CDJ
Chronic Diseases Journal
Chron Dis J 2026;14(1):36-47. doi:10.34172/cdj.910
http://cdjournal.muk.ac.ir

Systematic Review

Oral manifestations in patients with gastrointestinal malignancies: A Systematic Review

Hooman Tahmasebi[1], **Negin Samiee**[2*], **Yousef Moradi**[3*]

[1]Student Research Committee, Faculty of Dentistry, Kurdistan University of Medical Sciences, Sanandaj, Iran
[2]Oral and Maxillofacial Medicine Department, Faculty of Dentistry, Kurdistan University of Medical Sciences, Sanandaj, Iran
[3]Health Metrics and Evaluation Research Center, Research Institute for Health Development, Kurdistan University of Medical Sciences, Sanandaj, Iran

Article history:
Received: February 20, 2024
Revised: February 21, 2024
Accepted: March 5, 2024
ePublished: March 28, 2026

***Corresponding authors:**
Negin Samiee,
Email: Negin.samiei@gmail.com;
Yousef Moradi,
Email: Yousefmoradi211@yahoo.com

Abstract

Introduction: Roughly 1% of malignant lesions in the maxillofacial region are due to metastatic lesions, and 10% of these metastatic lesions are related to primary tumors located in the gastrointestinal tract. This systematic review examines the oral manifestations of metastatic lesions resulting from gastrointestinal malignancies based on age, gender, survival rates, and tumor characteristics. Given the importance of timely and accurate diagnosis of metastatic lesions originating from primary tumors in the gastrointestinal tract in improving patient prognosis and increasing survival time, the main objective of this systematic review is to identify oral manifestations of metastatic lesions in patients with gastrointestinal malignancies worldwide.

Methods: The review was conducted using international databases, including PubMed, Scopus, Web of Science, Google Scholar, and Ovid, with a deadline of June 2023. The search strategy included keywords such as "metastasis," "oral manifestations," "gastrointestinal malignancies," and "oral mucosa," and their synonyms were selected from Mesh to develop the search strategy.

Results: Seventy patients were included in this study, with 47 being male and 23 being female, and the average age of the patients was 64.5 years. Forty-four percent of the tumors were related to the colon, and 81% of all tumors were related to adenocarcinoma. The most common clinical symptom was the presence of a tumor or swelling, which was reported in 49% of cases, while the most common patient complaint was pain, experienced by 24% of patients. The mandible was the most commonly affected site of the metastatic lesion. The average survival time after diagnosis of oral metastatic lesions was approximately 6 months, and chemotherapy with or without surgery was the most commonly used treatment.

Conclusion: The prognosis for patients with metastatic lesions resulting from gastrointestinal malignancies is poor, and in some cases, it may be the first sign of gastrointestinal malignancy. Timely diagnosis and treatment can improve the quality of life and prognosis for these patients.

Keywords: Oral manifestations, Gastrointestinal neoplasms, Systematic review

Please cite this article as follows: Tahmasebi H, Samiee N, Moradi Y. Oral manifestations in patients with gastrointestinal malignancies: a systematic review Chron Dis J 2026;14(1):36-47. doi:10.34172/cdj.910

Introduction

Metastatic tumors of the oral cavity and maxillofacial region make up approximately 1% of all malignant lesions in this area, and according to dental and oral documentation, this area is not a common site for metastases from tumors located in other parts of the body.[1] As a general rule, metastatic malignancies in this area are considered a good indicator of the presence of a cancer with a high stage, indicating a poor prognosis for the patient, and according to previous studies, 90% of patients die within an average of 6 to 8 months after diagnosis.[2,3,4,5] However, diagnostic methods for malignancies and their metastases have made significant progress in recent years, providing patients with the opportunity to undergo a faster and more efficient diagnostic process and receive treatment sooner.[6] In 25% of patients, the first sign of a hidden distant tumor is the presence of a metastatic malignancy in the oral cavity and maxillofacial region[7], and in some patients, despite various tests and examinations to find the primary tumor, the site of malignancy remains unknown.[8] Reported metastases to the jawbones are more common in the bone tissue than in the soft tissue, and generally, the area of the mandibular molars is more involved.[7,8,9]

The clinical appearance of metastatic tumors in the soft tissue of the maxillofacial region can resemble hyperplastic lesions or benign soft tissue tumors such as fibroma, pyogenic granuloma, or hemangioma, which can make initial diagnosis difficult.[1,10] In some cases,

metastatic lesions can mimic malignant tumors such as squamous cell carcinoma, lymphoma, and salivary gland carcinomas.[11] Radiographic images showing an indeterminate radiolucent lesion are one of the most prominent signs of a malignant tumor, but this does not necessarily mean that the lesion is metastatic and it can be a primary lesion.[12]

Metastatic lesions in the maxillofacial region can present with various clinical symptoms such as rapid growth, numbness, pain at the site of the lesion, limited mouth opening, difficulty swallowing, and the presence of an exophytic mass. Other symptoms may be present that can mislead the dentist towards a diagnosis of odontogenic pain. Tooth mobility in the adjacent teeth or toothache and swelling in the maxillofacial area are among these misleading symptoms.[4,11,13,14]

The most common malignancies whose metastases involve the maxillofacial region differ between men and women. In men, lung cancer and then renal cell carcinoma are the most common malignancies that metastasize to the oral cavity and maxillofacial region. The most commonly reported primary tumors in women are breast and genital organ tumors, respectively.[7]

Despite advancements in diagnostic modalities, the subtle clinical manifestations of metastatic lesions in the maxillofacial region often elude detection. Dentists and healthcare providers may overlook these lesions, attributing symptoms to benign dental conditions. Consequently, there is a pressing need for enhanced awareness and diagnostic strategies to bridge this diagnostic gap and expedite appropriate management. Given the significance of timely and accurate diagnosis of metastases originating from primary tumors in the gastrointestinal tract in improving patient prognosis and increasing survival time, the main objective of this study is to systematically review the manifestations of oral metastases in patients with gastrointestinal malignancies worldwide.

Methods

The present study is a systematic review conducted and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The study included the following steps: search strategy development, article screening, final article selection, data extraction, and quality assessment. Due to the high heterogeneity of studies conducted worldwide on this topic, meta-analysis was not performed.

To perform the systematic review, international databases including PubMed, Scopus, Web of Science, and platforms such as Google Scholar and Ovid were searched. The deadline for conducting the search was until June 2023. The search keywords included "metastasis," "oral manifestations," "gastrointestinal malignancies," and "oral mucosa," and their synonyms were selected from Mesh for the search strategy. In addition, grey literature was accessed by reviewing the references of relevant articles and retrieving relevant reports from the websites of organizations such as WHO and CDC to access all published articles.

After retrieving all articles from international databases and grey literature, all results were entered into EndNote version 8 software, and article screening was conducted based on title, abstract, and full text. In this step, inclusion criteria for full study were considered.

The inclusion criteria for the present systematic review were all studies related to identifying the manifestations of oral metastases in patients with gastrointestinal malignancies. The studies included case reports or series, cohort studies, case-control studies, or other studies except for review articles, systematic reviews, or meta-analyses.

After screening the articles, final article selection and data extraction were performed. To extract the data in the present systematic review, first, the opinions of the authors' team and experts in this field were collected, and then a checklist was used for data extraction, including the authors' names, year of publication, study type, country, gender, age, site of primary tumor, site of metastasis, type of treatment received, clinical manifestation, and survival time. JBI's critical appraisal tools were used to assess the quality of the selected articles, based on the type of study.

The analysis of the present systematic review was performed using a qualitative analysis approach. Due to the heterogeneity of the studies, meta-analysis was not performed, and only a qualitative content analysis approach was used to analyze the selected studies' results. This article has resulted from a master's thesis approved and supported by the Kurdistan University of Medical Sciences with the code of ethics IR.MUK.REC.1401.316.

Results

According to this systematic review, after searching international databases and using grey literature, a total of 3812 articles were obtained, and out of these, 3657 were excluded based on title and 27 were excluded based on abstract. As a result, 116 full-text articles were reviewed, and ultimately, 57 studies were included in this article and thoroughly examined[2,4,5,8,11,15,16,17,18,19,20,21,22,23,24,25,26,27,28,29,30,31,32,33,34,35,36,37,38,39,40,41,42,43,44,45,46,47,48,49,50,51,52,53,54,55,56,57,58,59,60,61,62,63,64,65]. Among the 57 studies, there were three types of studies: 42 case reports, 7 case series reports, and 8 retrospective studies (Figure 1).

These studies were conducted in different countries and regions, with 25 studies related to the Asian continent, of which 10 were from Japan and 5 were from China. South Korea, India, and Iran each had 2 studies, and Taiwan, Israel, Malaysia, and Lebanon each had 1 study. 21 studies were related to Europe, of which 5 did not belong to Spain. Croatia, England, and Italy each had 3 studies, and France and Greece each had 2 studies. Germany, Switzerland, and Portugal each had 1 study. In North America, there were 8 relevant studies, one from Canada and the rest from the United States, and finally, there were 3 studies related to South America, all from Brazil (Table 1).

Overall, there were 70 cases of patients with metastasis due to gastrointestinal malignancies in the reviewed studies, with twice as many men as women. 67.1% (47

Table 1. Studies included in this systematic review

Author	Year	Country	Type	Number
C. Álvarez Álvarez[15]	2006	Spain	Case report	1
A. Andabak Rogulj[16]	2018	Croatia	Cohort	1
M. Baranović[17]	2015	Croatia	Case report	1
D. Bell[18]	2009	USA	Case series	1
L. Bodner[19]	2006	Israel	Case series	1
F. G. H. Coad[20]	2013	England	Case report	1
P. Colombo[21]	2005	Italy	Case report	1
Z. Dalirsani[22]	2020	Iran	Case report	1
Z. Dalirsani[23]	2021	Iran	Case report	1
M. Deutsch[24]	2002	USA	Cohort	1
D. Di Stasio[25]	2018	Italy	Case report	1
G. Favia[26]	2010	Italy	Case series	2
M. Fukuda[27]	2002	Japan	Case series	2
A. Hadhri[28]	2020	Japan	Case report	1
D. P. Ho[29]	2022	USA	Cohort	9
K. G. Hwang[30]	2007	South Korea	Case report	1
T. Iida[31]	2009	Japan	Case report	1
A. B. A. Jalil[32]	2009	Malaysia	Cohort	1
B. C. Jham[33]	2011	Brazil	Case series	1
I. G. Kalaitsidou[34]	2015	Greece	Case series	1
A. Kameta[35]	2017	Japan	Case report	1
A. Kolk[36]	2003	Germany	Case report	1
A. Khazzaka[37]	2016	Lebanon	Case report	1
N. A. A. Kuttan[38]	2006	USA	Case report	1
M. S. Kwon[39]	2006	South Korea	Case report	1
J. Landeyro[40]	2010	Spain	Case report	1
K. P. Lawes[41]	2013	England	Case report	1
J. C. Lutz[42]	2008	France	Case report	1
S. Majumdar[43]	2016	India	Case report	1
O. M. Maria[44]	2022	Canada	Case report	1
M. Miyake[45]	2015	Japan	Case report	1

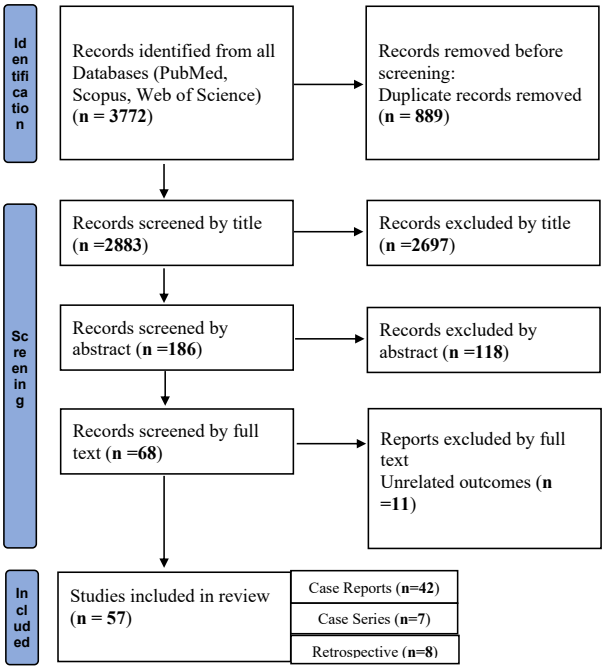

Figure 1. PRISMA 2020 flow diagram included searches of databases and registers only with their results

Table 1. Continued.

Author	Year	Country	Type	Number
P. Mojica-Manosa[46]	2006	USA	Case report	1
J. Murillo[4]	2013	Spain	Cohort	1
E. D. Neumann[47]	2021	Spain	Case report	1
N. Nishide[77]	2006	Japan	Case report	1
Y. T. Qiu[2,48]	2013	China	Cohort	1
Q. G. Ren[49]	2017	China	Case report	1
B. A. Rocha[2]	2020	Brazil	Case series	1
I. Romanet[50]	2018	France	Case report	1
K. J. Rosbottom[51]	2009	England	Case report	1
J. C. Salvador[52]	2018	Portugal	Case report	1
D. Sauerborn[11]	2011	Croatia	Case report	1
J. Seoane[5]	2009	Spain	Cohort	2
M. L. Shen[8]	2009	China	Cohort	2
S. Shimoyama[53]	2004	Japan	Case report	1
W. Smolka[54]	2004	Switzerland	Case report	1
A. B. Soares[55]	2011	Brazil	Case report	1
H. Soda[56]	2010	Japan	Case report	1
H. Su[57]	2017	China	Case report	1
M. Tomikawa[58]	2001	Japan	Case report	1
Z. Tsakiraki[59]	2021	Greece	Case report	1
N. Usman[60]	2014	India	Case report	1
M. Watanabe[61]	2016	Japan	Case report	1
C. C. Willard[62]	2002	USA	Case report	1
Z. Wu[63]	2017	China	Case report	1
R. H. Yang[64]	2014	Taiwan	Case report	1
A. Ziegler[65]	2019	USA	Case report	1

cases) were male and 32.9% (23 cases) were female. The mean age of the patients was 64.5 years and ranged from 14 to 92 years. The mean age of men was 61.9 years and the mean age of women was 69.8 years. 64.2% of the patients were in the age range of 60 to 80 years (Table 2).

In 44.3% (31 cases) of patients with gastrointestinal malignancies, the primary site of malignancy was in the colon, followed by 18.6% (13 cases) in the rectum and 17.1% (12 cases) in the stomach. The primary tumor was located in the small intestine in 7.1% (5 cases) and in the liver in 10% (7 cases). The primary tumor site was unknown in 2.9% (2 cases). The most common site of metastatic tumor in the oral cavity and maxillofacial region was the mandible in 62.9% (44 cases) and the maxilla in 22.9% (16 cases). In 14.2% (10 cases) of patients, the site of metastatic tumor was located in other areas such as the temporomandibular joint, tongue, etc.

The histological type of the primary malignancy determined by pathological tests was adenocarcinoma in 81.4% (57 cases) of the cases, of which 49.1% were colon adenocarcinomas. 5.7% (4 cases) of the tumors were squamous cell carcinoma, with 3 cases in the lung and 1 case in the colon. 3 (4.3%) of the malignancies were also gastrointestinal sarcomas, and one study was related to

Table 2. Demographic features, tumor location and received treatments in oral and maxillofacial metastatic cases

Case	Gender	Age	Site of primary tumor	Site of metastasis	Treatment
1[15]	M	62	Intestinal adenocarcinoma	right anterior mandibular gingiva	Palliative colostomy and chemotherapy
2[16]	F	84	Colon adenocarcinoma	Ulcerous tumor in mandible	Chemotherapy
3[17]	M	78	Rectal adenocarcinoma	alveolar mucosa of the upper jaw	Chemotherapy and surgery
4[18]	M	58	Failed to identify	base of the tongue	Glossectomy and inductive chemotherapy
5[19]	M	67	Rectal adenocarcinoma	Anterior of maxilla	Chemotherapy
6[20]	M	70	Rectal adenocarcinoma	right mandible	Trans-oral laser and palliative care
7[21]	F	61	Stomach	left hard palate	Surgery and chemotherapy and radiotherapy
8[22]	F	69	Colon adenocarcinoma	gingiva of the right upper jaw	Chemotherapy
9[23]	F	67	Small intestine T-cell lymphoma	left posterior part of the hard and soft palate and maxillary alveolar ridge	Surgery and chemotherapy
10[24]	M	14	Rectal adenocarcinoma	mandible	Chemotherapy and radiotherapy
11[25]	M	74	Colon adenocarcinoma	the right upper maxilla	Surgery
12[26]	F	66	Colon adenocarcinoma	right mandible	Surgery
13[26]	F	35	Colon adenocarcinoma	posterior region of left hemi-mandible	Surgery and chemotherapy and radiotherapy
14[27]	M	61	Esophagus Well-differentiated SCC	Bilateral mandibular region	Radical surgery and enucleation
15[27]	F	60	Stomach	zygomatic region	Radical Surgery and chemotherapy
16[28]	F	79	Colon adenocarcinoma	left mandible	Surgery and chemotherapy and radiotherapy
17[29]	M	60	Colon adenocarcinoma	Gingiva and Mandible (Posterior)	NA
18[29]	M	75	Colon adenocarcinoma	Gingiva	NA
19[29]	F	70	Colon adenocarcinoma	Gingiva	NA
20[29]	F	92	Colon adenocarcinoma	Gingiva	NA
21[29]	M	88	Colon adenocarcinoma	Gingiva and Mandible (Posterior)	NA
22[29]	M	69	Esophagus adenocarcinoma	Gingiva	NA
23[29]	M	57	Colon adenocarcinoma	Gingiva and Maxilla	NA
24[29]	F	81	Colon adenocarcinoma	Mandible (Anterior)	NA
25[29]	F	85	Colon adenocarcinoma	Gingiva and Mandible (Anterior)	NA
26[30]	M	58	Gastric adenocarcinoma	Buccal gingiva of upper right first molar area	Surgery and chemotherapy
27[31]	M	55	Rectal adenocarcinoma	frontal lower gingiva	Chemotherapy
28[32]	F	61	Rectal adenocarcinoma	Left retromolar	NA
29[33]	F	67	Esophageal adenocarcinoma	Mandible	Surgery
30[33]	M	53	Colon adenocarcinoma	Gingiva	Surgery and chemotherapy
31[34]	M	71	Gastric adenocarcinoma	Anterior teeth gingiva in mandible	Surgery and chemotherapy
32[35]	M	73	Colon adenocarcinoma	right premolar of mandible	Surgery and Chemotherapy
33[36]	F	36	Rectal adenocarcinoma	first left premolar gingiva of mandible	Neoadjuvant chemo radiotherapy
34[37]	M	51	Gastric adenocarcinoma	Left TMJ	Surgery and radio chemotherapy
35[38]	F	62	failed to identify	Mandibular symphysis	Palliative Radiotherapy
36[39]	M	65	Gastric adenocarcinoma	left mandibular canine and premolar gingiva	palliative care
37[40]	M	77	Sigmoid colon adenocarcinoma	Right maxillary gingiva	Chemotherapy and surgery
38[41]	M	69	esophageal adenocarcinoma	left mandible	Neo-adjuvant cisplatin and surgery
39[42]	M	68	ileum stromal tumor	Para symphysis and left molar mandibular area	Chemotherapy
40[43]	F	60	mucous adenocarcinoma of stomach	mandibular right first molar	No treatment
41[44]	M	77	duodenal GIST	Left palate	Surgery and radiotherapy
42[45]	F	65	Transverse colon adenocarcinoma	second left lower premolar	Surgery and chemotherapy

Table 2. Continued.

Case	Gender	Age	Site of primary tumor	Site of metastasis	Treatment
43[46]	M	66	rectal adenocarcinoma	mandibular symphysis and floor of mouth	Chemotherapy and surgery
44[4]	M	71	Rectum	right inferior gingiva	NA
45[47]	M	59	Colon adenocarcinoma	maxillary gingiva incisors area	Surgery and chemotherapy
46[77]	F	82	gastric adenocarcinoma	Gingival mass in anterior mandible	Surgery
47[48]	M	64	Colon carcinoma	Left TMJ	Chemotherapy
48[49]	M	60	Colon adenocarcinoma	gingival mucosa of the left mandible	Surgery and chemotherapy and radiotherapy
49[2]	M	61	squamous cell carcinoma of the esophagus	right side of the anterior mandible	Radiosurgery and radiotherapy and chemotherapy
50[50]	M	62	Colon adenocarcinoma	mandibular symphysis	surgical resection, chemotherapy and radiotherapy
51[51]	M	73	Colon adenocarcinoma	lower mandibular region	Surgery and chemotherapy
52[52]	M	70	Rectum adenocarcinoma	left buccomasseteric region of mandible	palliative chemotherapy and radiation therapy
53[11]	M	70	Gastric adenocarcinoma	left side of the mandible	Surgery and palliative care
54[5]	F	70	Colon adenocarcinoma	Hard palate	Palliative care
55[5]	M	59	Colon adenocarcinoma	Mandible	Palliative care
56[8]	F	75	Colon adenocarcinoma	Gingiva	NA
57[8]	M	55	Esophagus SCC	Mandible	NA
58[53]	M	56	Gastric adenocarcinoma	mandibular incisor and bilateral canine region	Surgery and chemotherapy
59[54]	M	67	adenocarcinoma of the cardia (stomach)	left TMJ	Surgery and chemotherapy
60[55]	M	42	Colon adenocarcinoma	buccal gingiva of mandible	Surgery and chemotherapy
61[56]	M	56	Rectal adenocarcinoma	retromolar pad of mandible	Surgery and chemotherapy
62[57]	M	51	clear-cell sarcomas of small intestine	Right parotid gland	Surgery and chemotherapy
63[58]	F	80	squamous cell carcinoma of the ascending colon	right lower gingiva of mandible	Surgery
64[59]	M	68	Cecal mixed adenoneuroendocrine carcinoma	left palatine tonsil	Surgery and chemotherapy
65[60]	M	60	Rectal adenocarcinoma	Left mandible	Surgery and chemotherapy and radiotherapy
66[61]	M	64	Rectal adenocarcinoma	anterior mandibular gingiva	Surgery and palliative radiotherapy
67[62]	M	41	esophageal adenocarcinoma	maxillary left third molar area	chemotherapy and radiotherapy
68[63]	M	75	Gastric adenocarcinoma	left upper gingiva	Surgery and chemotherapy and radiotherapy
69[64]	F	74	Colon adenocarcinoma	right mandibular gingiva	palliative treatment
70[65]	F	35	Colon adenocarcinoma	right lateral oral tongue	Surgery and chemotherapy and radiotherapy

T-cell lymphoma of the small intestine. In 7.1% (5 cases) of the patients, sufficient information about the tumor type was not provided (Table 3).

The most common clinical symptom among patients was the presence of a protrusion, tumor, or exophytic mass, which was reported in 48.6% (34 cases) of the studies. The most prominent feature on radiographs was the presence of a radiolucent area or bone erosion, which was present in almost one-third of the patients (32.9%). The main complaint of the patients was pain, which was reported in 24.3% (17 cases) of the studies. In 20% (14 cases) of the patients, a lesion with a hard consistency was reported, while in 10% (7 cases) a lesion with a soft or rubbery consistency was reported. Numbness and paresthesia in the maxillofacial region were reported in 15.7% (11 cases) of the patients (Table 3).

The survival time from the time of diagnosis of oral metastasis was determined in 45.7% (32 cases) of the patients, and in 2 cases, the survival time from the time of primary malignancy diagnosis was reported. In the remaining patients, either the survival time after the diagnosis of oral metastasis was not mentioned, or the patient was alive at the time of publication, or the study was published at the same time as the diagnosis of oral metastasis. The average survival time after the diagnosis of oral metastasis was 5.7 months for both genders, and in the two cases where the survival time from the diagnosis of primary malignancy was reported, one was 24.3 months and the other was 49 months.

80% of the patients in this study received treatment, and in one case, no treatment was performed. However, information about the treatment and prognosis of the

Table 3. Clinical charactristics of metastatic tumors and survival rates

Case	Clinical Manifestation	Survival
1	pain and swellings in the mandibular region/exophytic tumor/ 4 cms/ solid mass/ bony erosion	9 months
2	Ulcerous tumour	20 months
3	soft consistency with a whitish topmost area/ rapid growth/ 3 × 2 cm	4 months
4	oral bleeding/ firm mass/ ulcerated submucosal indurated mass/ 4.5 cm	NA
5	Exophytic mass	NA
6	jaw pain, numbness, difficulty swallowing and an enlarging mass/ bleeding/ 5*6 cm	3 months
7	firm and painless erythematous mass/ 4 cm	1 month
8	Granular exophytic lesion/ rapid growth and bleeding/ rubbery consistency	6 months
9	endophytic ulcer with a granular surface/ eroded surface/ pain and asymmetry/ 3*3	1 month
10	*	12 months
11	exophytic lesion/ irregular shape/ hemorrhagic/ eroded mucosal surface/ elastic-soft consistency	6 months
12	rapidly growing mass/ firm, solid swelling/ partially ulcerated mucosa	NA
13	slowly growing gingival swelling/ firm, solid swelling/ partially ulcerated mucosa	NA
14	Swelling/ 4 * 3,5 * 5	12 months
15	Swelling/ Osteolytic appearance/ 2.5 *2.5	6 months
16	Painful mass/ 6 cm long/ osteolytic lesion/	1 month
17	*	NA
18	*	NA
19	*	NA
20	*	NA
21	*	NA
22	*	NA
23	*	NA
24	*	NA
25	*	NA
26	painful swelling/ 3.0 * 2.0 cm/ exophytic growth/ bloody and necrotic tag/ bone loss	NA
27	enlarging soft reddish nodule	11 months
28	Cystic swelling	NA
29	Facial swelling	NA
30	Gingival swelling	NA
31	soft exophytic swelling/ 2 x 2 cm/ irregular surface/ exophytic growth/ foul odor/ bloody and necrotic tag/ radiolucent lesion	NA
32	Firm swelling and pain/ hemispheric mass/ paresthesia of the right lower lip/ 12 mm/ radiolucency	NA
33	exophytic gingival mass/ 5 cm	3 months
34	*	NA
35	Pain/ numbness involving her lower lip area/ edematous lesion/ 1.5 X 0.5 cm/ firm ovoid mass	4 months
36	gingival hypertrophy/ bleeding/ indurative mass /2.5 * 2.0	4 months
37	gingival mass / 3 x 4 cm/ destruction of the outer cortical bone/ firm	NA
38	palpable mass lesion/ numbness of the left lower and upper lip/ jaw pain/ trismus/ 'moth-eaten' appearance	NA
39	Painful swelling / Hypoesthesia of the chin and inferior lip/ 3 cm/ radiolucency	11 months
40	pinkish soft tissue growth/ 2 cm × 1 cm/ bleeded on probing	1 month
41	exophytic, fungating,painful lesion (3.7 * 3.7 cm) with central ulceration/ V2 cranial nerve paresthesia/ Bone erosion	12 month
42	partially pedunculated and moderately firm/ 24 * 20 mm/ surface color reddish pink/ right lower lip paralysis	NA
43	sclerotic lesion/ periosteal elevation/ numbness of the chin/ asymmetric-appearing/ eroding the mandible	2 months
44	Tumor/ paresthesia/ 3 cm	NA
45	exophytic neoformation/ rapidly growing lesion/ bone destruction	10 months
46	gradually enlarging mass/ gingival mass	NA
47	swelling and pain for 1 month/ asymmetry	3 months
48	bleeding, ulceration and edema/ reddish nodule/ tooth mobility	NA
49	gingival swelling/ firm/ dental mobility/ hypoesthesia on the lower lip/ 5.0 x 2.0 cm	1 month

Case	Clinical Manifestation	Survival
50	large inhomogeneous mass/ bone lysis/ mobile tooth	15 months
51	Painful/ rapidly growing/ large exophytic	NA
52	firm, adherent buccomasseteric mass/ 5 cm/ ill-defined lucency/ trismus	2 months
53	Exophytic mass/ 6.0 * 3.0 cm/ facial asymmetry/	3 months
54	*	24.3 from primary
55	*	49 from primary
56	Mass, bleeding	NA
57	Numbness of lower lip, mass, pain	NA
58	gray, fungating and friable swelling/ pain and bleeding on palpation	2 months
59	facial asymmetry/ trismus	NA
60	reddish, painless sessile nodule/ mobility/ rarefaction	NA
61	lytic radiolucent/ ulcerated	NA
62	Painless soft mass/ 20 mm × 20 mm	NA
63	dull pain/ hemispherical, moderately firm, and nonulcerated nodule/ erosion	6 months
64	ulcerated area/ enlarged tonsil/ 2.7 cm	NA
65	large proliferative growth/ bled on touch/ trismus/ osteolytic mass	4 months
66	firm mass/ 2.6 × 2.1 cm/ erosion at surface/ bony resorption	2 months
67	Pain/ radiolucency/ asymmetry	1 month
68	gray and painless neoplasm/ hemorrhage on palpation/ 2 cm diameter	NA
69	Bleeding after tooth extraction/ exophytic lesion/ tooth mobility	3 months
70	firm raised lesion/ 1.7 cm/ pain	NA

patients was not available for most cases. The most common treatment used for patients was chemotherapy, which was performed alone or in combination with other treatments in 60% (42 cases) of the patients. Other treatments such as surgery, radiotherapy, and palliative care were used alone or in combination with other treatments in 57.3% (40 cases), 24.3% (17 cases), and 14.3% (10 cases) of the patients, respectively (Table 4 and Figure 2).

Table 4. Distribution of clinical signs and symptoms

Clinical presentation/ symptom	Number of cases	Percentage
Exophytic tumor/ Swelling	34	48.6%
Bone erosion	23	32.9%
Pain	17	24.3%
Firm mass	14	20%
Ulcerated surface	11	15.7%
Numbness	11	15.7%
Soft mass	7	10%
Facial asymmetry	6	8.6%
Rapid growth	5	7.1%
Dental mobility	5	7.1%
Trismus	4	5.7%

Discussion

This study is about patients with metastatic tumors or a protruding mass or lump in the oral cavity. The most common clinical feature reported among the patients in this study was the presence of an exophytic tumor or mass, which was reported in 48.6% (34 cases) of the patients. Additionally, the presence of pain accompanied by clinical signs was observed in 21.4% of the patients and had a significant correlation. Information about the consistency of the lesion was available in 30% of cases, and according to them, the frequency of lesions with hard consistency was twice that of lesions with soft or rubbery consistency. Lesions with ulcerated surface were seen in 15.7% (11 cases) of the patients, mostly due to the entrapment of gas by the patient, indicating that the lesion had caused interference with tooth occlusion. In radiographic images of patients with metastatic tumors, a radiolucent lesion inside the bone is seen in most cases of metastatic tumors in the jawbone. However, metastatic tumors from breast and kidney cancers can present as osteoblastic, osteolytic, or a combination of both on radiographic images.[14] Most bone metastases from colorectal malignancies have an osteolytic radiographic appearance.[66] Nevertheless, in almost 5% of cases, radiography cannot help diagnose metastatic lesions in the jawbone because it does not show any significant pathological changes.[7]

According to the GLOBOCAN database, colorectal, gastric, and liver cancers were the third, fifth, and eighth most common new cancer cases reported in 2020, respectively, with a total of 2.6 million new cases. Breast cancer had the highest number of reported cases, affecting nearly 2.3 million people. However, the incidence of metastases caused by gastrointestinal malignancies involving the soft or hard tissue of the jaw and face is very low, and the available studies in this area mainly report on individual cases or small case series. This systematic review focused on the importance of common clinical signs and clinical appearance of lesion in early diagnosis and improved prognosis, based on studies published

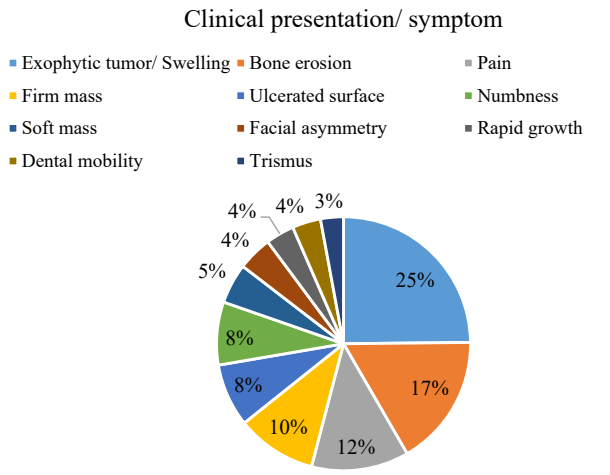

Figure 2. the frequency Clinical presentation/ symptom in patients

between 2000 and 2022.

In terms of gender, male patients with metastases caused by gastrointestinal malignancies in the oral cavity were twice as common as female patients. In Hirshberg et al's study, 673 patients with oral metastases were examined, of which 69 cases were related to colorectal, gastric, and liver metastases, and the male-to-female ratio was 1.4, while the ratio for all patients was 1.2 (360 male patients and 295 female patients, with gender not specified in 18 cases in the study).[7] In Iran's study 412 patients with metastatic lesions in the oral cavity from all parts of the body were examined, and the male-to-female ratio was 1.8 which was more close to this study.[10] The average age of patients in this study was 64.5 years, with male patients being about 8 years younger than female patients. In Kaplan et al's study, which examined 60 patients with maxillofacial metastatic tumors, the average age of patients was 67.7 years, with 5% of patients under the age of 40.[67] In the recent study, 5.7% of patients were under 40 years old. In Hirshberg et al's study, the average age of patients was 49.1 years, and most patients were in their fifth to seventh decade of life, whereas in our study, nearly two-thirds of patients were between 60 and 80 years old.

Intraosseous maxillofacial tumors commonly present with pain, paresthesia, and a growing mass.[7] According to clinical signs, pain was the most common symptom, observed in 24.3% (17 cases) of patients, which is somewhat similar to the Kirschnick LB study, where 31.6% of the 345 examined patients experienced pain.[68] In Labrador et al's systematic review of metastatic tumors of the oral cavity and maxillofacial region, among the 696 examined patients, 17.5% experienced pain as a clinical sign.[69] The second most common sign found in our study was anesthesia or paresthesia in a facial region, present in 15.7% (11 cases) of patients. In Labrador et al's study, the reported rate of paresthesia and numb chin syndrome was 8.6%, which is roughly half the rate in our study. Other symptoms were less common in patients, including facial asymmetry in 8.6% (6 cases), dental loosening caused by the tumor in 7.1% (5 cases), rapid growth of the lesion in 7.1% (5 cases), and limited mouth opening (Trismus) in 5.7% (4 cases).

In patients with colorectal malignancies, factors such as a disease-free interval of less than one year, the presence of non-hepatic metastases, and having more than 3 tumors in the body were all associated with poor prognosis.[60] In one-fourth of the reported cases in the Hirshberg et al study, a metastatic lesion was diagnosed before the primary tumor. The presence of metastatic lesions in the jaw and oral cavity generally lowers the patient's prognosis, and in one study, the median survival time from the time of diagnosis of jaw metastatic lesion was approximately 7 months.[7] In the Kirschnick et al study, the average survival time was also reported to be 8 months, but in our study, it was lower, with a median of 6.1 months in men and 4.7 months in women, and an average of 5.7 months in both genders.

Due to the low survival rate in these patients, the main goal of treatment is to improve their quality of life.[7] Treatments for these patients include surgery for primary or metastatic tumors, chemotherapy, and radiotherapy. Palliative treatments are used for patients with widespread metastases in the body and poor prognosis, which is a general term that can include previous treatments. Surgical removal of a metastatic tumor that only had that metastasis improved patient prognosis in several patients.[70] In our study, 60% of patients received chemotherapy, making it the most common treatment prescribed for patients. Surgery for metastatic or primary tumors was performed in 57.1% of the patients. Radiotherapy and palliative treatment were used for 24.3% and 14.3% of the patients, respectively. A combination of two or more of these treatments was used in 57.1% of the patients. Information about the treatment of 18.6% of the patients was not available, and one patient did not receive any treatment upon his request.

Metastatic tumors in the oral cavity tend to have a 2:1 ratio of involvement in the bony structures of the jaws to soft tissue, according to a study by Hirshberg et al.[7] Another study by Kirschnick LB found a ratio of 1.3:1.[68] In bone metastases of the jaws, the tendency for malignancy is greater in involving the lower jaw, and the blood supply is considered as a route for reaching these areas. The reason for greater involvement of the lower jaw is due to the presence of a higher number of hematopoietic cells in that area.[33,71] The most common site of metastatic tumor involvement among the soft tissues inside the mouth is the attached gingiva, and one of the ways that tumor cells are attracted to the gingiva is through the presence of inflammation in this area. In inflamed periodontal tissue, tumor cells may become trapped in a network of fibrosis and remain there.[7] Several different stages of tumor development, such as invasion, proliferation, angiogenesis, cellular shape change, and metastasis, have been linked to chronic inflammation.[72,73] In our study, contrary to previous reports, the ratio of soft tissue to bony lesions was 2.2:1, and 60% of metastatic lesions were located in the gingiva and oral mucosa, while approximately 27% were intraosseous, and the rest were located in other areas such as the tongue joint, temporomandibular joint,

tonsils, and parotid gland. As for the tendency to involve the upper and lower jaw, similar to previous studies, there was a tendency to involve the lower jaw, especially the posterior regions, and 62.9% of lesions were located in the mandible or its gingiva and soft tissue, while 22.9% were located in the maxilla and its gingiva and soft tissue.

Adenocarcinoma is the most common type of metastatic lesion in the oral cavity, accounting for 70% of cases.[3,74] Differentiating metastatic lesions from salivary gland adenocarcinoma is the main diagnostic challenge in these oral metastatic lesions.[75] Immunohistochemistry can be used to differentiate metastatic lesions from secondary adenocarcinoma of the salivary gland. In metastatic lesions, the levels of CEA in colorectal adenocarcinomas are often increased, and CK7 is not expressed, while CK20 is expressed.[76] In our study, adenocarcinoma was the most common histological type of malignant tumor, accounting for 81.4% of metastatic lesions. Other types of tumors included sarcoma, squamous cell carcinoma, and lymphoma. The most common primary site of the lesion was the colon. In Hirshberg et al's study, 10.3% of patients with oral metastasis had a primary tumor located in the gastrointestinal tract, of which approximately 58% were related to colorectal cancer.[7] The primary lesion originated from the colon in 62.9% of patients in our study, and adenocarcinoma of the colon accounted for 40% of all primary tumors. The next most common site was the rectum, and the least common site was the small intestine.

Lesion size was described using two methods in 41.4% (29 cases) of cases. In one method, the two-dimensional dimensions of the lesion were described, while in the other category, the size of the lesion was described based on its diameter. In Labrador et al's review, the average size of lesions in both genders was 2.3 cm.[69] In our study, the average size was larger, with an average lesion size of 3.26 cm in both genders. In studies where lesions were described in two-dimensional dimensions, lesion size ranged from 0.5 to 6 cm.

There were several limitations in conducting this systematic review that may have affected the study's results, and therefore we mention them. In some studies, the full text of the article was not available, and in others, articles were available in languages other than English, making it impossible to review these studies. Oral metastases resulting from gastrointestinal malignancies are often a significant challenge to diagnose and are often misdiagnosed as other lesions. In addition, the reported cases of these cases are low, and most studies are case reports or case series, so a limited sample size is available for analysis. Previous studies also lacked sufficient and accurate information in most cases. Another limitation is the lack of comprehensive information on the lesion and the failure to address the features and symptoms of the lesion. For example, in many studies, the size of the lesion was not discussed, and in cases where the size of the lesion was described, it was discussed in some studies in two-dimensional dimensions, and in others, the diameter of the lesion was mentioned. This makes it difficult to perform numerical analysis of lesion size. Also, due to the lack of sufficient numerical information on the tumor and the relative survival rate, it was not possible to perform a meta-analysis in this study. In other systematic reviews, the investigation of metastatic lesions from all parts of the body to the oral and maxillofacial region was performed, but in our study, for the first time, metastatic lesions resulting from gastrointestinal malignancies were investigated, and the features of the lesion, survival rate since the diagnosis of oral metastasis, and the type and prevalence of tumors in this area were discussed.

Conclusion

Generally, metastatic lesions of the oral and maxillofacial region resulting from gastrointestinal malignancies are more common in men, and the most common site of the tumor is the colon, with most cases being adenocarcinomas. The presence of pain and an exophytic lesion were reported as the most common manifestations of these patients. Cases of these metastatic lesions are rare and have a poor prognosis, and in some cases, they occur as the first indication of malignancy. Therefore, the findings of this study can help clinicians and dentists in the early diagnosis of these patients and improve their quality of life.

Acknowledgments

Not applicable.

Authors' Contribution

Conceptualization: Hooman Tahmasebi, Negin Samiee, Yousef Moradi.
Data curation: Hooman Tahmasebi.
Formal analysis: Yousef Moradi.
Funding acquisition: Negin Samiee, Yousef Moradi.
Investigation: Hooman Tahmasebi, Negin Samiee.
Methodology: Yousef Moradi.
Project administration: Yousef Moradi.
Resources: Yousef Moradi.
Software: Hooman Tahmasebi.
Supervision: Negin Samiee, Yousef Moradi.
Validation: Negin Samiee, Yousef Moradi.
Visualization: Hooman Tahmasebi.
Writing–original draft: Hooman Tahmasebi.
Writing–review & editing: Negin Samiee, Yousef Moradi.

Competing Interests

No conflict of interest for the present review.

Ethical Approval

This study was approved by the Ethics Committee of Kurdistan University of Medical Sciences, Sanandaj, Iran (Ethical Code: IR.MUK.REC.1401.316.). As this study is a systematic review of previously published data, no direct involvement of human participants was required.

Funding

This article has resulted from a master's thesis approved and supported by the Kurdistan University of Medical Sciences.

References

1. Hirshberg A, Berger R, Allon I, Kaplan I. Metastatic tumors to the jaws and mouth. Head Neck Pathol 2014;8(4):463–74.

doi:10.1007/s12105-014-0591-z
2. Rocha BA, Paranaíba LM, Dantas CD, de Carvalho MG, de Melo-Filho MR, Lima LM, et al. Two rare cases of oral metastasis arising from lung adenocarcinoma and esophageal carcinoma. J Clin Exp Dent 2020;12(10):e999–e1004. doi:10.4317/jced.57125
3. van der Waal RI, Buter J, van der Waal I. Oral metastases: report of 24 cases. Br J Oral Maxillofac Surg 2003;41(1):3–6. doi:10.1016/s0266-4356(02)00301-7
4. Murillo J, Bagan JV, Hens E, Diaz JM, Leopoldo M. Tumors metastasizing to the oral cavity: a study of 16 cases. J Oral Maxillofac Surg 2013;71(9):1545–51. doi:10.1016/j.joms.2013.03.017
5. Seoane J, Van der Waal I, Van der Waal RI, Cameselle-Teijeiro J, Antón I, Tardio A, et al. Metastatic tumours to the oral cavity: a survival study with a special focus on gingival metastases. J Clin Periodontol 2009;36(6):488–92. doi:10.1111/j.1600-051X.2009.01407.x
6. Miller KD, Siegel RL, Lin CC, Mariotto AB, Kramer JL, Rowland JH, et al. Cancer treatment and survivorship statistics, 2016. CA: A Cancer Journal for Clinicians 2016;66(4):271–89. doi:10.3322/caac.21349
7. Hirshberg A, Shnaiderman-Shapiro A, Kaplan I, Berger R. Metastatic tumours to the oral cavity - pathogenesis and analysis of 673 cases. Oral Oncol 2008;44(8):743–52. doi:10.1016/j.oraloncology.2007.09.012
8. Shen ML, Kang J, Wen YL, Ying WM, Yi J, Hua CG, et al. Metastatic tumors to the oral and maxillofacial region: a retrospective study of 19 cases in West China and review of the Chinese and English literature. J Oral Maxillofac Surg 2009;67(4):718–37. doi:10.1016/j.joms.2008.06.032
9. Kumar G, Manjunatha B. Metastatic tumors to the jaws and oral cavity. J Oral Maxillofac Pathol 2013;17(1):71–5. doi:10.4103/0973-029x.110737
10. Irani S. Metastasis to the oral soft tissues: A review of 412 cases. J Int Soc Prev Community Dent 2016;6(5):393–401. doi:10.4103/2231-0762.192935
11. Sauerborn D, Vidakovic B, Baranovic M, Mahovne I, Danic P, Danic D. Gastric adenocarcinoma metastases to the alveolar mucosa of the mandible: a case report and review of the literature. J Craniomaxillofac Surg 2011;39(8):645–8. doi:10.1016/j.jcms.2010.10.020
12. Cai J, He B, Li X, Sun M, Lam AK, Qiao B, et al. Regulation of tumorigenesis in oral epithelial cells by defined reprogramming factors Oct4 and Sox2. Oncol Rep 2016;36(2):651–8. doi:10.3892/or.2016.4851
13. McClure SA, Movahed R, Salama A, Ord RA. Maxillofacial metastases: a retrospective review of one institution's 15-year experience. J Oral Maxillofac Surg 2013;71(1):178–88. doi:10.1016/j.joms.2012.04.009
14. D'Silva NJ, Summerlin DJ, Cordell KG, Abdelsayed RA, Tomich CE, Hanks CT, et al. Metastatic tumors in the jaws: a retrospective study of 114 cases. J Am Dent Assoc 2006;137(12):1667–72. doi:10.14219/jada.archive.2006.0112
15. Alvarez-Alvarez C, Iglesias-Rodríguez B, Pazo-Irazu S, Delgado-Sánchez-Gracián C. Colonic adenocarcinoma with metastasis to the gingiva. Med Oral Patol Oral Cir Bucal 2006;11(1):E85–7.
16. Andabak Rogulj A, Tomasovic Loncaric C, Muller D, Blivajs I, Andabak M, Vucicevic Boras V, et al. Solid malignant metastases in the jaw bones. Br J Oral Maxillofac Surg 2018;56(8):705–8. doi:10.1016/j.bjoms.2018.07.013
17. Baranović M, Vidaković B, Sauerborn D, Perić B, Uljanić I, Mahovne I. Colorectal Adenocarcinoma Metastasizing to the Oral Mucosa of the Upper Jaw. Srp Arh Celok Lek 2015;143(5-6):314–6. doi:10.2298/sarh1506314b
18. Bell D, Kupferman ME, Williams MD, Rashid A, El-Naggar AK. Primary colonic-type adenocarcinoma of the base of the tongue: a previously unreported phenotype. Hum Pathol 2009;40(12):1798–802. doi:10.1016/j.humpath.2009.01.028
19. Bodner L, Sion-Vardy N, Geffen DB, Nash M. Metastatic tumors to the jaws: a report of eight new cases. Med Oral Patol Oral Cir Bucal 2006;11(2):E132–5.
20. Coad FH, Thayalasekaran S, Booth J. An unusual presentation of metastasis from a rectal adenocarcinoma. Qjm 2013;106(10):943–5. doi:10.1093/qjmed/hcs122
21. Colombo P, Tondulli L, Masci G, Muzza A, Rimassa L, Petrella D, et al. Oral ulcer as an exclusive sign of gastric cancer: report of a rare case. BMC Cancer 2005;5:117. doi:10.1186/1471-2407-5-117
22. Dalirsani Z, Mohtasham N, Samiee N. Metastasis of Colon Adenocarcinoma to Maxillary Gingiva and Palate. Iran J Otorhinolaryngol 2020;32(112):327–31. doi:10.22038/ijorl.2020.42693.2394
23. Dalirsani Z, Pakfetrat A, Saghravanian N, Samiee N, Salari S. Metastasis of Non-Hodgkin's T-cell lymphoma to the palate and maxillary alveolar ridge: case report. Tehran-Univ-Med-J 2021;79(1):61.
24. Deutsch M, Wollman MR. Radiotherapy for metastases to the mandible in children. J Oral Maxillofac Surg 2002;60(3):269–71. doi:10.1053/joms.2002.30573
25. Di Stasio D, Montella M, Cozzolino I, Cicciù M, Cervino G, Paparella RS, et al. Multidisciplinary Diagnostic and Surgical Management of Adenocarcinoma Gingival Metastases. J Craniofac Surg 2018;29(6):e531–e4. doi:10.1097/scs.0000000000004632
26. Favia G, Maiorano E, Lo Muzio L. Image of the month. Gingival metastasis from colonic adenocarcinoma. Clin Gastroenterol Hepatol 2010;8(4):A28. doi:10.1016/j.cgh.2009.07.010
27. Fukuda M, Miyata M, Okabe K, Sakashita H. A case series of 9 tumors metastatic to the oral and maxillofacial region. J Oral Maxillofac Surg 2002;60(8):942–4. doi:10.1053/joms.2002.33868
28. Hadhri A, Abidi R, Ben Rejeb M, Yahyaoui S, Nasr C. Metastasis of colon adenocarcinoma to the mandible: A case report. Tunis Med 2020;98(6):518–21.
29. Ho DP, Wilkinson PE, Vogel RI, Gopalakrishnan R, Argyris PP. Metastatic Tumors to the Oral Soft Tissues and Jawbones: A Retrospective Analysis of 40 Cases and Review of the Literature. Head Neck Pathol 2022;16(3):802–13. doi:10.1007/s12105-022-01451-8
30. Hwang KG, Park CJ, Paik SS, Shim KS. Gingival metastasis from gastric adenocarcinoma. Otolaryngol Head Neck Surg 2007;137(1):169–70. doi:10.1016/j.otohns.2007.01.014
31. Iida T, Sasaki T, Akita H, Sasaki M, Shiba H, Yanaga K. Metastatic gingival tumor from rectal cancer diagnosed with CDX2. Clin J Gastroenterol 2009;2(3):175–7. doi:10.1007/s12328-009-0081-0
32. Jalil AbA, Lau S-H. Metastatic Tumours of the Oral Cavity in Malaysians: a Retrospective Study (1967–2007). Asian Journal of Oral and Maxillofacial Surgery 2009;21(3):101–5. doi:10.1016/S0915-6992(09)80005-8
33. Jham BC, Salama AR, McClure SA, Ord RA. Metastatic tumors to the oral cavity: a clinical study of 18 cases. Head Neck Pathol 2011;5(4):355–8. doi:10.1007/s12105-011-0286-7
34. Kalaitsidou IG, Astreidis IT, Kontos KI, Lazaridou MN, Bourlidou ET, Gerasimidou DK, et al. Metastatic Tumours to the Oral Cavity: Report of Three Cases. J Oral Maxillofac Res 2015;6(4):e5. doi:10.5037/jomr.2015.6405
35. Kameta A, Oda T, Ogura I, Ono J, Kanri Y, Okada Y, et al. Metastasis of colon adenocarcinoma to the mandible: A case report. Oral Science International 2017;14(1):22–5. doi:10.1016/S1348-8643(16)30023-4
36. Khazzaka A, El Rassy E, Sarkis R. An Unusual Case of Oral Metastasis from Rectal Adenocarcinoma Precipitated by Iatrogenicity. J Gastrointest Cancer 2016;47(3):336–7. doi:10.1007/s12029-016-9807-7
37. Kolk A, Sader R, Zeilhofer HF, Becker I, Westermark A, Horch

HH. [Condylar reconstruction after resection of an intracapsular stomach carcinoma metastasis]. Mund Kiefer Gesichtschir 2003;7(5):306–10. doi:10.1007/s10006-003-0496-6
38. Kuttan NA, Flemming DK, Dane JN, Ang DB. Metastatic lesion of the anterior mandible with an occult primary: a case report. Spec Care Dentist 2006;26(2):76–80. doi:10.1111/j.1754-4505.2006.tb01514.x
39. Kwon MS, Ko SO, Cho NP, Kim OH, Shin HK, Baek JA, et al. Gastric signet-ring cell adenocarcinoma metastatic to the gingiva: a case report. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2006;102(1):62–6. doi:10.1016/j.tripleo.2005.08.029
40. Landeyro J, Raventós A, Mommsen J et al. (2010) Gingival and submandibular lymph node metastasis of sigmoid colon adenocarcinoma. Journal of Clinical and Experimental Dentistry 2010;2(1):e46-49.
41. Lawes KP, Danford M, Di Palma S. Delayed metastasis to the mandible of esophageal adenocarcinoma. Head Neck Pathol 2013;7(4):416–20. doi:10.1007/s12105-013-0450-3
42. Lutz JC, El-Bouihi M, Vidal N, Fricain JC, Robert M, Deminière C, et al. Mandibular metastases from an ileum stromal tumor. Rev Stomatol Chir Maxillofac 2008;109(6):399–402. doi:10.1016/j.stomax.2008.09.010
43. Majumdar S, Uppala D, Boddepalli R, Rao AK. A rare case of mucous adenocarcinoma with gingival metastasis: A case report and review of literature. Journal of Oral and Maxillofacial Surgery, Medicine, and Pathology 2016;28(2):197–201. doi:10.1016/j.ajoms.2015.09.002
44. Maria OM, Alghamdi O, Baabdullah R, El-Hakim M, Al-Halabi H, Makhoul NM. Gastrointestinal stromal tumor with maxillary metastasis: a case report and literature review. Oral Surg Oral Med Oral Pathol Oral Radiol 2022;133(1):e1–e5. doi:10.1016/j.oooo.2021.06.017
45. Miyake M, Takebayashi R, Ohbayashi Y, Kushida Y, Matsui Y. Metastasis in the gingiva from colon adenocarcinoma. J Maxillofac Oral Surg 2015;14(Suppl 1):279–82. doi:10.1007/s12663-013-0487-6
46. Mojica-Manosa P, Rigual N, Tan D, Sullivan M. An unusual case of a metastatic adenocarcinoma of the rectum to the mandible: a case report and review of the literature. J Oral Maxillofac Surg 2006;64(9):1436–9. doi:10.1016/j.joms.2005.11.063
47. Neumann ED, León Vintró X, Vega García C, Quer Agustí M. Oral cavity colon adenocarcinoma metastases: case report with surgical approach and review of more than 30 years literature. Oral Maxillofac Surg 2021;25(1):99–101. doi:10.1007/s10006-020-00887-y
48. Qiu YT, Yang C, Chen MJ, Qiu WL. Metastatic spread to the mandibular condyle as initial clinical presentation: radiographic diagnosis and surgical experience. J Oral Maxillofac Surg 2013;71(4):809–20. doi:10.1016/j.joms.2012.07.026
49. Ren QG, Huang T, Yang SL, Hu JL. Colon cancer metastasis to the mandibular gingiva with partial occult squamous differentiation: A case report and literature review. Mol Clin Oncol 2017;6(2):189–92. doi:10.3892/mco.2016.1102
50. Romanet I, Lan R, Ordioni U, Albertini AF, Campana F. A rare case of oral metastasis of colon adenocarcinoma. J Stomatol Oral Maxillofac Surg 2018;119(3):229–31. doi:10.1016/j.jormas.2018.02.003
51. Rosbottom KJ, Michie B, Boyce S. Metastasis of recurrent colonic adenocarcinoma to the mouth. BMJ Case Rep 2009;2009. doi:10.1136/bcr.03.2009.1663
52. Salvador JC, Rosa D, Rito M, Borges A. Atypical mandibular metastasis as the first presentation of a colorectal cancer. BMJ Case Rep 2018;2018. doi:10.1136/bcr-2018-225094
53. Shimoyama S, Seto Y, Aoki F, Ogawa T, Toma T, Endo H, et al. Gastric cancer with metastasis to the gingiva. J Gastroenterol Hepatol 2004;19(7):831–5. doi:10.1111/j.1440-1746.2002.03234.x
54. Smolka W, Brekenfeld C, Büchel P, Iizuka T. Metastatic adenocarcinoma of the temporomandibular joint from the cardia of the stomach: a case report. Int J Oral Maxillofac Surg 2004;33(7):713–5. doi:10.1016/j.ijom.2003.10.013
55. Soares AB, Thomaz LA, Duarte MT, de Camargo de Moraes P, de Araújo VC. Metastatic adenocarcinoma of the colon: early manifestation in gingival tissue. Head Neck Pathol 2011;5(2):140–3. doi:10.1007/s12105-010-0222-2
56. Soda H, Doi K, Kinoshita T, Yamamoto H, Nagata M, Takiguchi N, et al. Mandibular bone metastasis of rectal cancer: Report of a case. Surg Today 2010;40(12):1188–91. doi:10.1007/s00595-009-4197-0
57. Su H, Liu WS, Ren WH, Wang P, Shi L, Zhou HT. Multiple clear-cell sarcomas of small intestine with parotid gland metastasis: A case report. World J Gastroenterol 2017;23(12):2258–65. doi:10.3748/wjg.v23.i12.2258
58. Tomikawa M, Higuchi Y, Saku M, Takeshita M, Yoshida K, Sugimachi K. Carcinoma of the colon metastatic to the lower gingiva. Dig Surg 2001;18(4):333–5. doi:10.1159/000050166
59. Tsakiraki Z, Delides A, Damaskou V, Psarogiorgou S, Athanasiadis I, Spathis A, et al. Palatine tonsil metastasis of cecal mixed neuroendocrine-non-neuroendocrine neoplasm (MiNEN): A unique case. Clin Case Rep 2021;9(7):e04460. doi:10.1002/ccr3.4460
60. Usman N, Kattepur A, Gopinath KS. Metachronous metastasis to the oral cavity from carcinoma rectum - a case report and review of literature. Indian J Surg Oncol 2014;5(4):303–6. doi:10.1007/s13193-014-0334-3
61. Watanabe M, Tada M, Satomi T, Chikazu D, Mizumoto M, Sakurai H. Metastatic rectal adenocarcinoma in the mandibular gingiva: a case report. World J Surg Oncol 2016;14(1):199. doi:10.1186/s12957-016-0958-6
62. Willard CC, Weber CR, Buche W. Metastatic esophageal adenocarcinoma involving the maxilla. J Oral Maxillofac Surg 2002;60(12):1496–9. doi:10.1053/joms.2002.36137
63. Wu Z, Tang J, Li Y, Lu H, Xu J, Lv D. Successful management of rare gingival metastasis from gastric adenocarcinoma: a case report and literature review. World J Surg Oncol 2017;15(1):141. doi:10.1186/s12957-017-1215-3
64. Yang RH, Chu YK, Li WY. Unusual site of metastasis detected with FDG PET/CT in a case of recurrent rectosigmoid cancer. Clin Nucl Med 2014;39(4):355–7. doi:10.1097/rlu.0000000000000293
65. Ziegler A, Thorpe E. Oral tongue cancer in a patient with hereditary nonpolyposis colorectal cancer: A case report and review of the literature. Oral Oncol 2019;92:92–3. doi:10.1016/j.oraloncology.2019.03.008
66. Santini D, Tampellini M, Vincenzi B, Ibrahim T, Ortega C, Virzi V, et al. Natural history of bone metastasis in colorectal cancer: final results of a large Italian bone metastases study. Ann Oncol 2012;23(8):2072–7. doi:10.1093/annonc/mdr572
67. Kaplan I, Raiser V, Shuster A, Shlomi B, Rosenfeld E, Greenberg A, et al. Metastatic tumors in oral mucosa and jawbones: Unusual primary origins and unusual oral locations. Acta Histochem 2019;121(8):151448. doi:10.1016/j.acthis.2019.151448
68. Kirschnick LB, Schuch LF, Cademartori MG, Vasconcelos ACU. Metastasis to the oral and maxillofacial region: A systematic review. Oral Dis 2022;28(1):23–32. doi:10.1111/odi.13611
69. Labrador AJP, Marin NRG, Valdez LHM, Sanchez KBT, Zabarburu W, Ibazetta KAR, et al. Metastasis to the oral and maxillofacial region. A systematic review. J Stomatol Oral Maxillofac Surg 2022;123(5):e474–e83. doi:10.1016/j.jormas.2021.12.009
70. Nakamura T, Ishimaru J-I, Mizui T, Kobayashi A, Toida M, Makita H, et al. Osteosarcoma metastatic to the mandible: A case report. Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology 2001;91(4):452–4.

doi:10.1067/moe.2001.113107
71. Muttagi SS, Chaturvedi P, D'Cruz A, Kane S, Chaukar D, Pai P, et al. Metastatic tumors to the jaw bones: retrospective analysis from an Indian tertiary referral center. Indian J Cancer 2011;48(2):234–9. doi:10.4103/0019-509x.82894
72. Mantovani A. Cancer: inflammation by remote control. Nature 2005;435(7043):752–3. doi:10.1038/435752a
73. Aggarwal BB, Shishodia S, Sandur SK, Pandey MK, Sethi G. Inflammation and cancer: how hot is the link? Biochem Pharmacol 2006;72(11):1605–21. doi:10.1016/j.bcp.2006.06.029
74. Meyer I, Shklar G. MALIGNANT TUMORS METASTATIC TO MOUTH AND JAWS. Oral Surg Oral Med Oral Pathol 1965;20:350–62. doi:10.1016/0030-4220(65)90167-2
75. Hirshberg A, Leibovich P, Buchner A. Metastatic tumors to the jawbones: analysis of 390 cases. J Oral Pathol Med 1994;23(8):337–41. doi: 10.1111/j.1600-0714.1994.tb00072.x
76. Kende AI, Carr NJ, Sobin LH. Expression of cytokeratins 7 and 20 in carcinomas of the gastrointestinal tract. Histopathology 2003;42(2):137–40. doi:10.1046/j.1365-2559.2003.01545.x
77. Nishide N, Kanamura N. The value of carcinoembryonic antigen staining to determine the primary malignancy in metastatic carcinoma to the gingiva. Am J Clin Oncol 2006;29(3):316–7. doi:10.1097/01.coc.0000164005.25685.13