Metastatic colon carcinoma in the maxilla: Highlighting the importance of perioperative oral management: A case report

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Abstract. Metastatic colorectal carcinoma involving the maxilla is a rare phenomenon, and existing literature regarding the significance of perioperative oral function management (POM) in managing such cases is limited. In the present case report the clinical details of a 58-year-old male referred to the oral and maxillofacial department for POM. The patient had previously undergone segmental bowel resection due to stage IIIb colon cancer. A comprehensive approach encompassing a thorough medical history, meticulous physical examination, radiographic imaging and immunohistopathology was employed, and a definitive diagnosis of metastatic adenocarcinoma in the left maxillary gingiva originating from a colorectal carcinoma was reached. Additionally, concomitant metastases were detected in the lungs and liver. Despite the daunting prognosis associated with the metastases in the oral cavity, the patient's quality of life exhibited discernible improvements owing to the implementation of palliative care interventions. Notably, this interdisciplinary approach facilitated the patient's survival for over a year. The present case report strongly advocates for the prompt integration of POM in the surgical management of cancer patients with oral manifestations, which can optimize both the quality of life and overall survival.

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Abbreviations: CA19-9, carbohydrate antigen 19-9; CEA, carcinoembryonic antigen; CK, cytokeratin; CT, computerized tomography; HBsAb, hepatitis B surface antibody; MOF, multiple organ failures; POM, perioperative oral function management; TNM, cancer staging system

Key words: perioperative oral management, colon cancer, oral metastasis, gingival cancer, case report

Introduction

Metastatic tumors in the oral region are extremely rare, constituting <1% of all malignancies (1,2). They primarily affect individuals aged 50-70 years-old, with no significant sex disparity. The mandible and gingiva are the predominant sites for jawbone and soft tissue metastases, respectively; however, the frequency varies depending on the primary lesion (3-8). In men, oral metastases commonly arise from lung, kidney, liver and prostate cancers, whereas in women, breast, genital and kidney cancers are frequently associated with oral metastases (6). The metastasis of colorectal cancer to the oral cavity is relatively uncommon (only 1-2% of all cases) (5-10).

The significance of perioperative oral function management (POM) in preventing and mitigating post-operative complications, including surgical site infections and pneumonia, and improving the overall quality of life of the cancer patient, is increasingly evident (11-16). POM interventions have demonstrated positive outcomes, including reduced hospital stays, decreased medical costs, and improved patient survival rates, consequently gaining recognition as an indispensable procedure during the perioperative period (11-18). However, limited literature exists regarding the effectiveness of POM in managing oral metastases, particularly in the context of colorectal cancers.

The present case report presents a rare case of metastases to the maxillary gingiva originating from a stage IIIB tumor-node-metastatic (TNM) colorectal carcinoma. The patient's condition improved with the POM, resulting in a significant enhancement in the quality of life. In contrast to expectations, the patient defied prognostic predictions and survived for over a year before succumbing to multiple organ failure (MOF). These findings underscore the urgent need for timely administration of POM to improve the quality of life and survival rates of surgical patients with a history of cancer and oral symptoms.

Case report

A 58-year-old man complaining of an uncomfortable swelling on the left side of the upper jaw and decreased oral intake was referred to the Department of Oral and Maxillofacial Functional Rehabilitation in March 2018 for a POM consultation. The patient had a surgical history of segmental bowel resection due to TNM stage IIIB colorectal cancer, with elevated serum carcinoembryonic antigen (CEA; recorded value, 5.9 ng/ml; reference value, 0.0-4.0 ng/ml) and serum hepatitis B surface antibody (HBsAb; recorded value, 104.04 mIU/ml; reference value, 0.00-9.99 mIU/ml) levels, and normal liver function test values. In January 2015, the patient had a history of melena and occasional hematochezia. TNM stage IIIB colorectal adenocarcinoma was diagnosed following a thorough clinical evaluation, and the patient was surgically treated using the Hartmann procedure (13) under general anesthesia in March 2015. Thereafter, the patient was followed up ~1 year without evidence of recurrence or metastatic disease. After March 2016, the patient was lost to follow-up for two years. However, the patient returned in March 2018 with complaints of abdominal pain and oral symptoms. Additionally, the patient had a history of a remnant root following extraction of the left maxillary second premolar; the family history was unremarkable.

Upon examination, the patient was cachectic and sick looking with mild pallor, a tinge of jaundice, and cervical lymphadenopathy on the left side. Extraoral examination indicated facial asymmetry and swelling of the left cheek. Intraoral investigations revealed a large, ulcerative, moderately-tender, irregular mass (size, 22x20x18 mm) with focal areas of necrosis extending distally from the left maxillary first premolar (Fig. 1).

The patient underwent radiological, hematologic and histological examinations, with a differential diagnosis of a gingival tumor invading the maxillary sinus. Orthopantomography and computed tomography (CT) were performed in the radiology department. The orthopantomograms showed horizontal bone resorption in the jaw, particularly in the left maxillary molar root region and around the second premolar (Fig. 2). CT scan of the oral cavity showed a large, poorly demarcated soft tissue mass extending into the left maxillary sinus, with generalized bone resorption around the left second premolar and the base of the maxillary sinus (Fig. 3). CT scans of the chest and abdomen showed relatively distinct nodules in the lung and tumor recurrence in the residual bowel. Liver metastases were also detected. The hematology and blood biochemistry test results are shown in Table I. The levels of the tumor markers CEA and carbohydrate antigen 19-9 (CA19-9), also known as Sialyl-LewisA, were exponentially elevated; other blood parameters were essentially unremarkable.

Fresh surgical biopsy specimens from the jaw tumor underwent histopathological analysis in the university hospital pathology department, conducted by at least 2 pathologists. This involved the utilization of hematoxylin and eosin (H&E) staining and immunohistochemistry (IHC). For H&E staining, the process commenced by sectioning the specimen into 4-μm thick segments following fixation with 96% ethanol. Subsequently, these sections were immersed in a 10% formalin solution for 24 h. Hematoxylin staining was initiated for 30 sec, followed by a 5-min water rinse and a 15-sec eosin Y counterstaining. Dehydration using 96 and 99.8% ethanol, along with xylene fixation and cover slipping with a mounting medium, followed suit. Diagnostic images were captured via a Nikon Eclipse Ci microscope equipped with a Nikon DS-Fi3 camera with a 4X objective (Nikon Corporation).

Figure 1. Intraoral photograph showing a mass (size, 22x20x18 mm) on the gingiva corresponding to the maxillary second premolar on the left side.

Figure 2. Panoramic radiograph showing the residual root of the left maxillary molar along with resorption of the surrounding bone.

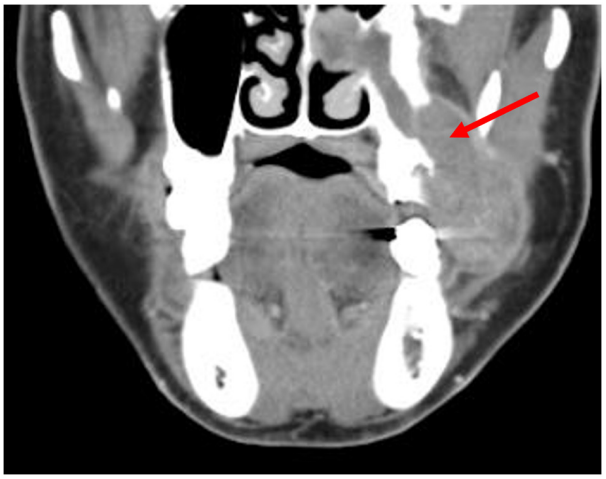

Figure 3. Compute tomography image showing bone resorption around the maxillary tooth 6 on the left side of the maxillary sinus.

Table I. Hematology and blood biochemistry findings.

Test parameter	Obtained value	Reference range	Unit
Initial hospital visit			
WBC	10,900	4,000~9,000	Ml
s-Glu	117	70~110	mg/dl
HB_sAb	104.04	0.00~9.99	mIU/ml
CEA	5.9	0.0~5.0	Ng/ml
CA19-9	<2.0	0.0~37.0	U/ml
Emergency visit			
WBC	10,200	4,000-9,000	Ml
AST (GOT)	46	13~37	IU/l
ALT (GPT)	30	8~45	IU/l
LDH	1,212	122~228	IU/l
ALP	1,749	118~335	IU/l
γ-GT	870	8~33	IU/l
ALB	3.3	4.1~5.2	g/dl
BUN	14.6	7.8~18.9	mg/dl
CREA	0.77	0.45~0.82	mg/dl
s-Glu	92	70~110	mg/dl
HB_sAb	29.79	0.00~9.99	mIU/ml
CEA	10,945.4	0.0~5.0	Ng/ml
CA19-9	<2.0	0.0~37.0	U/ml
5-S-CD	2.7	1.5~8.0	

WBC, white blood cell count; AST (GOT), aspartate transaminase (glutamic oxaloacetic transaminase); ALT (GPT), serum glutamate-pyruvate transaminase or serum glutamic-pyruvic transaminase; LDH, lactate dehydrogenase; ALP, alkaline phosphatase; γ-GT, gamma-glutamyl transferase; ALB, albumin blood test; BUN, blood urea nitrogen; CREA, creatinine test; s-Glu, blood glucose; glycated hemoglobin; HB_sAb, hepatitis B surface antibody; CEA, carcinoembryonic antigen; CA19-9, cancer antigen 19-9; 5-S-CD, serum 5-S-Cysteinyldopa.

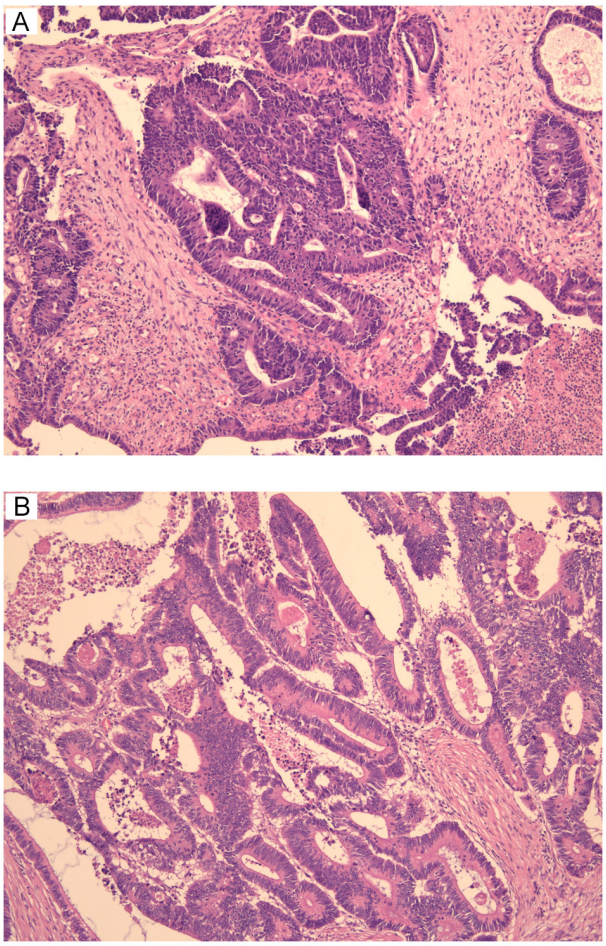

Figure 4. Histopathological images of the patient. (A) H&E staining of the maxillary gingiva (magnification, x40). (B) H&E staining of the sigmoid colon (magnification, x40). The formation of a tubular structure by the proliferating atypical cells and necrotic tissue indicated a moderately-differentiated adenocarcinoma.

For IHC, the streptavidin-peroxidase technique was employed on 4-μm thick specimen sections. Following rinsing with phosphate-buffered saline (PBS) and a 10-min pepsase activity for antigen retrieval, sections were incubated in methanol alongside 3% hydrogen peroxide to deactivate endogenous peroxidases. Subsequently, blocking with PBS 0.5% Tween-20 (PBS-T; MilliporeSigma), containing 3% bovine serum albumin (MilliporeSigma), occurred for 1 h at room temperature. Incubation at 4˚C overnight with primary antibodies including cytokeratin (CK)7 and CK20 was performed. As an example, the primary antibody for CK7, rabbit anti-CK7 (1:1,600; cat. no. ab199718; Abcam), was utilized. Following three PBS washes, a secondary antibody, goat anti-rabbit IgG H&L (HRP) (1:500; cat. no. ab97051; Abcam), was introduced, along with fresh Diaminobenzidine as the substrate. Negative controls employed PBS instead of the primary antibody. Philips IntelliSite Pathology Solution (Philips) was employed for image acquisition.

H&E staining analysis unveiled atypical cell growth within tubular structures coupled with necrotic tissue, indicating a moderately-differentiated adenocarcinoma (Fig. 4). Furthermore, IHC demonstrated CK20 positivity and CK7 negativity in the atypical glandular ducts, implying metastasis from the colorectal carcinoma (Fig. 5).

Based on the results of the POM examination, the oral lesion was diagnosed as metastatic colorectal adenocarcinoma of the maxillary gingiva. In addition, metastases were observed in the lung and liver. After thorough consultations among the surgeons and considering several factors, including the patient's general condition and the late stage of the disease, the patient was treated with adjuvant chemotherapy and radiotherapy with removal of the remaining root tooth, rather than aggressive surgical treatment of the tumor in the oral cavity. Chemotherapy was initiated using a combination of XELOX: capecitabine (Xeloda®; Chugai Pharmaceutical Co., Ltd.) plus oxaliplatin (Yakult Honsha Co., Ltd.), and bevacizumab (BV). A total of seven doses of XELOX (170 mg) plus BV (450 mg) were followed by 21 doses of cetuximab; cetuximab administration started with a single dose of 620 mg, which was reduced to 390 mg once daily. The oral cavity and primary tumor were treated by radiation therapy (8 Gy each). The patient's oral intake improved after the extraction of the residual tooth and the comprehensive implementation of POM, which included

Table II. Showing some reported cases of colorectal cancer metastasis in the maxillary gingiva.

Case	Authors	Publication year	Age	Sex	Prognosis	Other metastasis sites
1	Cama *et al* (24)	2002	57	Female	<1 year	Not indicated
2	Kataoka *et al* (23)	2003	37	Female	3.6 years	Lung, brain
3	Koizumi *et al* (21)	2004	69	Male	3.7 years	Lung, liver
4	Kitamura *et al* (22)	2007	64	Male	1 Year	None
5	Baranović *et al* (25)	2015	78	Male	<1 year	Liver
6	Dalirsani *et al* (26)	2020	69	Female	<1 year	Not indicated
7	Nair *et al* (27)	2021	50	Male	<1 year	Lung, liver, adrenal and vertebral
8	Prasad *et al* (28)	2021	51	Male	<1 year	Not indicated
9	Neumann *et al* (29)	2021	59	Male	26 other cases were listed, reported over 30 years (mostly with poor prognosis)	Peritoneum
10	Todorova *et al* (30)	2021	73	Male	Not indicated	Locoregional lymphatic nodes
11	Present case	2023	58	Male	>1 Year	Lung, liver, bone

Table III. Shows suggested diagnostic criteria for oral metastatic tumors.

Item number	Criterion	(Refs.)
1	Clinical and histological evidence of a primary tumor	(31)
2	The histological similarity between the primary tumor and the metastases	
3	No previous tumor in the metastatic area	
4	No direct invasion from the primary tumor or other metastases	
1	Histopathological similarity to the primary tumor	(32)
2	Sufficient clinical and histological suspicion of metastatic disease	
3	A tumor suspected to be metastatic must not resemble a primary tumor arising in the oral cavity	

customized hygiene, chemoprophylaxis, collaborative efforts from an interdisciplinary medical team, pain management, and patient education. Subsequently, an improvement in the patient's quality of life was observed for >12 months before his clinical condition deteriorated due to multiple organ metastases. The patient succumbed to MOF in March 2019.

Discussion

Metastases in the oral cavity are rare, and studies on the efficacy of POM for managing such cases are limited. Patients with metastatic tumors in the oral cavity can present with various symptoms, such as swelling, pain, nerve paralysis and dental issues (tooth mobility or displacement). Gingival metastases may be asymptomatic or manifest as painless granulomatous masses (7,8). Therefore, it is crucial to differentiate metastatic oral tumors from other dental conditions accurately.

Colorectal carcinomas account for ~18% of all malignancies, with sigmoid carcinoma constituting ~30% of these cases (8). Orofacial metastatic tumors can potentially originate from various organs, such as the lungs and kidneys; nonetheless, the rare occurrence of oral metastases stemming from colorectal cancer can pose complex challenges in both diagnosis and treatment (7-10). A precise diagnosis of metastatic tumors in the oral cavity is vital for identifying the primary tumor and any metastases to other organs (9,11-20). Furthermore, distinguishing between primary and metastatic tumors in the oral cavity is crucial for selecting the appropriate treatment approach.

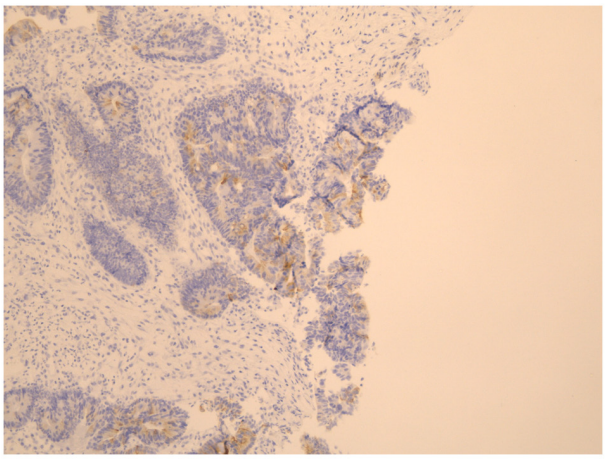

Figure 5. Histopathological images of the maxillary gingiva showing positive immunostaining for CK20 (magnification, x40).

The diagnostic criteria for metastatic tumors include the presence of a primary tumor or the absence of other tumor lesions (Tables II and III) (21-32). Additionally,

histopathological similarities to the primary tumor and the clinical metastatic status are considered during the diagnosis (32). In the present case report, histopathological examination revealed a moderately-differentiated adenocarcinoma. Immunostaining with CK20 and CK7 aided in establishing its correlation with the primary site (19,33-35). The positive CK20 and negative CK7 results were consistent with the findings of metastatic colorectal carcinoma (32). The elevated serum levels of CEA and CA19-9 and the CT images confirmed cancer infiltration in the liver and lungs.

The metastasis of sigmoid carcinoma to the liver and lungs is considered to occur via the portal vein system and to other sites (such as the oropharyngeal region) via the inferior vena cava and pulmonary veins (36,37). The mandible commonly serves as the primary site for metastatic tumors due to its high vascularity, while the rich capillary network in the gingiva facilitates the infiltration of tumor cells (8,20,38). In the present case report, chronic gingival irritation resulting from a retained root fragment in the left upper second premolar may have contributed to the dissemination of cancer cells through the bloodstream.

Consistent with the findings in this case, metastatic tumors in the oral and maxillofacial regions are frequently encountered as multiple metastases and exhibit a high fatality rate (22,23). A comprehensive evaluation of the primary tumor and the presence or absence of metastases is crucial in determining an effective treatment plan. POM during the perioperative period is widely recognized as a critical procedure in the surgical management of patients with cancer, offering notable advantages (11-16). Kurasawa *et al* (39) investigated the impact of POM on pneumonia and the mortality of patients with cancer and reported its effectiveness in decreasing the incidence of pneumonia across various cancer types, including musculoskeletal, lung, brain, head and neck, thyroid gland, pancreatic, stomach, and esophageal cancers. In addition, POM was beneficial for patients with compromised immune systems and respiratory dysfunction. Factors such as preoperative conditions, nutritional status, oral hygiene, and the relationship between the operative field and airway were identified as crucial determinants of the effectiveness of POM. Importantly, POM was associated with decreased mortality rates, particularly in lung and pancreatic cancer, which was attributed to enhanced oral hygiene and swallowing function. Additionally, a case report by Nashi *et al* (40) underscored the significance of standardized techniques and guidelines for oral management to prevent complications, especially in patients with cardiac conditions, which served as a reminder for healthcare practitioners to prioritize appropriate POM protocols. In another study, Suzuki *et al* (41) reported that preoperative periodontal treatment improved oral health before and after cardiac valve surgery; the intervention group also experienced fewer postoperative fever days. Although the present case report had certain limitations, the results suggested that preoperative treatment may help mitigate the risk of postoperative infections, thus emphasizing the necessity for perioperative oral health interventions and education. Conversely, a retrospective review on POM conducted at a cancer treatment hospital demonstrated positive outcomes, such as reduced complications and improved patient experiences; however, the authors observed challenges associated with POM due to the absence of standardized practices and limited collaboration between medical and dental professionals (42). The present case report highlighted the importance of education and early intervention in oral management to optimize cancer treatment outcomes.

In the present case report, the proactive implementation of POM significantly enhanced the patient's quality of life via comprehensive assessment and palliative care, despite the advanced stage of the disease. This interdisciplinary approach prolonged survival by over a year before the eventual demise of the patient. Metastatic tumors in the oral cavity were promptly identified through POM, although surgery was deemed not feasible due to liver and lung involvement. Prompt consideration of clinical findings, differentiation of oral symptoms from tumor lesions, and emphasis on oral care in systemic disease through effective collaboration between medical and oral/dental professionals are crucial for the perioperative oral management of patients with malignant tumors.

In conclusion, the present case report highlighted the rarity of metastases, especially colon carcinoma metastasis, to the maxilla. An accurate diagnosis, differentiation from dental conditions, and POM are indispensable for the effective treatment of patients in this condition. POM offers significant advantages in preventing pneumonia, reducing mortality, and improving oral health. Standardized practices and interdisciplinary collaboration are imperative for optimizing the outcomes. Further research on POM can enhance the management of oral metastases and improve the well-being of the patient.

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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 and EHN contributed to the drafting of the manuscript. MM, EHN and NK performed the literature search. MM, EHN, NK, IK, SJ, MN,KT, SY and NH collected the data and assisted in drafting the case report section. MM, EHN, SY and NH critically revised the manuscript. All authors confirm the authenticity of all the raw data. All authors have read and approved the final version of the manuscript.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

Written informed consent for the publication of the patient's clinical information and images was obtained from the patient.

Competing interests

The authors declare that they have no competing interests.

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