performed under general anesthesia (range: mandibular right first premolar to the central ramus of the mandible) (Fig. 3A, B). Good hemorrhaging was observed at the amputation edges. For mucosal defects, suture manipulation from the oral cavity was difficult because of inadequate mouth opening (Fig. 3C). Therefore, the wound was closed completely using the Gambee suture technique for intestinal anastomosis via a cervical approach (Fig. 3D). The watertight wound closure could be performed in the oral cavity, and the wound edge was everted on the oral side. The operative time was 3.5 hours, and the hemorrhage volume was small.

2.8 Postoperative course

The patient was intubated and admitted to the intensive care unit postoperatively. She was extubated on the first postoperative day and was confirmed to have a good respiratory condition. She did not eat on the day of surgery or the first postoperative day. Given her severe AS, dehydration and excessive infusion were carefully managed. Pre-hospitalization interviews revealed a daily intake of 700–800 kcal, and the same level of caloric intake was planned

postoperatively. Accordingly, 40 kcal was administered via infusion, and 600 kcal of enteral nutrition was started on the second and third postoperative days. Blood tests on the third postoperative day revealed a serum potassium level of 3.0 mmol/L and phosphorus level of 2.0 mg/dL (Table 3), representing significant decreases when compared with preoperative levels; thus, RFS was suspected. In accordance with the National Institute for Health and Care Excellence (NICE) guidelines [8], caloric intake was reduced to approximately 10 kcal/kg/day (300 kcal), and vitamin B_1 supplementation was initiated. Thereafter, caloric intake was increased by 150 kcal every few days with the confirmation of the nutritional support team (NST). Oral intake became possible on the 8th postoperative day, and the final caloric intake was increased to 1,200 kcal without complication (Fig. 4). There were no findings suggestive of RFS, such as arrhythmia or signs of heart failure.

The wound showed no dehiscence or obvious signs of infection (Fig. 5A, B), and the patient was discharged on postoperative day 26. At 12 months postoperatively, the pain had largely resolved, and the infection was under control (Fig. 5C, D). There was no wound dehiscence or bone exposure in the oral cavity, and the wound was completely healed. She exhibited a slight improvement in mouth opening (approximately 1.5 finger breadths) and an increase in body weight (32 kg). She mainly ingested food processed in a blender, with oral enteral nutrition as a supplement. Although rightward deviation of the mandible was observed, the initial treatment objectives were generally achieved overall, and the patient's quality of life improved. She maintained independence in ADL but developed peripheral artery disease (PAD) in her lower limbs, which made walking difficult. Thirteen months after the mandibulectomy, she was admitted to our cardiology department to treat the PAD. Blood tests at 22 days, 5 months, and 13 months postoperatively are also shown in Table 3.

3. Discussion

Segmental mandibulectomy was performed in an older patient with underweight status and mandibular ORN. Decision-making regarding the treatment plan was difficult because of the patient's cognitive decline. However, after clarifying the treatment priorities, the characteristics of each treatment method were repeatedly explained and discussed with the patient and her family members, and the treatment decision was made in accordance with the patient's wishes and general condition [9]. Furthermore, the patient was considered at high risk for RFS because of severe emaciation. Therefore, perioperative management was performed to avoid RFS.

RFS is a metabolic disorder caused by the rapid resumption of nutritional administration in patients with malnutrition. RFS is characterized by hypokalemia, hypophosphatemia, and hypomagnesemia, which are associated with the development of neurological symptoms and heart failure. Severe cases can lead to death, necessitating extreme caution [10]. In the NICE guidelines [8], patients at high risk of RFS are defined as follows: 1) one or more of the following: i) BMI less than 16 kg/m^2; ii) unintentional weight loss of 15% or more in the past 3 to 6 months; iii) minimal or no nutritional intake for more than 10 days; iv) hypokalemia, hypophosphatemia, or hypomagnesemia before refeeding; 2) two or more of the following: i) BMI less than 18.5 kg/m^2, ii) unintentional weight loss of more than 10% in the past 3 to 6 months, iii) very little or no nutritional intake for more than 5 days; iv) history of alcohol dependence or use of insulin, anticancer drugs, antacids, or diuretics.

As the patient's BMI was 14.2 kg/m^2, she was thus considered at high risk for RFS. Nevertheless, she had the same caloric intake before and after admission (700–800 kcal). Since there was almost no fasting period and her caloric requirement was approximately 1200 kcal, we believed it was fine to start the initial postoperative nutritional intake at the same level as before surgery while taking RFS into consideration. However, hypokalemia and hypophosphatemia were observed immediately after the patient was started on enteral feeding, and RFS was suspected. At this point, there were no clinical symptoms suggestive of RFS;

therefore, the condition was considered imminent RFS (i.e., one step before RFS) [11]. Thus, even though the patient did not have acute nutritional intake, we believed that early intervention could avoid progression to full RFS. In this case, imminent RFS may have occurred due to chronically biased nutrition from the preoperative period and decreased self-regulation due to old age. Previous reports have also suggested that RFS can occur even after a short period of fasting [12]. In cases such as the present case, where the risk of RFS is high, the intervention of the NST seems necessary prior to surgery and hospitalization.

Populations potentially at high risk of RFS may have decreased intake (dysphagia, anorexia nervosa, mental health disorders, and chronic alcoholism), decreased nutrient absorption (inflammatory bowel disease), or increased metabolic demand (in cancer and surgery) [10, 13, 14]. The incidence rate of RFS among malnourished individuals, mostly including geriatric patients and those with underlying diseases, is estimated to range from 0% to 38% [15]. Most reports of RFS in the head and neck region focused on patients with cancer [16, 17]. Some patients scheduled for oral surgery are at risk of developing RFS due to advanced oral cancer and severe infections that make it difficult to ingest food. In one previous report, the authors noted that surgical treatment with management for RFS prevented the onset of RFS in a patient with severe odontogenic infection [18]. Patients with refractory osteomyelitis who are also candidates for highly invasive surgery are at a higher risk of developing RFS. It is assumed that the risk of RFS is further increased in older patients and those with cognitive decline, as in the present case (Fig. 1). The recognition of RFS in surgery is considered low [7, 18]. RFS should always be considered in older adults undergoing surgical treatment for refractory osteomyelitis, and great care should be taken in perioperative management. In this case, it was difficult to suture the mucosal defect via an oral approach due to severe trismus. As precise suturing was necessary given her post-irradiation status, we adopted the Gambee suture method, which involves inverting the cervical approach into the oral cavity [19]. This allowed

us to close the intraoral wound from the neck, and wound healing occurred without subsequent wound dehiscence.

4. Conclusion

Advanced refractory osteomyelitis tends to lead to poor nutritional status in older adults due to difficulties in food intake. When surgery is more invasive, careful attention should be paid to perioperative management, including nutritional management for RFS.

Consent for publication

The patient and her family provided written informed consent for the publication of this report.

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FIGURE LEGENDS

Figure 1. Development of malnutrition and underweight due to refractory osteomyelitis and associated factors

As refractory osteomyelitis progresses, difficulty in dietary intake predisposes patients to trismus and severe pain. Radiation therapy and medication treatment—coupled with the conditions that necessitate them, advanced age, and cognitive decline—can also lead to malnutrition and underweight.

Figure 2. Facial and imaging findings during pain enhancement

A) Redness and swelling were observed in the right mandibular angle. B) Panoramic X-ray revealed a fracture in the right mandibular angle. C) Three-dimensional reconstruction computed tomography (CT) image showing bone destruction and fracture in the right mandibular angle. D) CT image showing bone destruction from the right lower quadrant to the ramus of the mandible.

Figure 3. Intraoperative findings and suture schema

A) Status of the mandible, including the fractured area. The fracture area was identified, and the resection area was set from the right lower fourth to the middle of the mandibular ramus. B) After segmental mandibulectomy, good hemorrhaging was observed from the resection edge. C) Confirmation of connection to the oral cavity at the mucosal defect. D) Scheme at the time of suturing, which was performed using the Gambee suture method.

Figure 4. Changes in preoperative and postoperative caloric intake and electrolyte balance

Enteral feeding was started 2–3 days postoperatively. Serum potassium and phosphorus levels

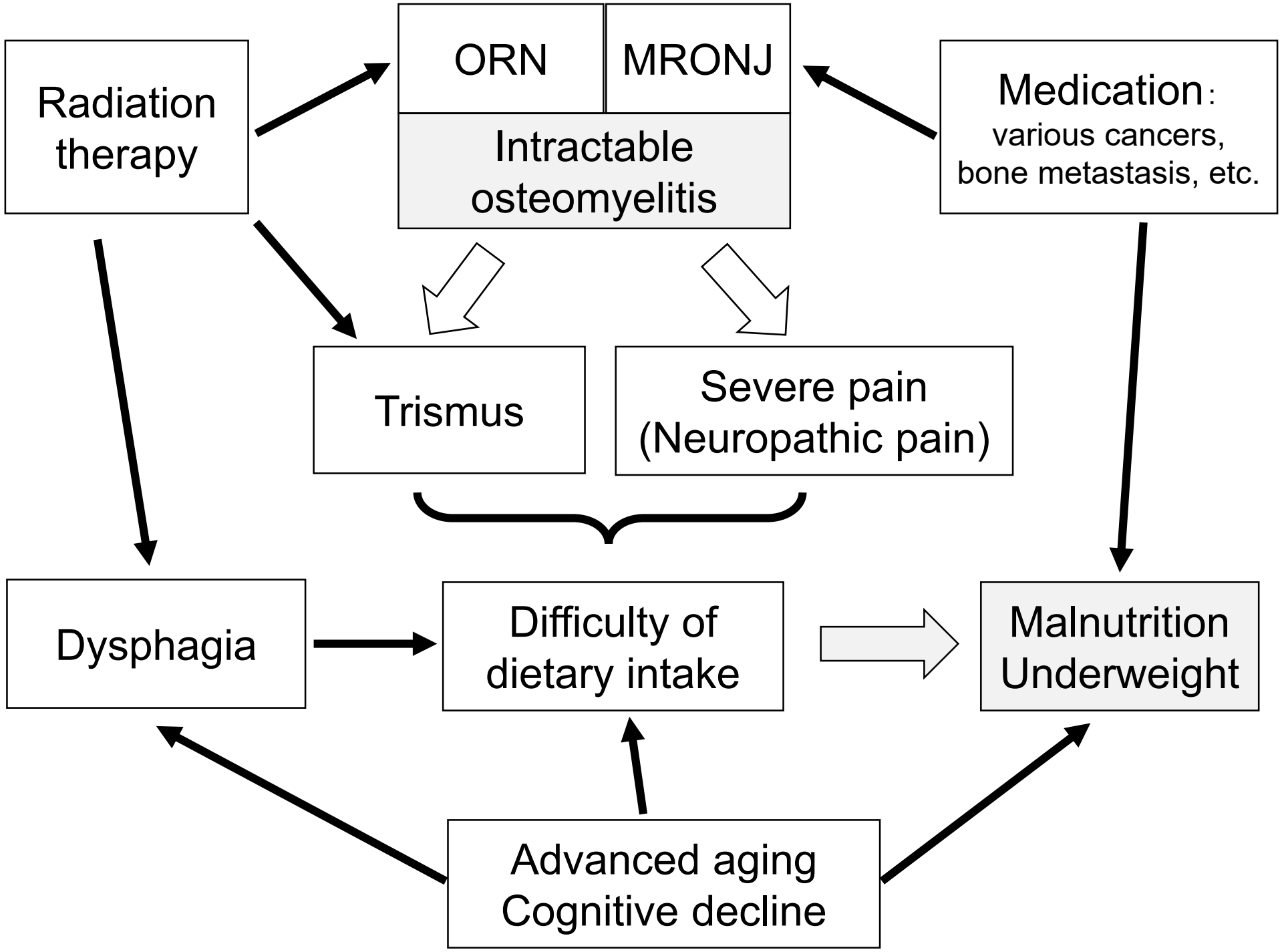
decreased after the start of enteral nutrition, and serum phosphorus decreased by approximately 39% (2.0 mg/dL) compared with the preoperative level (3.3 mg/dL). The serum magnesium levels remained within the reference values. Oral intake was initiated on postoperative day 8.

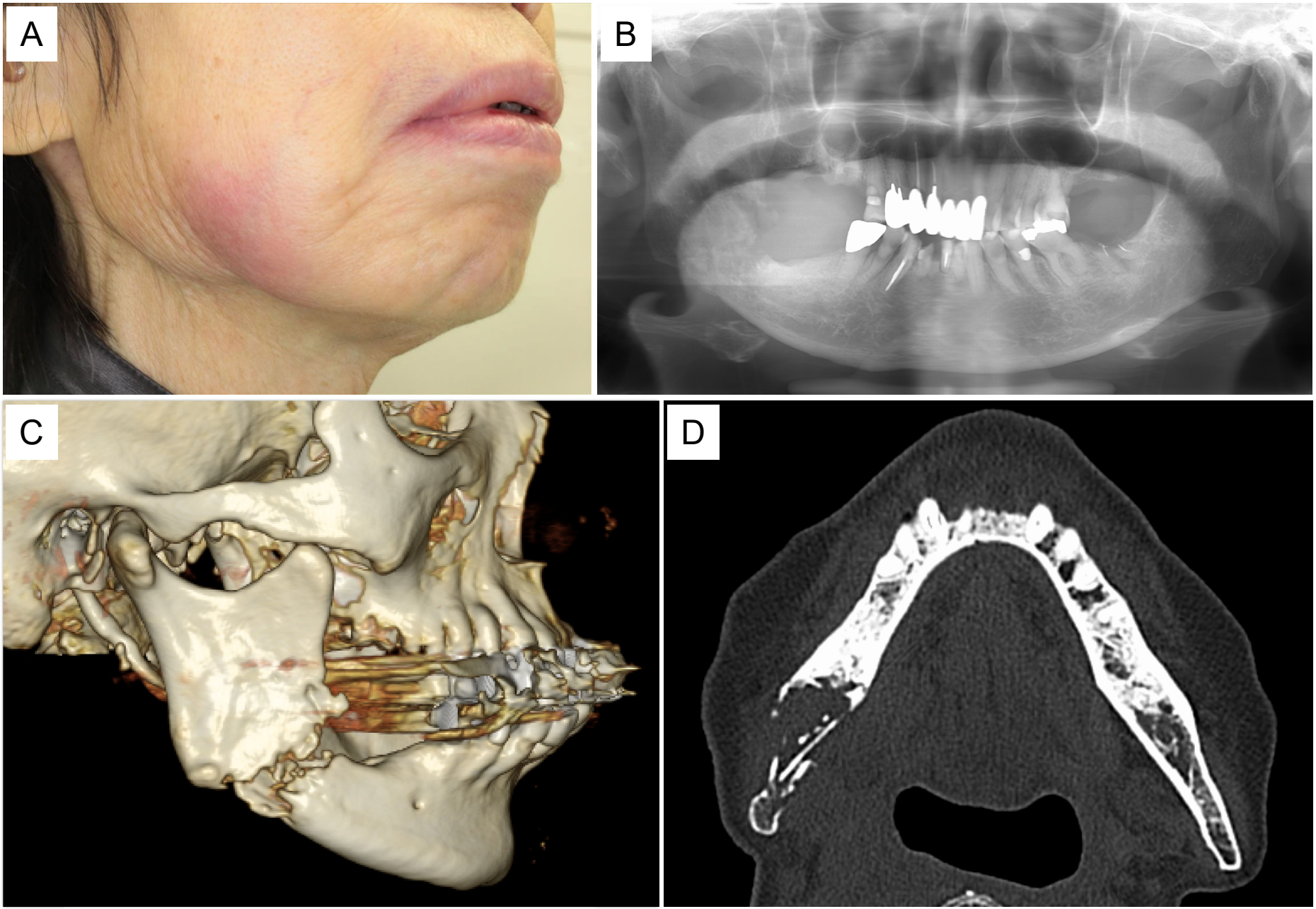
Pre-op, pre-operation

Bar chart: total calorie intake (kcal); blue line: serum potassium (mmol/dL); red line: serum phosphorus (mg/dL); black line: serum magnesium (mg/dL).

Figure 5. Postoperative wound healing and panoramic X-ray findings

A) Wound findings on postoperative day 11. The wound was mildly erythematous, but no wound dehiscence or fistulas were observed. B) Panoramic X-ray findings on postoperative day 20. C) Wound findings at 12 months postoperatively. No evidence of infection or fistula was observed. D) Panoramic X-ray findings 12 months after surgery. No abnormal resorption of the bony transection was observed.


Radiation therapy
ORN
MRONJ
Intractable osteomyelitis
Medication:
various cancers,
bone metastasis, etc.
Trismus
Severe pain
(Neuropathic pain)
Dysphagia
Difficulty of dietary intake
Malnutrition
Underweight
Advanced aging
Cognitive decline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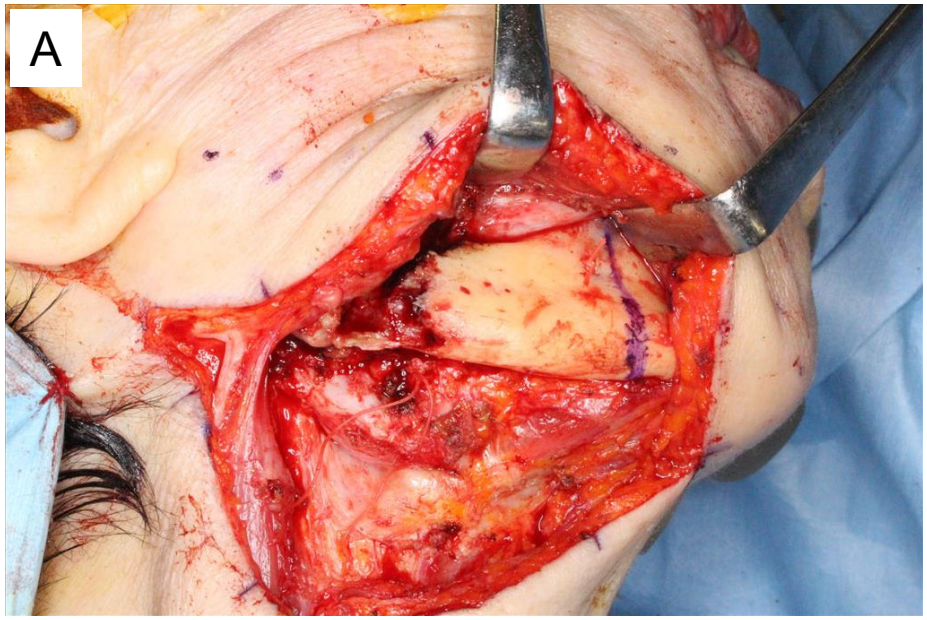
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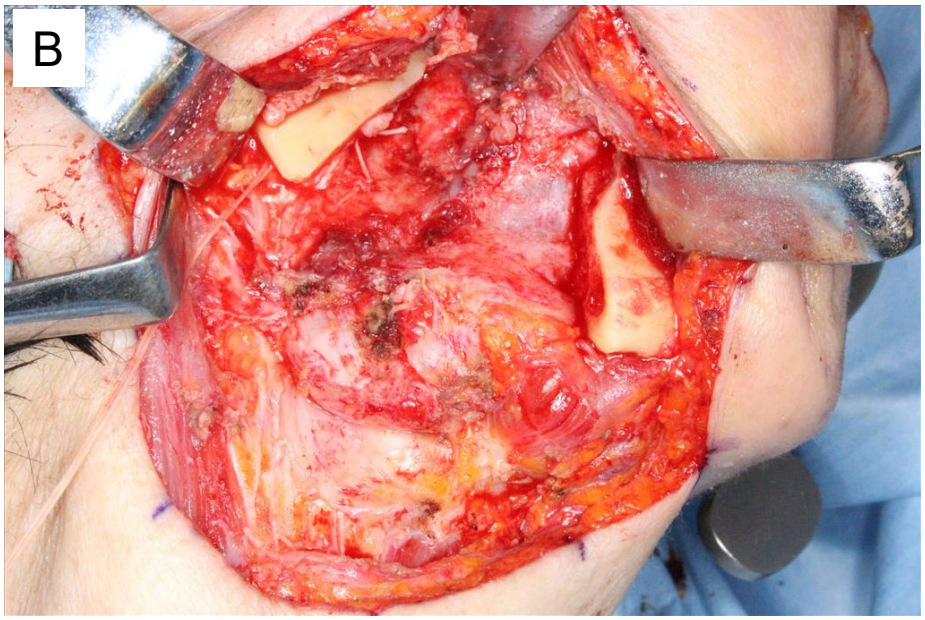
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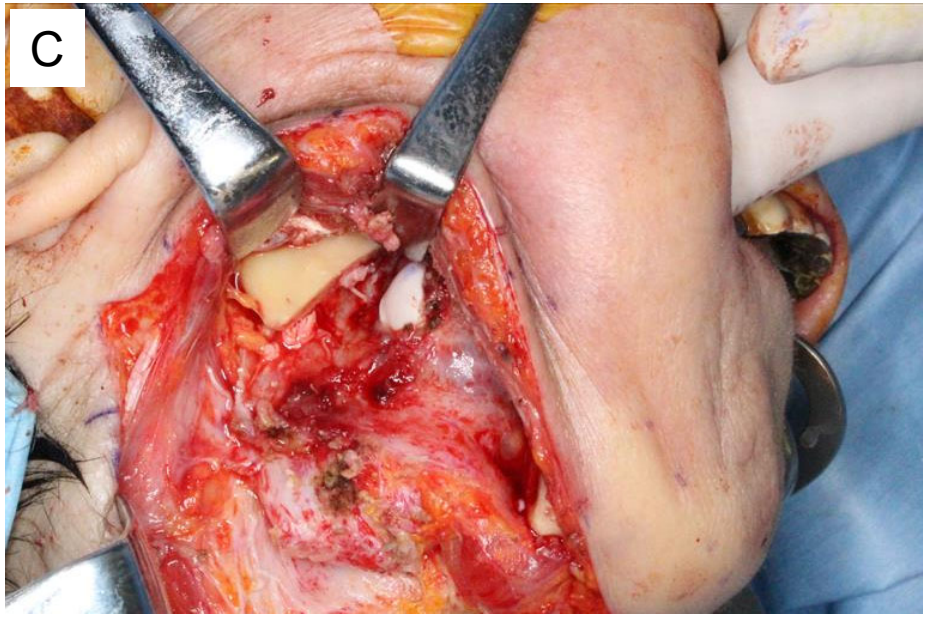
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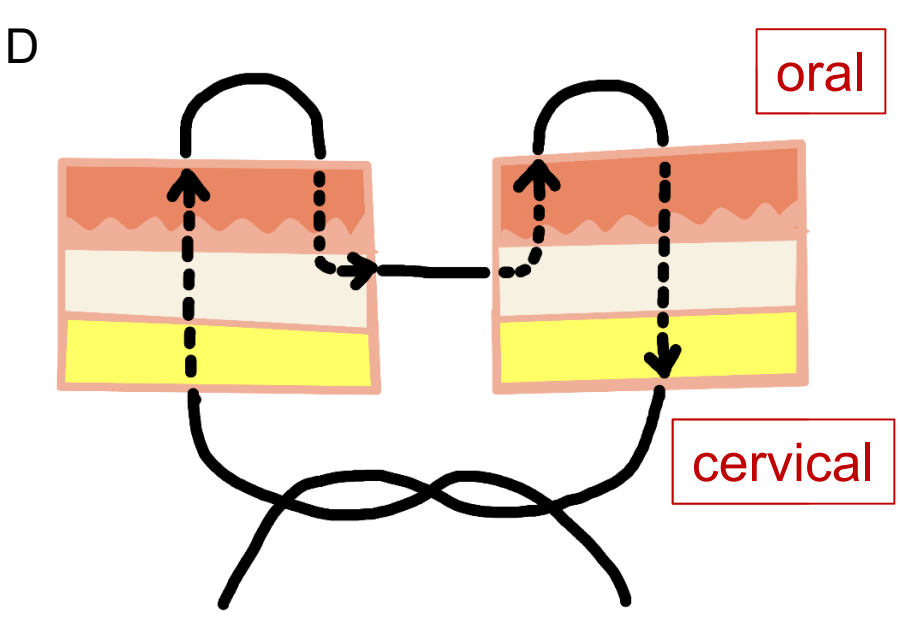
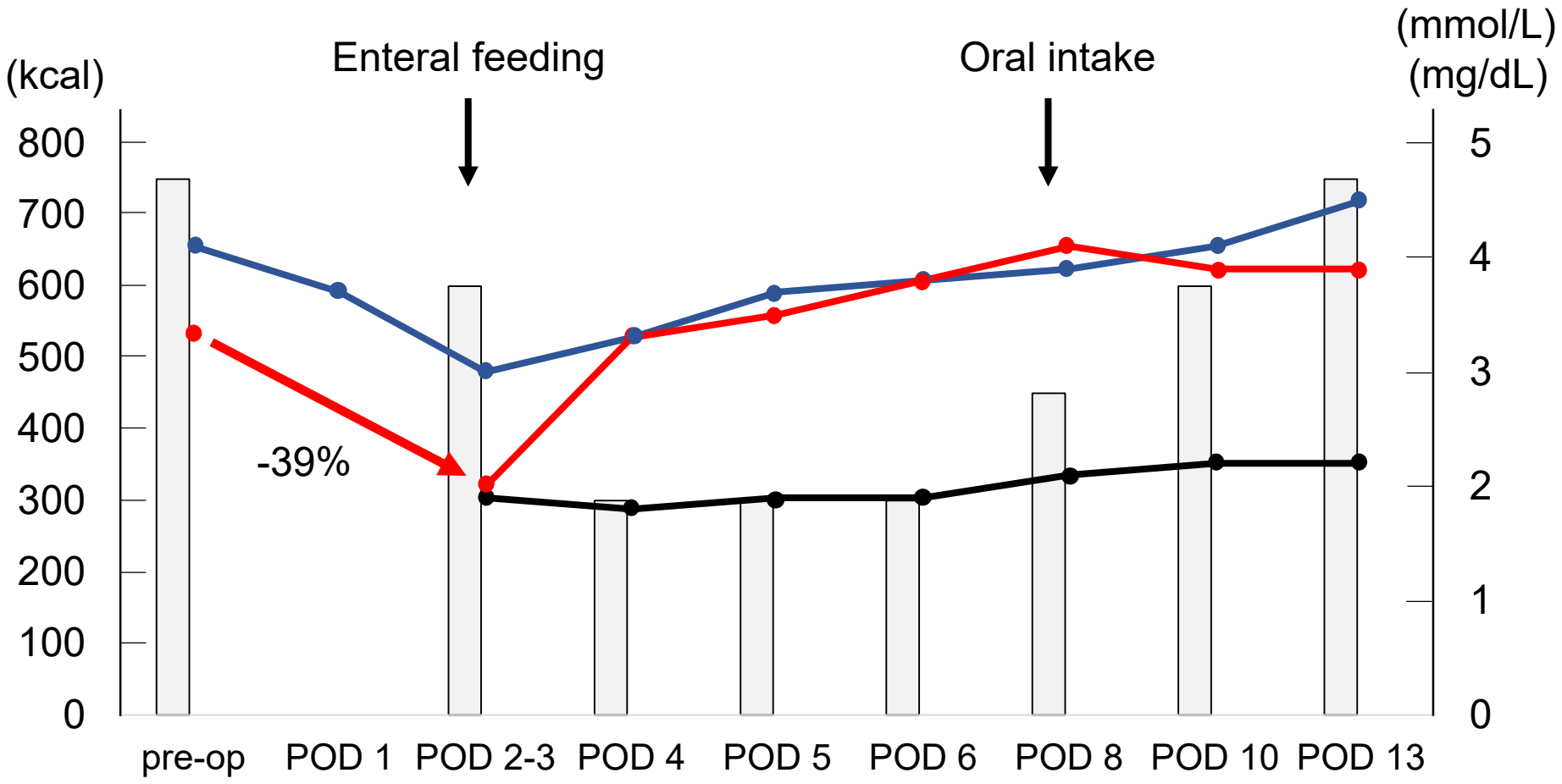

D
oral
cervical


(kcal)
Enteral feeding
Oral intake
(mmol/L)
(mg/dL)
800
700
600
500
400
300
200
100
0
5
4
3
2
1
0
-39%
pre-op
POD 1
POD 2-3
POD 4
POD 5
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POD 13

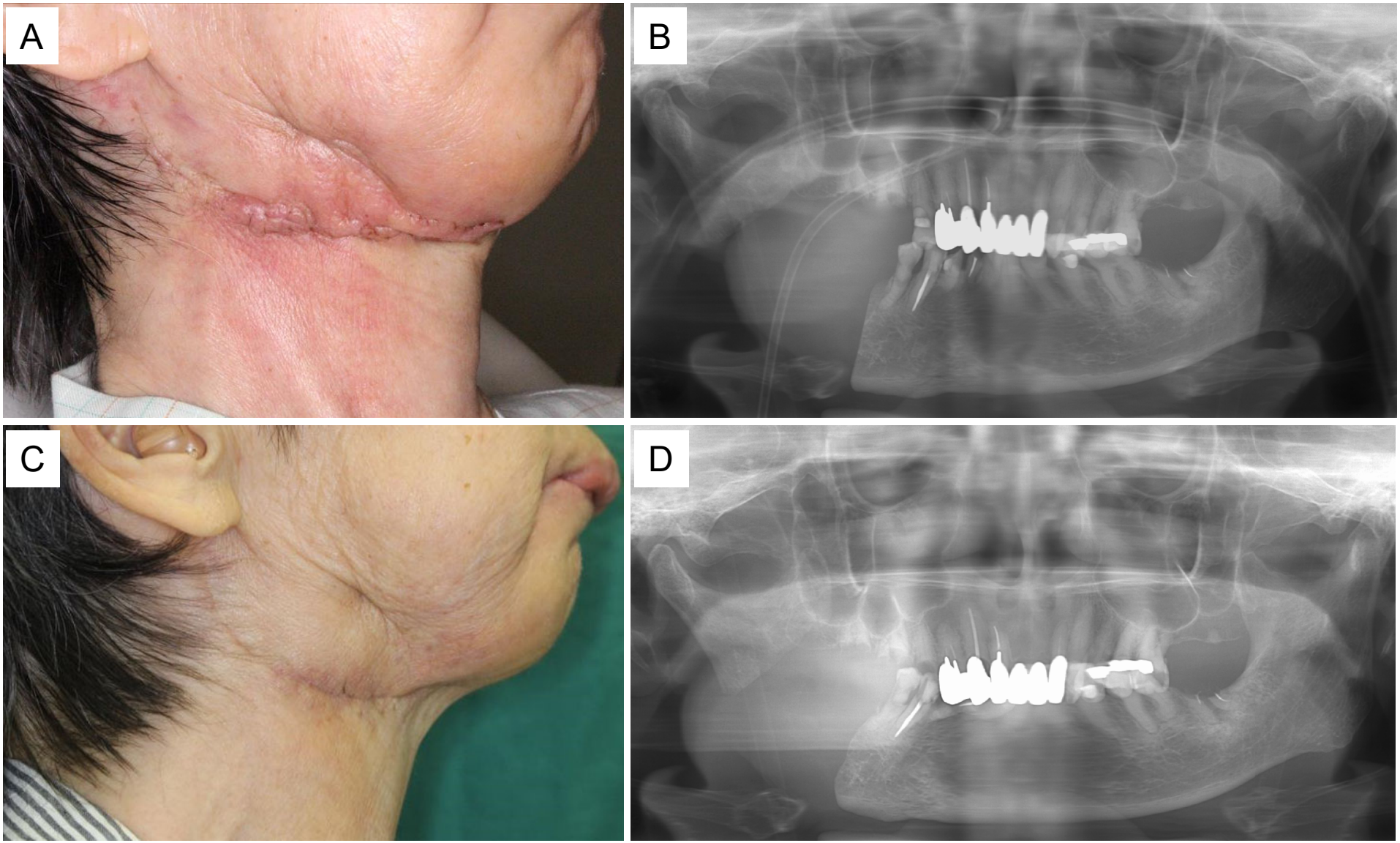
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Table 1. Blood test findings on admission

Variables	
Complete blood count	
White blood cell ($\times 10^3/\mu L$)	5.3
Neutrophil (%)	69.2
Lymphocyte (%)	16.9
Red blood cell ($\times 10^6/\mu L$)	3.5
Hemoglobin (g/dL)	10.6
Hematocrit (%)	31.9
Platelet ($\times 10^4/\mu L$)	36.8
Coagulation examination	
Activated partial thromboplastin time (s)	34.8
Prothrombin time (%)	88.2
PT-INR	1.08
Biochemical examination	
C-reactive protein (mg/dL)	0.18
Aspartate aminotransferase (U/L)	21
Alanine aminotransferase (U/L)	10
γ-glutamyl transpeptidase (IU/L)	19
Creatine kinase (U/L)	43
Cholinesterase (U/L)	221
Lactate dehydrogenase (U/L)	196
Sodium (mmol/L)	130
Potassium (mmol/L)	4.4

Chlorine (mmol/L)	96
Calcium (mmol/L)	9.0
Phosphorus (mg/dL)	3.6
Blood urea nitrogen (mg/dL)	11.5
Uretic acid (mg/dL)	3.2
Creatinine (mg/dL)	0.64
eGFR (mL/min/1.73m^2)	66.4
Total protein (g/dL)	6.1
Albumin (g/dL)	3.3
Total cholesterol (mg/dL)	264
Triglycerol (mg/dL)	107
Glucose (mg/dL)	79
Brain natriuretic peptide (pg/mL)	99.6

PT-INR, prothrombin time international normalized ratio; eGFR, estimated glomerular filtration rate

Table 2. Effectiveness and limitations of each treatment method

	Surgical treatment	Nerve destruction	Conservative treatment
Pain	I	I or U	U or E
Trismus	U or I	U	U or E
Swallowing function	U or E	U	U
Facial deformity	E	U	U
Infectious control	I or E	U or E	U or E
QOL after treatment	I or E	I or U	U or E
Risk of perioperative complication	Yes	Yes	No

QOL, quality of life

I, improved; U, unchanged; E, exaggerated

Table 3. Postoperative blood test findings

Variables	3 days	22 days	5 months	13 months
Complete blood count				
White blood cell ($\times 10^3/\mu L$)	14.6	6.4	6.4	5.8
Neutrophil (%)	90.4	75.6	72.2	
Lymphocyte (%)	3.5	11.9	15.3	
Red blood cell ($\times 10^6/\mu L$)	3.7	2.8	3.6	3.3
Hemoglobin (g/dL)	11.1	8.6	11.0	10.3
Hematocrit (%)	33.6	26.1	33.3	31.3
Platelet ($\times 10^4/\mu L$)	35.3	51.0	29.1	26.5
Biochemical examination				
C-reactive protein (mg/dL)	12.17	0.73	0.14	0.06
Aspartate aminotransferase (U/L)	29	36	31	25
Alanine aminotransferase (U/L)	12	29	17	14
γ-glutamyl transpeptidase (IU/L)	17	29	14	11
Creatine kinase (U/L)	364	27	52	46
Cholinesterase (U/L)	201	202	260	
Sodium (mmol/L)	132	127	135	137
Potassium (mmol/L)	3.0	4.6	4.3	4.1
Chlorine (mmol/L)	95	90	98	103
Calcium (mmol/L)	9.1		9.8	9.8
Phosphorus (mg/dL)	2.0		3.8	3.8
Blood urea nitrogen (mg/dL)	5.9	14.3	17.5	19.9
Uretic acid (mg/dL)	2.0	3.9	4.9	4.8

Creatinine (mg/dL)	0.50	0.57	0.83	0.84
eGFR (mL/min/1.73m^2)	87.0	75.4	49.8	49.2
Total protein (g/dL)	6.3	6.1	6.9	6.5
Albumin (g/dL)	3.2	2.9	4.0	3.3

2 eGFR, estimated glomerular filtration rate