CASE REPORT

Atypical mandibular metastasis as the first presentation of a colorectal cancer

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SUMMARY

We describe a case of a 70-year-old man presenting with a mandibular metastasis as the first sign of a mucinous adenocarcinoma of the rectum. After 6 months of a protracted toothache, the patient presented with a palpable mandibular mass and trismus, precluding adequate clinical evaluation. A CT scan was performed, and imaging findings suggested an aggressive primary jawbone tumour, most likely an osteosarcoma. However, biopsy and further patient's management proved to be a metastasis. Metastasis to the oral cavity account for only 1%–3% of all malignant oral tumours, and the mandible is the most frequent site. Clinical presentation can be quite variable, and most often a primary malignancy is already known. Jawbone metastases are a sign of disseminated malignant neoplasms, with poor prognosis and usually an indication for palliative therapy.

BACKGROUND

Metastases to the oral region represent only 1%–3% of all malignant oral neoplasms.¹ However, they are of great clinical significance as approximately 25% are the first sign of a disseminated malignancy and 23% are the first sign of a distant unknown neoplasm.² The mandible is the most common location,^{1,2} usually involving the molar region, which is rich in red bone marrow.^{2–5} In early stages, patients present with unspecific symptoms and signs, which are frequently mistaken for benign tumours or odontogenic infections.⁶ Toothache, lower lip or mental numbness, trigeminal neuralgia, temporomandibular joint disorders or facial swelling are the most common presenting symptoms.^{6,7} Radiographically, they are most often osteolytic² but can also be sclerotic or mixed, depending on the primary neoplasm,⁸ and periosteal reaction is an uncommon feature. Treatment of these patients is usually palliative since they tend to be associated with widely disseminated disease and with poor prognosis.

CASE PRESENTATION

A 70-year-old man was referred to our institution with a large mass in the left buccomasseteric region and palpable cervical lymphadenopathies. On physical examination, a firm, adherent buccomasseteric mass with about 5 cm was detected. The patient complained of trismus and of lumbar pain aggravated by movement and was otherwise asymptomatic. There was a history of weight loss of more than 12 kg in the last 2 months. Laboratory assessments revealed a normocytic normochromic anaemia of

8.8 g/dL of haemoglobin and a thrombocytopaenia of 41 000 µ/L of platelets.

Relevant clinical history included basal cell carcinoma of the left nasolabial fold and superior lip removed surgically 5 years before and for a left inferior wisdom toothache, which began 6 months prior to presentation. The investigation of this toothache included a contrast-enhanced CT scan of the maxillofacial region ([figure 1](#)), which showed an ill-defined lucency surrounding an impacted 38, interpreted as infectious/inflammatory changes and no signs of local recurrence of the basal cell carcinoma. The patient underwent tooth extraction, with amelioration of the pain.

INVESTIGATIONS

A contrast-enhanced CT scan of the neck and maxillofacial region, performed to investigate the origin of the buccomasseteric mass ([figure 2](#)), showed a bulky, permeative and destructive lesion, centred at the left mandibular ramus, with an aggressive ‘sunburst’ pattern of periosteal reaction and a large soft tissue component, predominantly cystic/necrotic, which demonstrated thick peripheral contrast uptake. Bilateral cervical lymphadenopathies were also noted, the largest measuring 28×25×18 mm, located in level Ib, ipsilateral to the mandibular lesion, showing central cystic/necrotic degeneration ([figure 2](#)).

The imaging features and interval growth compared with the maxillofacial CT scan performed 6 months prior suggested an aggressive sarcomatous lesion, most likely an osteosarcoma or a primary odontogenic sarcoma (ameloblastic fibrosarcoma or ameloblastic fibro-odontosarcoma) with nodal metastases. Other less likely diagnoses should include a primary or secondary squamous cell cancer or minor salivary gland (MSG) carcinoma (intraosseous or by direct invasion of an alveolar ridge or retromolar trigone tumour), a primary odontogenic carcinoma (ameloblastoma carcinoma and clear-cell odontogenic carcinoma) or an aggressive haematological malignancy such as Burkitt lymphoma. Although the patient had a history of a basal cell cancer, these tumours can recur and invade locally but do not metastasise.

Further investigation with US-guided fine-needle aspiration cytology of the cervical lymphadenopathies revealed a mucinous background with atypical epithelial cells expressing CK20, suggesting metastases of a mucinous adenocarcinoma.

The search for the primary tumour included a CT of the thorax, abdomen and pelvis ([figure 3](#)) to

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Figure 1 Axial CT scan in both soft tissue (A) and bone windows (B), revealing an ill-defined lucency around tooth 38 (arrow), interpreted as infectious/inflammatory changes.

investigate for a possible gastrointestinal tract tumour and to stage the disease. This CT scan disclosed irregular, parietal thickening of the lower rectum invading the perirectal fat, bilateral inguinal lymphadenopathies, multiple pericentimetric hypodense lesions in the liver and a sclerotic lesion in the L4 vertebral body. These findings suggested a primary mucinous adenocarcinoma of the rectum with nodal, hepatic and bone metastases.

A biopsy of the rectum confirmed the presumed diagnosis of a primary rectal mucinous adenocarcinoma (figure 4). Due to

Figure 2 Axial (A, B and D) and coronal (C) CT scan after contrast administration, revealing a bulky, permeative and destructive lesion, centred at the left mandibular ramus and molar region, with an aggressive 'sunburst' pattern of periosteal reaction (arrows) and a large soft tissue component, predominantly cystic/necrotic, with thick peripheral contrast uptake. This 72×65×52 mm lesion involves the mastication muscles (masseter and both pterygoids), spreads superficially to the buccal space, infiltrates Stenson's duct and is in close contact with the superficial lobe of the parotid gland. Superiorly, the lesion extends into the infratemporal fossa, encompassing the coronoid process and the mandibular notch. Note also in figure parts C and D the presence of necrotic lymph node metastasis (*).

Figure 3 Axial CT scan after contrast administration of the pelvis (A) and abdominal region (B) showing an irregular and ill-defined thickening of the posterolateral wall of the rectum (white arrow) and also small hypodense lesions in the liver (the largest pointed out by a black arrow), compatible with liver metastases.

its large size, distinctive features compared with the L4 vertebral lesion, presence of periosteal reaction and to the fact that mandibular metastases of colorectal cancer are rare, a fine-needle aspiration cytology of the mandibular lesion was deemed necessary to exclude the possibility of two different, unrelated, primary tumours. This proved the metastatic nature of the mandibular lesion which, in this case, was the first sign of a metastatic rectal cancer (figure 4).

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of a rapidly growing, destructive lesion of the mandible should raise the following differential diagnosis:

Figure 4 Mucinous adenocarcinoma. Biopsy of the rectum (A) (H&E, medium power) and cytology of the mandible (B) (May-Grünwald-Giemsa, high power) revealing clusters of atypical epithelial cells within pools of extracellular mucin.

1. Sarcomatous lesions:
 - Osteosarcoma, chondrosarcoma, fibrosarcoma, malignant histiocytic sarcoma and Ewing sarcoma.
 - Odontogenic sarcomas (ameloblastic fibrosarcoma and ameloblastic fibro-odontosarcoma).
 - Direct invasion from a rhabdomyosarcoma.
2. Primary and secondary carcinomas:
 - Direct invasion from squamous cell carcinoma (SCC) or MSG carcinomas of the oral cavity.
 - Primary intraosseous SCC (solid type or arising from an odontogenic keratocyst).
 - Primary intraosseous MSG carcinomas.
3. Primary odontogenic carcinomas:
 - Ameloblastoma carcinoma.
 - Clear-cell odontogenic carcinoma.
 - Ghost-cell odontogenic carcinoma.
4. Haematological malignancies:
 - Lymphoma (Burkitt lymphoma).
 - Chloroma (granulocytic sarcoma).
 - Plasmocytoma/multiple myeloma.
5. Malignant nerve sheath tumour of the inferior alveolar nerve.
6. Calcifying epithelial odontogenic tumour (benign and locally aggressive).
7. Aggressive osteomyelitis.
8. Metastases (most common from lung, breast, kidney and bone origin).

TREATMENT

Due to the poor prognosis of this widely disseminated disease (stage IV), the patient was offered palliative chemotherapy and radiation therapy to the symptomatic bone metastases in the L4 vertebra and mandible.

OUTCOME AND FOLLOW-UP

Unfortunately, the patient died 2 months after the diagnosis.

DISCUSSION

Oral metastasis is a late complication of a disseminated malignant neoplasm, with an estimated median survival of 6 months after its diagnosis.⁹ Of all oral cavity metastases, the mandible is the most common site, comprising 80%–90% of cases.^{1 2 6 10} Metastases to the mandible are a consequence of distant haematogenous spread and affect preferentially areas with active haematopoietic bone marrow, such as the molar region.^{2–5} This active bone marrow is connected with sinusoidal vascular spaces, which act as a nidus for the deposition and growth of circulating malignant tumour cells. Mandibular metastization must be a complex and asymmetric mechanism that should be further investigated, once it is clear the predilection for this site when comparing with other oral regions with the same blood supply, such as the maxilla and soft tissues of this region.² About 80% of oral metastases are of epithelial origin.¹¹

Accounting for only 1%–2% of all malignant lesions of the oral cavity,⁹ metastasis tend to be misdiagnosed and underestimated, due to non-specific clinical presentation, often mistaken for common inflammatory/infectious dental disease.^{5 6 12} Symptoms can vary, depending mainly on the lesion size and the involvement of adjacent structures. Pain, mimicking a toothache, is one of the most common and often the single early finding of a mandibular metastasis.^{2 6} It is, therefore, not uncommon that patients undergo unnecessary tooth extractions in an attempt to resolve the pain.¹³ Although it is reasonable to think that the metastasis is already there, it is also known that chronic inflammation and

trauma promotes deposition of metastatic cells.^{13 14} Additionally, it is estimated that only 1.2% of cases of dental pain is associated with mandibular metastases.¹⁵ Moreover, in early stages, radiographic evaluation is of little help, showing normal findings or subtle areas of osteolysis or sclerosis surrounding one or more teeth, interpreted as periodontitis or periapical cementosis,^{6 12 13} conditions with a high prevalence in the general population. It is understandable that, in these early stages, a high degree of suspicion is needed to suggest the diagnosis of a mandibular metastasis.^{2 5} Tooth extraction does not help expedite the diagnosis as the extracted teeth, and the thin rim of tissue adjacent to the roots does not routinely undergo histopathological examination. Persistent pain and delayed, prolonged healing should raise the question of an infected extraction socket or an underlying lesion.

In later stages, clinical signs become more worrisome and include trismus, facial swelling and 'numb chin syndrome'.^{6 7} These signs mandate a search for infection (osteomyelitis) or for a primary or secondary malignancy. Specifically, 'numb chin syndrome' is a worrisome and suspicious symptom, present in 20%–50% of patients.^{3 5 7 12} Pain and pathological fractures are a sign of poor prognosis.¹⁶

Radiographically, jawbone metastases do not have distinctive features, and the best clue to the diagnosis is a prior history of a malignant tumour. Their imaging appearance depends on the site and histology of the primary tumour, which may elicit a predominantly osteolytic or osteoblastic response depending on the inhibition of activation of osteoblasts or osteoclasts.² However, up to 90% of lesions present as osteolytic lesions.² Periosteal reaction is not a common finding in mandibular metastases. This feature has been shown to correlate better with the growth rate of a lesion than with its particular histology.

MRI and bone scintigraphy can help in the differential diagnosis with other primary and secondary lesions and, most importantly, in the detection of early disease, confined to the marrow cavity. MRI is quite sensitive due to its remarkable ability to show signal changes within the bone marrow infiltrated by tumour, low signal intensity on T1-weighted images (T1W), high signal intensity on T2-weighted images (T2W), homogeneous or heterogeneous contrast uptake and restricted diffusion on DWI. Occasionally, signal intensity can be used to further refine the diagnosis.

Bone scintigraphy with ^{99m}Tc-pertechnetate is also a very sensitive technique to depict increased osteoblastic activity. However, it lacks specificity and misses predominantly osteolytic lesions. 18 Fluorodeoxyglucose Positron-Emission Tomography CT (¹⁸FDG-PET-CT) is also a very sensitive, non-specific technique in early depiction of bone lesions.¹⁷ All these functional techniques have the advantage of all body imaging, which allows the detection of additional lesions and may contribute to further refinement of the diagnosis.

As in other metastases, histological and immunohistochemical findings follow that of the primary tumour. However, histological characterisation is often difficult attending to frequent poorly differentiated lesions, making it a challenge to identify the primary location in unknown tumours.¹⁸ Adenocarcinoma tends to be the most common type of mandibular metastasis, usually from breast, lung, prostate and gastrointestinal tract origin.^{2 6 10} Colorectal cancer metastasises primarily to the liver and lungs.¹⁹ Mandibular metastases from colorectal carcinoma are rare, comprising 5%–7% of all mandibular metastasis in some series of cases.^{2 3 6 12} Regarding case reports, only 15 cases were found in the literature, even rarer as the first presenting sign. Clinical and radiological features of these lesions are summarised on [table 1](#).

As far as we know, this is the first case of secondary colorectal mandibular lesion with this kind of radiological appearance.

Table 1 List of case reports of colorectal mandibular metastases found in literature

Article	Clinical presentation	Radiological findings
Amin <i>et al</i> ²¹	Paresthesia and swelling.	Well-defined soft-tissue mass with bone destruction.
Bentley and Worrall <i>et al</i> ²²	Swelling.	–
Chen <i>et al</i> ²³	Trigeminal neuralgia, trismus and swelling.	Osteolytic lesion with soft-tissue component.
Hsu <i>et al</i> ²⁴	Swelling.	Well-defined soft-tissue mass with bone destruction.
Kameta <i>et al</i> ²⁵	Swelling, pain and paresthesia.	Ill-defined osteolytic lesion with soft-tissue component.
Mason <i>et al</i> ²⁶	Swelling and pain.	Ill-defined soft-tissue lesion with bone destruction.
Matt and McGee ²⁷	Swelling and pain.	Ill-defined soft-tissue lesion with bone destruction.
Naylor <i>et al</i> ²⁸	Swelling.	Ill-defined osteolytic lesion.
Qiu <i>et al</i> ²⁹	Swelling and pain.	Ill-defined soft tissue lesion with bone destruction.
Rentschler <i>et al</i> ³⁰	Swelling.	–
Rogers <i>et al</i> ³¹	Loose tooth.	Ill-defined osteolytic lesion.
Sheen <i>et al</i> ³²	Loose tooth, non-healing tooth socket.	Ill-defined osteolytic lesion.
Soda <i>et al</i> ³³	Pain.	Osteolytic lesion.
Woo <i>et al</i> ³⁴	Pain.	Ill-defined osteolytic lesion with pathologic fractures and soft-tissue component.
Yang <i>et al</i> ³⁵	Swelling, persistent bleeding after tooth extraction.	Soft-tissue lesion with irregularity of cortical bone.
Salvador <i>et al</i> (2018)	Pain, swelling and trismus.	Ill-defined soft tissue lesion with bone destruction and 'sunburst' type of periosteal reaction.

Although we believe that, in our case, further imaging at the time of first presentation could have anticipated the presence of a more aggressive mandibular lesion, it is not sensible to recommend sophisticated imaging such as MRI or bone scintigraphy to all patients with toothache and subtle periodontal lucencies. However, suspicion should be raised in cases of persistent pain, delayed or prolonged healing of dental extraction sockets and in the presence of worrisome clinical symptoms (trismus, facial swelling and hypoesthesia).

Fine-needle aspiration or core biopsy must be performed to confirm the nature of an aggressive-looking mandibular lesion, unless the patient has a known primary malignancy and multiple, similar-appearing bone metastases elsewhere.²

The present case also highlights the importance of colorectal cancer screening by faecal occult blood testing and sigmoidoscopy/colonoscopy in adults over 50 years of age.²⁰ Unfortunately, this patient with no family history of colorectal cancer was never screened, which might have avoided this late presentation and fatal outcome.

Treatment of choice for these patients is usually palliative, since jawbone metastases often represent a disseminated malignancy, with a very low overall prognosis. Depending on the clinical condition and the stage of disseminated disease, radiotherapy or even surgical excision may be an option, especially for pain control and preservation of oral function. Chemotherapy is always guided by the nature of the primary lesion.

Learning points

- ▶ The mandible is the most common site for oral cavity metastases, although they represent only 1%–3% of the oral cavity malignant lesions.
- ▶ A mandibular metastasis tends to involve the molar region, due to the presence of red bone marrow, and can be the presenting sign of a disseminated unknown neoplasm.
- ▶ Early clinical and radiological findings are unspecific and often mistaken for common benign infectious/inflammatory conditions; therefore, a high degree of suspicion is required for the diagnosis.
- ▶ CT scan usually reveals a lytic lesion with ill-defined margins, but a blastic appearance or even a mixed-type is possible.
- ▶ Palliative therapy is usually the treatment of choice since mandibular metastases represent widely disseminated disease with poor outcome.

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