# Combination treatment with paclitaxel, carboplatin and cetuximab in maxillary sinus cancer: A case report

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**Abstract.** The standard treatment for maxillary sinus cancer is surgery; however, surgery for advanced cases often leads to significant aesthetic and functional disability. Combination treatment (induction chemotherapy) with paclitaxel, carboplatin and cetuximab (PCE) can be effective in head and neck cancer. The present study describes the case of a patient with advanced maxillary sinus cancer that was successfully treated using the PCE regimen. A 69-year-old man presented to the Department of Dentistry and Oral Surgery, Hokuto Hospital (Obihiro, Japan) with left buccal swelling and an irregular mass on the left maxillary gingiva. The lesion filled the ethmoid and maxillary sinus, and destroyed the pterygoid process. Numerous lymph node metastases were suspected in the bilateral cervical region. The patient was diagnosed with left maxillary sinus cancer T4aN2cM0 and treated with PCE. The size of the tumor was markedly reduced after the initial treatment. After six cycles of PCE, bioradiotherapy (BRT; 66 Gy/33 Fr) was performed for the remaining lesion, and a complete response was achieved. Ten months after BRT, the tumor recurred in the anterior wall of the left maxillary sinus, which was treated by partial maxillary resection and split-thickness skin grafting. No local or cervical recurrence was observed 2 years after the surgery. These findings suggested that PCE could be considered as the first step for the treatment of highly advanced malignant tumors in the head and neck.

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*Abbreviations:* ORR, objective response rate; SCC, squamous cell carcinoma

*Key words:* maxillary sinus cancer, paclitaxel, carboplatin, cetuximab, induction chemotherapy, bioradiotherapy

## Introduction

Maxillary sinus cancer is relatively rare among head and neck cancers (1). If the tumor extends superiorly, it can destroy the orbital floor and lead to ocular symptoms such as double vision (2). The tumor that extends posteriorly may destroy the pterygoid process, making it even more difficult to open the mouth (3). The tumor that spreads inward can fill the nasal cavity and cause symptoms such as nasal obstruction (4). If tumor expansion causes damage to the alveolar process, tumor may be exposed in the oral cavity (5). Treatment options for maxillary sinus cancer include surgery, radiation therapy (RT), and drug therapy (6). However, there is little evidence regarding the choice of treatment. Although surgery is often selected as the initial treatment, surgery for advanced cases significantly impacts the functional aspects and facial appearance due to its location and significantly reduces the quality of life (7,8).

Combination treatment with paclitaxel, carboplatin, and cetuximab (PCE) as a new induction chemotherapy regimen for advanced head and neck cancer has been recently reported (9). This treatment is characterized by a high completion rate and low toxicity (10). Post-treatment options include RT alone, chemoradiotherapy (CRT) with concurrent high-dose cisplatin (CDDP), bioradiotherapy (BRT), and surgery; these can be selected on a case-by-case basis, taking into account the patient's general condition, the size and location of residual tumor, and the effectiveness of PCE (11). Although PCE is reported to be highly effective for head and neck cancers, there are no detailed reports on the efficacy of PCE for maxillary sinus cancer.

Herein, we report a case of a patient with highly advanced maxillary sinus cancer with bilateral cervical metastatic lymph nodes who was successfully treated with PCE followed by BRT. The tumor was subsequently controlled via minimally invasive surgery following recurrence.

## Case report

A 69-year-old man presented to the Department of Dentistry and Oral Surgery, Hokuto Hospital (Obihiro, Japan) in June 2019 with left buccal swelling and an irregular mass on the left maxillary gingiva that had gradually increased in size over the past month. He had no extraordinary personal or

family medical history. Extraoral findings included left buccal swelling, trismus, left nasal obstruction, and enlarged bilateral cervical lymph nodes. Other findings, such as abnormal ocular position, diplopia, or lacrimation, were not observed. A mass (diameter, 50 mm) in the left palate, beyond the midline, and an ulcer on the left buccal alveolar region were observed within the oral cavity (Fig. 1). Magnetic resonance imaging showed that the lesion filled the ethmoid and maxillary sinus and destroyed the pterygoid process (Fig. 2A). Contrast-enhanced computed tomography and 18-fluoro-2-deoxyglucose positron emission tomography (FDG-PET) revealed multiple cervical lymph node metastases extending distally, including level V on the left side and level III on the right side (Fig. 2B and C). There was no evidence of distant metastasis. Biopsy revealed features of squamous cell carcinoma (SCC), and the patient was diagnosed with the left maxillary sinus cancer T4aN2cM0. Although the tumor was not considered unresectable, PCE treatment was provided as initial treatment owing to the invasive nature and postoperative functional implications of the surgery. The PCE regimen consisted of paclitaxel (100 mg/m$^2$ on Days 1, 8), carboplatin (AUC 2.5 on Days 1, 8), and cetuximab (400 mg/m$^2$ on Days 1, 250 mg/m$^2$ on Days 8, 15) for 3 weeks for a maximum of six cycles. At the end of the 1st cycle, the tumor in the maxilla had collapsed and opened widely in the maxillary sinus. By the end of the 6th cycle, the tumor had markedly shrunk and remained only partially anterior to the pterygoid process (Fig. 3A and B). No signs of metastasis were seen in the cervical lymph nodes. During the course of PCE treatment, the patient was diagnosed with neutropenia (Grade 2-4) and treated with cetuximab only. The residual tumor was treated by BRT (66 Gy/33 Fr) with weekly doses of cetuximab (250 mg/m$^2$). Subsequently, the lesion disappeared, and a complete response to the treatment was achieved. Cetuximab was continued weekly after BRT. Ten months after completion of BRT, an erosive lesion was detected on the anterior wall of the left maxillary sinus via PET (Fig. 4A and B). Following a biopsy which revealed SCC, cetuximab was discontinued, and partial maxillectomy along with split-thickness skin grafting was performed under general anesthesia. An incision was made along the nasal wing, and the superficial layer of the maxilla was lifted up to the zygomatic bone; the anterior and lateral walls of the maxillary sinus and the sinus mucosa-like scar containing the recurrent tumor were resected (Fig. 5A and B). The pathological diagnosis was SCC, with negative margins and no bone invasion. The patient was treated with the anticancer drug S-1 (120 mg/day, 2-week administration followed by one week of rest) for 1 year as adjuvant therapy. The patient could survive with minimal functional disability and a dento-maxillary prosthesis. No local or cervical recurrence was observed at the two-year follow-up after surgery.

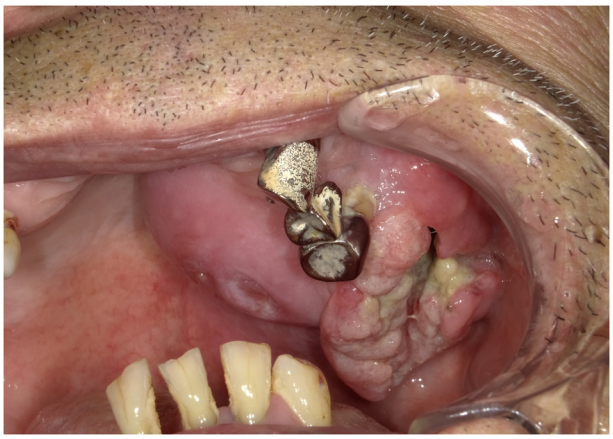

Figure 1. Intraoral photograph at the initial examination. A mass with a diameter of 50 mm was observed in the left palate beyond the midline. Additionally, an ulcer was seen in the left buccal alveolar region.

## Discussion

According to the National Comprehensive Cancer Network guidelines (12), surgical treatment involves total maxillectomy and bilateral neck dissection, which are invasive and cause significant postoperative functional impairment. In addition, the patient was diagnosed with numerous distal lymph node metastases in the bilateral cervical regions, and there was a high possibility of distant metastasis. Arterial injection chemotherapy was one option, but bilateral neck dissection could not be avoided; therefore, PCE was selected as the initial treatment. The conventional induction chemotherapy, which comprised the combination of docetaxel, cisplatin, and 5-fluorouracil (TPF), had significant toxicity issues. In 2010, PCE was introduced as a novel induction chemotherapy regimen for advanced head and neck cancer (9). It is characterized by high completion and response rates and low toxicity. Additionally, it has the advantages of being administered in an outpatient setting and allowing the use of chemoradiotherapy (CRT) as post-treatment. In this study, six weeks of PCE treatment resulted in an objective response rate (ORR) of 96% (complete response, 19%; partial response, 77%), indicating a very good response rate. This regimen has been reported to have a high response rate of 65% to 97% as induction chemotherapy for locally advanced head and neck cancer (11,13-17). However, only one recent study by Takenaka *et al* (11) reported using this regimen as induction chemotherapy for sinonasal carcinoma; two cycles of PCE were used as preoperative chemotherapy, and two out of four patients with sinonasal sinus cancer responded to the treatment (ORR, 50%).

This case demonstrated the possibility of treating maxillary sinus cancer using a minimally invasive method, which may be applied to other head and neck cancers. Post-treatment after a PCE regimen may include RT alone, CRT with CDDP, BRT, or surgery. The TREMPLIN trial (18) showed that the efficacy of CRT was similar to that of BRT after TPF. However, no such comparative study has been conducted for PCE, and there are no criteria for selecting the appropriate post-treatment method at present. Enokida *et al* (14) performed PCE for eight weeks, followed by CRT with CDDP, and showed that the completion rate of CRT was 97% and the response rate was 93.8%. Takenaka *et al* (11) performed two cycles of PCE followed by RT, CRT, or surgery, depending on the tumor site and condition. The post-treatment method for laryngeal and hypopharyngeal carcinoma was selected based on a chemoselection strategy. Therefore, CRT and BRT may be effective for the post-treatment of maxillary sinus cancer

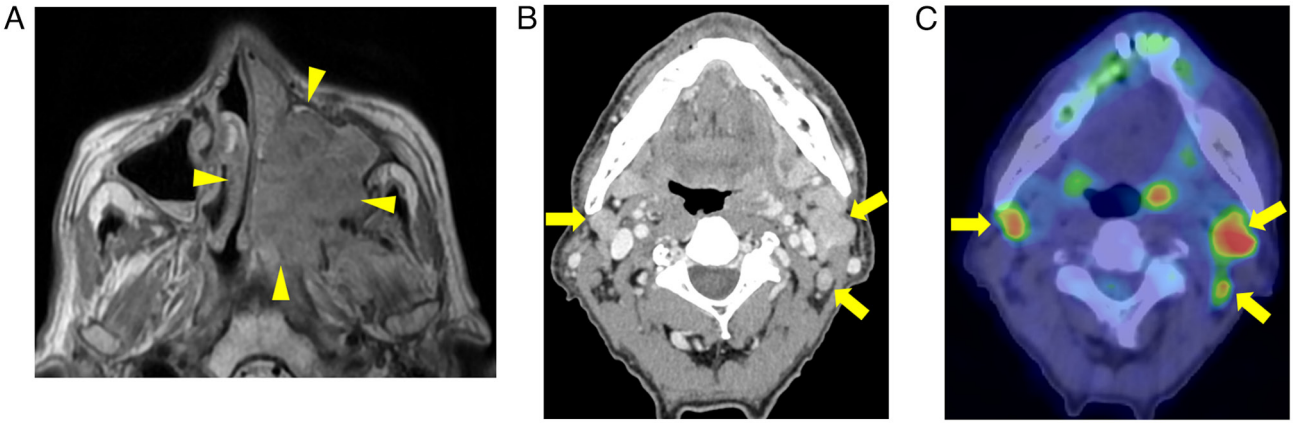


Figure 2. Various imaging findings before treatment. (A) Magnetic resonance imaging showed a tumor that filled the ethmoid and maxillary sinuses and destroyed the pterygoid process. The arrowheads point to the tumor. (B) Contrast-enhanced computed tomography and (C) 18-fluoro-2-deoxyglucose positron emission tomography showed multiple enlarged lymph node metastases in the bilateral cervical regions. The arrows indicate metastatic nodes.

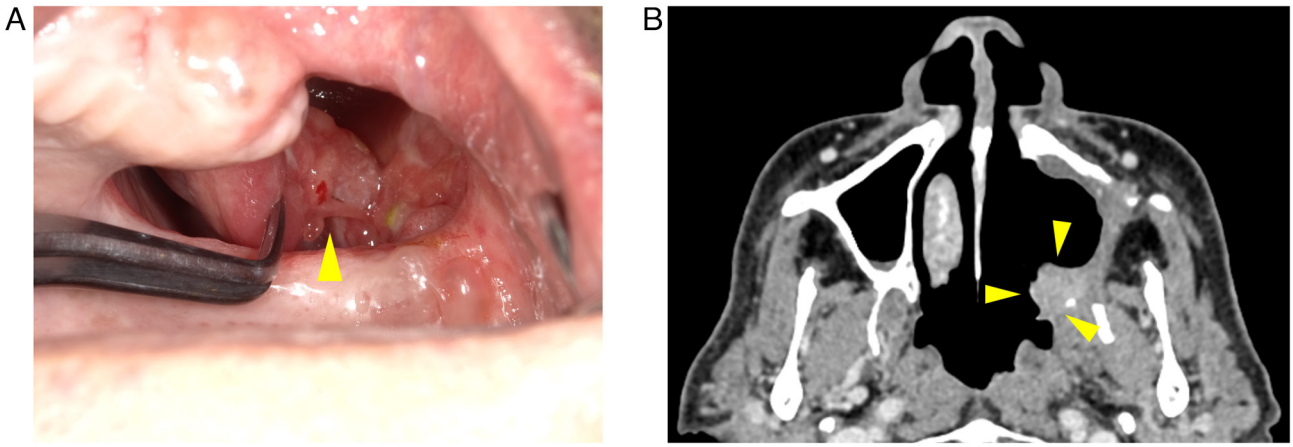


Figure 3. The residual tumor after six cycles of paclitaxel, carboplatin and cetuximab. (A) Intraoral photograph of the residual tumor was shown. (B) Computed tomography showed that the tumor remained only partially anterior to the pterygoid process. The arrowheads indicate residual tumor.

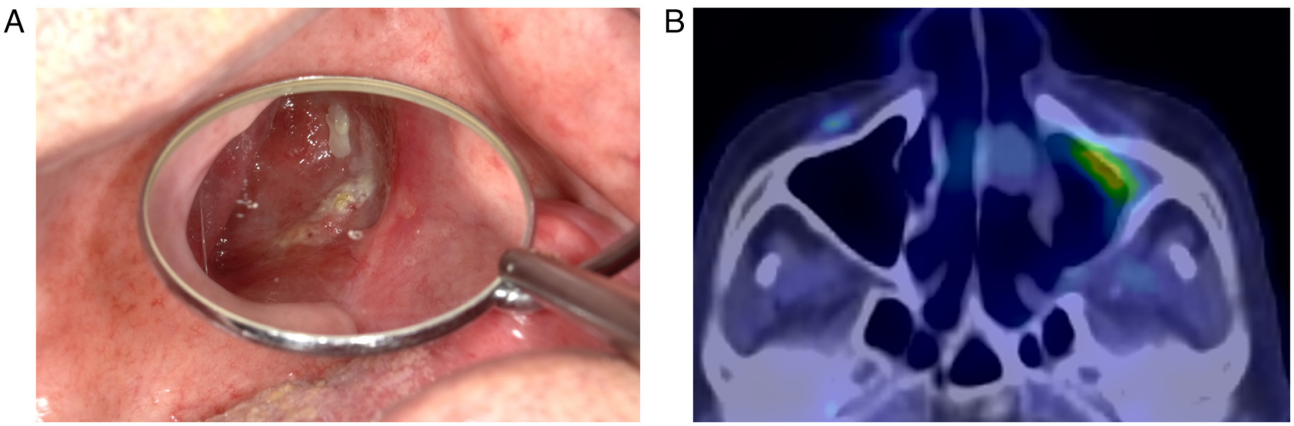


Figure 4. Recurrent lesion observed 10 months after the completion of bioradiotherapy. (A) An erosive lesion was observed in the anterior wall of the left maxillary sinus. (B) FDG positron emission tomography shows a high uptake of FDG in the same area. FDG, 18-fluoro-2-deoxyglucose.

that has responded well to PCE. BRT is more manageable than CRT due to the possibility of developing myelosuppression and renal dysfunction by CDDP. However, BRT may cause severe infusion reactions and interstitial pneumonia. In the current case report, the tumor continued to shrink during PCE, and continuing cetuximab was considered considerably beneficial; therefore, BRT was chosen as post-PCE therapy, which resulted in a good outcome.

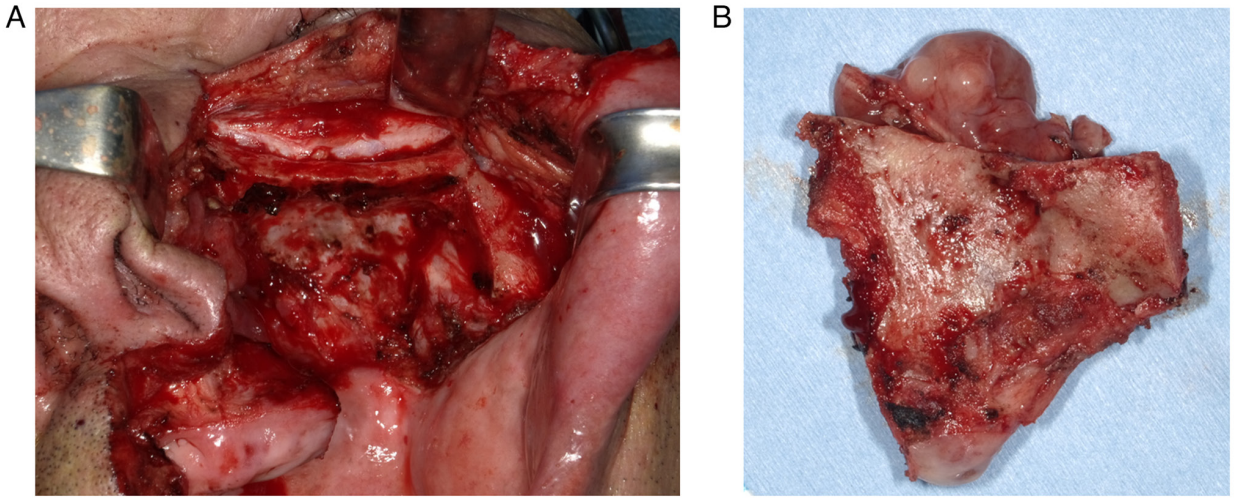


Figure 5. Surgery for removing the recurrent tumor. The patient underwent partial maxillary resection and split-thickness skin grafting. (A) The anterior and lateral walls of the maxillary sinus were resected, and the sinus mucosa-like scar containing the recurrent tumor was dissected. (B) The resected specimen was shown.

This report demonstrates the effectiveness of PCE and BRT as post-treatment methods for advanced maxillary sinus cancer. In patients initially treated with PCE, careful imaging evaluations, assessment of the treatment efficacy, and selection of the appropriate post-treatment method will lead to improved outcomes.

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**Availability of data and materials**

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

**Authors' contributions**

MM, MT, TS and SM discussed the treatment strategy. MT and SM treated the patient with PCE. MM, MT and TS performed surgery for the recurrent lesion. MM, MT, TS and SM performed follow-up observations. MM, MT and SM drafted the manuscript. All authors approved the final version of the manuscript.

**Ethics approval and consent to participate**

Not applicable.

**Patient consent for publication**

The patient provided written informed consent for publication.

**Competing interests**

The authors declare that they have no competing interests.

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