Isolated Metastasis of the Ascending Ramus of the Mandible of Thyroid Follicular Carcinoma: A Case Report and Literature Review

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Case report

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Abstract

Objectives: The mandibular metastatic spread of carcinoma from the thyroid gland is exceedingly rare. In August 2020, we treated a 69-year-old woman exhibiting thyroid follicular carcinoma metastasis to the ascending ramus region of the mandible showing evidence of detailed radiological and pathological features.

Methods: We present a case report of thyroid carcinoma that metastasized to the ascending ramus region of the mandible at 21 years after partial thyroidectomy. We also present relevant information in a literature review of 35 articles, consisting of 43 cases (including our case) of thyroid carcinomas with jaw bone metastasis. We statistically analyzed the demographical and clinical results in terms of age, sex, type of primary cancer, site and time of metastasis, treatment, and outcome.

Results: Unlike most of the other cases, in our case, the thyroid cancer had metastasized to the ascending ramus region of the mandible, which made the diagnosis relatively difficult. The patient underwent partial mandibular resection, thyroidectomy, and iodine-131 treatment. The patient was followed up regularly, and no new symptoms were observed at seven months after post-treatment.

Conclusions: Surgery is the most common treatment for thyroid metastases of the mandible. Clinicians should ask thyroid cancer patients for follow-up to monitor whether any new complications have occurred. Patients must undergo complete examination of the maxillofacial bone for up to 40 years or more. Otolaryngologists and stomatologists should pay extra attention to patients with thyroid cancer or nodules to avoid misdiagnosis or missing the recognition of thyroid metastatic cancer.

Background

Follicular thyroid carcinoma (FTC) is the second most common type of thyroid carcinoma and accounts for approximately 10–15%^[1] of all thyroid cancers. FTC is a slow growing, solitary thyroid nodule^[2] that occurs in 0.22–1.35% of children and 4% of adults^[3]. The mean age at onset of FTC is between 40–60 years, and women are typically more affected than men, with a 3:1 ratio^[1]. The most common initial treatment for FTC is surgery; however, with disease progression, other therapeutic strategies are employed, including non-radioiodine avid and external beam radiotherapy (EBRT) as well as systemic therapies for unresectable lesions. Although FTC grows inert, its prognosis is not satisfactory. Several factors have been identified in contributing to the poor outcome of FTC. Patients of old age exhibit a propensity for angiovascular invasion of structures, regional lymph nodes, and distant regions, resulting in a high incidence of distant metastasis and mortality^[3]. The prognosis of FTC is still not satisfactory due to distant metastasis.

Distant metastases develop in 6–20% of FTC cases and 10–40% of these cases decrease the 10-year survival compared with those without distant metastases^[4–7]. Distant metastases may be the initial presentation of the disease condition or may occur after initial treatment for cancer.^[8] The most common organ sites of distant metastasis in FTC are the bones, lungs, and liver.^[3] One study found that patients with skeletal metastases did not survive more than 10 years^[9]. At present, there is no definite treatment strategy for bone metastasis (BM) of FTC, especially for skeletal metastases, which may attribute to the loss of large sample data and insufficient research attention. Surgical excision, EBRT, stereotactic body radiation therapy, or other local therapies are used to treat symptomatic isolated skeletal metastases or asymptomatic cases with metastases in weight-bearing sites.^[10–12] If the lesion can be completely removed, surgical resection is the primary choice^[10]. Besides, for those who cannot be resected surgically, non-radioactive iodine deficiency and progressive disease, EBRT and systemic therapies can be considered^[10].

FTC metastasis to the mandible is exceedingly rare and its diagnosis and treatment are challenging. In this case report, a woman possessing FTC metastasizing to the ascending ramus region of the mandible presented a painless lump in the right parotid region. This case was the first case of thyroid cancer with isolated metastasis to the ascending ramus region of the mandible reported in the last three decades. Because of the special anatomical location of this metastasis (adjacent to the temporomandibular joint), which can be misdiagnosed as a primary tumor of the mandible or a parotid gland mass, diagnosis and treatment may be difficult. This case report describes FTC metastatic to the ascending ramus region of the mandible with detailed radiological and pathological features, which may provide insights to help guide future cases.

Methods

In August 2020, a 69-year-old woman was referred to the otorhinolaryngology department of the China-Japan Union Hospital of Jilin University complaining of facial swelling in the right parotid region without any pain for 2 years. The patient was advised to undergo magnetic resonance imaging (MRI) scan of the head, which confirmed a lump in the right parotid region. She visited our clinic seeking the best treatment options for relief from swelling. During this period, the volume of the mass increased slightly. After examining the case history, we found that she had a long-term history of partial thyroidectomy from an enlarged thyroid gland that caused shortness of breath in 1999. She underwent operation and postoperative pathology reports revealed a right FTC along with capsular and vascular invasion. However, she did not receive any adjuvant treatment after resection. She had no history of tobacco or alcohol abuse, and her body mass index (BMI) was also stable (normal BMI ranges are typically 18.5–24 in China). Further clinical examination detected the existence of a smooth, soft lesion approximately 3 cm in size in the right parotid region. These complications did not cause any cervical lymphadenopathy and limited mouth opening. Ears, nose, and throat showed normal functions, and facial nerves were intact. Computed tomography (CT) scan was performed on the chest and the results were normal. Therefore, we made a preliminary diagnosis of parotid gland mass and believed that it was a benign mass.

We next performed CT angiography of the carotid, which identified the space-occupying lesions at the right mandible and the lateral pterygoid muscle (Figure 1). This led us to reconsider our initial diagnosis. Even with the ultrasound scan of the cervical lymph nodes, no abnormalities were found. We considered that the mass might be a malignant tumor of the primary mandible and conducted further needle biopsy. Ultrasound-guided needle biopsy of the lump confirmed

the presence of thyroid follicular cells. Immunohistochemical analysis further confirmed these findings and revealed thyroid transcription factor-1 (TTF-1), paired box gene-8 (PAX-8), galectin-3 and thyroglobulin positivity, as well as partial cytokeratin-7 (CK7) positivity; the expressions of cytokeratin-19 (CK19) and cluster differentiation-56 (CD56) were negative; and the Ki67 index was approximately 5% (Figure 2). Positron emission tomography–CT was performed; however, the scan reports did not reveal further pathology. Laboratory test results revealed normal T4 and T3 levels, along with a thyroid-stimulating hormone (TSH) level of 4.64 mIU/L (normal < 4.94 mIU/L); however, serum thyroglobulin level was elevated at 108.50 ng/ml (normal < 23 ng/ml).

The patient then underwent a right segmental mandibulectomy. After administration of general anesthesia, an S-shaped incision of 2 cm was made from the front region of the tragus under the mandible. Intraoperative findings revealed a round mass measuring up to 5 cm with clear demarcation. The mass was found on the deep face of the facial nerve that enters into the parotid gland of the posteromedial surface reaching the skull base and cervical transverse process and covering the ascending ramus region of the mandible. The facial nerve was free on the surface of the tumor and it was gently pulled upwards to fully expose the superficial surface of the tumor. To release the tumor, the ascending ramus region of the mandible was sawed laterally at 2 cm below the lower pole of the tumor, and the internal pterygoid muscle was cut off. The external carotid artery was lying adjacent to the tumor, and a branch entered the tumor. The tumor was completely removed after ligation of the external carotid artery (Fig. 3). We performed quick pathological examination of the incisional margin during the operation and found no infiltration of cancer cells at the incisional margin. Immunohistochemical analysis of the tumor indicated TTF-1 and thyroglobulin positivity and partial CK19 positivity; staining for P53 and CD56 were negative; and the Ki67 index was approximately 5% (Fig. 4 and Table 1). The integrity of the facial nerve was maintained during the whole operation and there was no facial paralysis during the first 2 days after the surgery. The incisions healed well with little scar formation after 7 days of surgery. Because of the compressive bandage, there was slight swelling and bruising on the right side of the face, and mouth opening was not restricted. After the patient recovered, she was transferred to the thyroid department to undergo total thyroidectomy and postoperative adjuvant therapy, such as radioactive iodine therapy. The patient was followed up regularly, and no new symptoms appeared at seven months of post-treatment.

Results

We performed a systematic literature review using PubMed and Medline databases for better understanding of the disease. Relevant articles were gathered using the key terms “thyroid,” AND “metastasis,” “mandible,” AND “cancer,” “Oral cavity,” AND “Orbit”. We obtained information on 43 cases (including our case). Among the 43 cases, 35 cases of thyroid carcinoma with jawbone metastasis were identified (Table 2) using appropriate key terms. Among the overall 43 cases, there were 34 female patients, 8 male patients, and 1 patient of unspecified sex. The female predominance, with a male-to-female ratio of 4:17, may be attributed to the higher prevalence of the disease in women^[1].

Table 1
Immunohistochemistry results of needle biopsy and postoperative sample

	TTF-1	PAX-8	galectin-3	thyroglobulin	CK7	CK19	CD56	Ki67	P53
Needle biopsy	+*	+	+	+	Scattered(+)	- †	-	5%+	ND‡
Postoperative	+	ND	ND	+	ND	Focal weakly(-)	Part(-)	5%+	-
* positivity † negative ‡ Not described (ND)									

Table 2
Clinical data of 43 cases of thyroid carcinoma with oral metastasis

Author	Age (year)	Gender	Histology	Symptom of metastasis	Time to metastasis	Location of metastasis	Treatment	Outcome (length of follow-up)
Lavanya et al. ^[36]	76	Male	FTC	Left painless jaw tumor	First manifestation	Left mandibular body	Refer to an oncologist, not report	Not report
Kundan Kisanrao Nawale et al. ^[37]	60	Female	PTC	Not report	No (not report)	Mandible	Mandibulectomy	Not report
	42	Female	PTC	Not report	No (not report)	Mandible	Biopsy, not report	Not report
	50	Female	PTC	Not report	No (not report)	Mandible	Mandibulectomy	Not report
	56	Female	PTC	Not report	No (not report)	Mandible	Mandibulectomy	Not report
Ihsen Slim et al. ^[38]	67	Female	PTC	Left pain cheek tumor	7years	Left malar, maxilla and orbit	Surgical resection of the malar mass, thyroidectomy, radioiodine (I131) therapy	Alive (not report)
Algahtani et al. ^[39]	66	Female	FTC	Left cheek swelling, lower lip numbness, difficulty chewing, pathological fracture	First manifestation	Left mandibular body and ramus	Total thyroidectomy, lateral neck dissection, mandibular lesion resection	Alive (not report)
Nikolaos Get al ^[40]	63	Male	PTC	Right painful maxillary swelling	2 years	Right maxilla, sternum, ribs, left tibia	Radiotherapy, chemotherapy	Alive (2 years)
A Agarwal et al, ^[41]	45	Female	FTC	Facial swelling	First manifestation	Left mandibular body	Hemimandibulectomy	Alive (2 weeks)
S Anil et al. ^[19]	61	Female	FTC	Right pain swelling of the mandibular angle, erythematous change in oral mucosa	8 years	Right mandibular angle and ramus	Incision biopsy, not report	Not report
Chetan J Bhadage et al, ^[42]	40	Female	FTC	Lower left facial swelling, neck lump, tooth extraction	First manifestation	Left mandibular body	Biopsy, transfer treatment (not report)	Not report
Caliaperoumal Santhosh Kumar et al, ^[43]	31	Female	FTC	Painful swelling, mobile teeth	First manifestation	Posterior maxilla	Thyroidectomy, radioiodine (I131) therapy	Alive (7years)
T Heferet al, ^[44]	52	Male	FTC	Left hard palate discomfort	Six months	Left maxilla	Left maxillectomy	Alive (2 years)
Mahnaz Fatahzadehet al. ^[45]	43	Female	PTC	Hemorrhagicmass in the right maxilla noted	No (not report)	Right maxilla	Radiotherapy	Not report
Antonio Azoubel Antunes et al. ^[46]	13	Female	PTC	Not report	Not report	Maxilla	Not report	Not report
	64	Female	FTC	Not report	Not report	Mandible	Not report	Not report
	75	Female	FTC	Not report	Not report	Mandible	Not report	Not report
Mohammad Zandiet al. ^[47]	73	Male	TC	Right painful mandible mass	First manifestation	Body of right mandible	Palliative therapy	Not report
Ugur Anil Bingol et al. ^[48]	33	Female	PTC	Right angulus mandibular mass	13 years*	Right angulus mandible	Right hemimandibulectomy and reconstructed with costochondral rib graft	Death due to multisystem metastases (5 years)
Giuseppe Colella et al. ^[49]	50	Female	PTC	Pain and swelling in right mandible	5 years	Right mandibular body	Not report	Not report
B W Draper et al. ^[50]	Not report	Female	PTC	Oral ulcers	Not report	Mandibularbody, skull	Radiotherapy	Not report

Author	Age (year)	Gender	Histology	Symptom of metastasis	Time to metastasis	Location of metastasis	Treatment	Outcome (length of follow-up)
T Erdaget al. ^[51]	53	Female	PTC	Right cheek swelling	Not report	Right mandible (not report)	Surgery, radiotherapy	Alive (2.5 years)
L Essakalli et al. ^[52]	50	Female	PTC	Painful jaw swelling	Not report	Mandible (not report)	Surgery, radiotherapy	Alive (2 months)
M A Germain et al. ^[53]	50	Female	PTC	Lymphadenopathy	13 years	Mandibular body	Interruptive mandibulectomy, reconstruction with a free composed vascularized fibular transplant	Alive (17 months)
Sumairi Bin Ismailel al. ^[17]	70	Female	FTC	Painful swelling in the left side of the angle of the mandible, loose teeth	First manifestation	Left mandibular body	Biopsy, not report	Not report
M A Kahn et al. ^[34]	82	Female	FTC	Painful mandibular vestibular swelling	32 years [†]	Mandibularbody	Radiotherapy, radioactive iodine therapy, resection	Died from cardiovascular failure (1.5 years)
Rayadurgam Venkata Kishore Kumar et al. ^[54]	58	Female	FTC	Slow-growing painless swelling on the left lower jaw	First manifestation	Left body of the mandible	Segmental mandibular resection, total thyroidectomy with midline neck dissection, postoperative radioiodine therapy	Alive (2 years)
E Vuralet al. ^[20]	64	Female	FTC	Right progressively enlarging preauricular mass	First manifestation	Right mandibular angle and ramus	Totalthyroidectomy, radical resection, radioactive iodine therapy	Not report
Paranjyothi Magadi Vishveshwaraiah et al. ^[55]	56	Female	FTC	Right painless lower facial swelling, paresthesia	First manifestation	Right mandibular body	Biopsy, referred to an oncologist [‡]	Not report
Leila Vazifeh Mostaan et al. ^[56]	58	Female	FTC	Right facial swelling on mandibular angle, teeth extraction	12 years	Right mandibular angle and ramus	Segmental mandibulectomy	Not report
F Tovi et al. ^[57]	33	Male	FTC	Large intraoral mass of the left molar area	10 years	Left mandibular angle and ramus	Radioactive iodine therapy [§]	Died of thyroid crisis (17 days)
Demetrio Tamiolakis et al. ^[18]	69	Female	PTC	Facial swelling, nasal obstruction, epistaxis	Not report	Mandible (not report)	Inoperable	Died of disease(1 month)
	Not report	Not report	TC	Facial swelling, oral mucosal ulcerations	Not report	Mandible (not report)	Resection	Not report
Ajay Prakash Pasupula et al. ^[58]	40	Female	FTC	Painful swelling in the left parotid region, intermittent low-grade fever	First manifestation	Left mandibular body and ramus	Total thyroidectomy, resection of metastatic tumor of the mandible	Not report
Alejandro Ostrosky et al. ^[59]	72	Male	FTC	Slight toothache	First manifestation	Left mandibular body	Total thyroidectomy, resection and reconstruction of the mandible	Not report
I Meyer et al. ^[60]	51	Female	FTC	Not report	Not report	Not report	Not report	Not report
Lin Liu et al. ^[35]	66	Male	FTC	Left cheek lump	22 years	Mandible (not report)	Radical resection of the mandibular tumor, radioactive iodine therapy	Alive (3years)

Author	Age (year)	Gender	Histology	Symptom of metastasis	Time to metastasis	Location of metastasis	Treatment	Outcome (length of follow-up)
JD Osguthorpe et al. ^[28]	53	Male	FTC	Slowly enlarging right parotid area mass	First manifestation	Right mandibular ramus	Partial mandibulectomy	Alive (3 years)
H Nishikawa et al. ^[61]	83	Female	FTC	Swelling and pain in the median lower jaw	2 years	Median mandible	None	Died of disease (19 months)
A Markitziu et al. ^[29]	69	Female	PTC	Left facial swelling	First manifestation	Left ascending ramus of the mandible and parotid	Irradiation, chemotherapy	Alive (1.5 years)
R K McDaniel et al. ^[62]	77	Female	FTC	Pain and swelling in the right mandible	First manifestation	Right mandibular posterior body and ramus	Right hemimandibulectomy, total parotidectomy	Alive (4 years)
	48	Female	FTC	Swelling in left mandible of thyroid parotid area, numbness of left lower lip	First manifestation	Left mandibular ramus	Not report	Alive (not report)
Present case	69	Female	FTC	Painless lump in the right parotid region	21 years	Right ascending ramus of the mandible	Right segmental mandibulectomy, thyroidectomy, radioactive iodine therapy	Alive (7 months)
<p>* The patient had a history of thyroid surgery because of PTC at the age of 20. Six years later, she underwent surgery again because of recurrence and received radioactive iodine treatment at the age of 30. The patient underwent two surgeries due to metastases of the pelvis and humerus.</p> <p>† This patient had undergone a thyroidectomy when she was 51 years old because of the presence of an unspecified tumor. Four years later, a mediastinal tumor of unknown nature was excised. After 5 years, the patient was diagnosed with hyperthyroidism. When she was 77, in February 1980, she developed a metastatic focus of thyroid carcinoma in the tibia. Between 1980 and 1985, metastases invaded the lungs and pelvis.</p> <p>‡ The patient had undergone an incisional biopsy elsewhere, which was diagnosed as an odontogenic tumor.</p> <p>§ The patient had undergone a subtotal thyroidectomy when she was 23 years old because of the existence of a cold nodule in the left lobe. Six years later, deformation of the seventh to ninth thoracic vertebrae was found, but the patient refused laminectomy and subsequently became paraplegic. In addition to the mandible, metastases were also found in the vertebrae, mediastinum, parietal bone, and femur.</p>								

The patient age ranged from 13 years to 83 years, and the median age of patients was 57 years. This observation is consistent with the fact that metastatic tumors are reported to be the most common diseases in the fifth to seventh decade of life^[13]. Among the histological types of thyroid carcinoma, 25 of the 43 cases (58.1%) were follicular carcinomas and 16 of these cases (37%) were considered as papillary carcinoma; for the remaining 2 cases, the primary tumor was reported as thyroid carcinoma without further clinical description. Although the incidence of papillary thyroid carcinoma (PTC) was higher than FTC, FTC shows high vascularity and a higher rate of vascular invasion^[14]. This may account for the higher incidence of FTC with maxillofacial metastasis.

The clinical symptoms of maxillofacial metastasis include pain in the gums, swelling, loosening of tooth, paraesthesia of the lower lip and chin, trismus, growth of tumor projecting out from the soft tissue, and pathologic fracture^[15]. The lesion can also cause pain in the temporomandibular joint region or as osteomyelitis in the jaw or as trigeminal neuralgia^[16]. However, some cases do not show symptoms. Sometimes the symptoms or signs may be the only manifestation of an undiscovered malignancy^[17]. Among the 43 cases, 16 cases were diagnosed with distant metastasis as the initial presentation, while in 9 cases, the timing between the diagnosis of the primary and metastatic disease was not specified. In the other 18 cases, patients developed distant metastases after the initial treatment for thyroid carcinoma, with an average of 7 years after treatment (ranging from 6 months to 32 years). This may be related to the slow growth rate of thyroid carcinoma and thus metastases in the bone may be undetected or may remain dormant for a longer period.

Oral metastatic carcinoma accounts for approximately 1% of all oral cancers^[18]. Compared with metastases in other bones, metastatic tumors to the jawbones are very rare and the true incidence is not known. The most frequent location for metastasis in the jawbone is the mandible. We found that 36 cases out of the 43 identified cases had metastasis in the mandible. Metastasis to the maxilla was seen in 6 cases out of 43 cases. Most (84%) metastasis involving jaw bones occurs in the mandible, and the molar area is the most frequent site of metastasis.^[18, 19] This may be due to the presence of more hematopoietic tissue in the mandible^[20]. Patients with metastases in the maxilla were relatively young, with an average age of 45 years; in comparison, the mean age of patients with metastasis to the mandible was 59 years.

Rection, EBRT, or embolization for bone metastases in patients in whom these are symptomatic^[21]. Unfortunately, only a few cases have been cured after the diagnosis of bone metastases with FTC. Recent studies have documented the significant role of the sodium iodide symporter (NIS) in several extrathyroidal cancers such as pancreatic cancer, prostate cancer, colon cancer, ovarian cancer, breast cancer, cervical cancer, and testicular cancer^[22]. Moreover, balanced regulation of the transcription and translocation of NIS is monitored by TSH^[23]. NIS is also essential to establish an I⁻ gradient in thyrocytes, thereby achieving the synthesis of thyroid hormones^[24]. Furthermore, various studies have reported overexpression of NIS in thyroid cancer cells and its oncogenic

effects. Hence, the overexpression of NIS in cancer cells has indicated the utility of radioiodide treatment application for the targeting of thyroid cancer^[25]. Radioactive iodide (131I) has been used as the standard treatment for FTC with distant metastases of lung or bone, and treatment results are dependent on the expression of NIS expression in cancer cells^[25]. The efficacy of 131I treatment for FTC depends on the differentiation of the cancer cells^[26]. In our literature review, 23 cases underwent surgery and 2 cases (a total of 5 deaths in 43 cases) died. This may also indicate that the prognosis of jawbone metastases is better than that of other bone metastases for thyroid carcinoma (TC). There is evidence that resection of solitary bony metastasis, along with total thyroidectomy, may increase the survival among patients with TC, possibly due to increased radioactive iodine uptake and effects used to treat the potential micrometastases elsewhere in the body after surgery^[20]. Extremely high vascular density in FTC with bone metastases may not only lead to diagnostic dilemmas but also high surgical mortality and morbidity^[20]. Therefore, we should focus on the selection of surgical methods and the avoidance of bleeding and post-surgery complications. In recent decades, the extent of surgery for TC has changed. Surgery has become more conservative, with an emphasis on treating the patient on a case-by-case basis. The clinician and patients should discuss the expectations regarding the quality of life as well as the risks and benefits associated with the treatment strategy. This will allow for the best personalized treatment option. Treatment decisions must weigh the rate of tumor progression and quality of life without treatment against the efficacy and side effects of therapy.

Discussion

Our literature review identified 390 articles that mentioned metastasis in mandibular and maxillary bones. Hirshberg et al^[14] observed that breast is the most frequent primary site of metastasis in women while the primary sites of metastatic carcinoma of the mandible region are mainly lung cancer in men^[27]. Of the maxillofacial metastases, 60–80% occur in the mandible and are mainly concentrated in the molar and premolar areas^[18]. Metastases to the mandible from thyroid cancer are uncommon.

Of the 43 cases we collected, the case reported by Osguthorpe^[28] alone has a complaint of parotid sialography, which was diagnosed and a lateral displacement of the superficial lobe and destruction of the mandible from the angle to the neck of the condyle were found. This case occurred in the 1980s when the technology did not provide any complete images of the mandible. Furthermore, the authors selected the partial mandibulectomy and inferior alveolar nerve en bloc specimen for pathological examination, so whether the tumor is just invading the ascending ramus region of the mandible is not clear. Another case reported by Markitziu^[29] involved the ascending ramus region of the mandible and the parotid gland. Although the tumor mass in our case report also consists of the parotid region, which lies between the superficial and deep lobes of the parotid gland, the parotid gland was not invaded and the capsule of the parotid gland was intact. Therefore, our case was the first to report thyroid cancer isolated metastasis to the ascending ramus region of the mandible in the last three decades.

Metastasis is the result of a complex biological cascade that begins when tumor cells detach from the primary tumor and spread into the tissue; the cells then invade lymphatic vascular structures and survive in circulation^[13]. The microvascular system of the target organ provides a hiding place for metastatic tumor cells, which spread, proliferate and invade the target tissue. Angiogenesis is necessary to provide adequate oxygen and nutrients when tumor cells are overloaded with more than 2–3 mm^[30]. Because the mode of metastasis is hematogenous, the neoplastic cells are deposited in areas where there is vascular tissue^[31]. Some investigators believe that metastasis to the jawbone through the hematogenous route requires the presence of hematopoietically active bone marrow that is well connected with the sinusoidal vascular spaces at the site of deposition of malignant cells^[32]. This may be one of the reasons why the involvement of the jaw in metastasis seems to be less common than other bones. The amount of red bone marrow and blood vessels in the jaw tends to decrease with age, which may be from the gradual replacement of red bone marrow by yellow or fatty bone marrow^[13]. We found that jawbones are not always included in radiographic skeletal surveys for metastasis, according to the National Comprehensive Cancer Network (NCCN) guidelines^[10] for thyroid cancer treatment, which does not mention the mandible in the periodic bone examination of patients after thyroid cancer surgery. Therefore, clinicians should also monitor the maxillofacial features in the diagnosis and follow-up of patients with thyroid cancer, rather than focusing only on the common sites of metastasis such as lung and bone.

The most common site of metastasis to the mandible is the molar area^[18, 19]. There are usually no significant blood vessels or nerves in this area, and the main considerations may be the amount of blood loss during the operation and how the mandible is reconstructed. Unlike most previous case reports, in this case, the mass was located close to the temporomandibular joint, which makes the diagnosis difficult. It is difficult to distinguish from the primary mandibular tumor or parotid gland tumor by imaging and clinical manifestations. Therefore, preoperative puncture biopsy is particularly important. A clear diagnosis of the disease is very important to the choice of treatment. Extremely high vascular density in FTC with bone metastases may not only lead to diagnostic dilemmas but also may lead to high surgical mortality and morbidity. Therefore, CT or MRI alone cannot fully evaluate the condition of the tumor; hence, CT angiography or MRI angiography is necessary to further resolve the tumor condition. Vural et al^[20] reported a case of FTC metastasis to the mandible with preoperative selective embolization. We evaluated preoperatively and decided not to perform the embolization process. Although we reported the existence of vascular abnormalities of the tumor, in this case, intraoperative blood loss was within a normal range. After the surgery, there was some bleeding due to compression, and the skin of the patient returned to normal within two weeks. We can make a better decision whether to choose preoperative embolization with the help of CT angiography and other imaging techniques. FTC metastatic to mandible can cause significant morphological, functional and esthetic alterations due to disease progression, so it needs aggressive therapy. In terms of reconstruction of the mandible, this case is different from other cases. Instead of using fibula or other bone with blood vessels, our preoperative vision was to use an in vitro titanium plate tailored to the preoperative normal jaw bone of the patient. The patient would be advised to wear it or remove it as needed, just like dentures. However, the patient's occlusal condition and appearance did not appear to be a major problem after the surgery, and the pre-customized titanium plate was not used.

Pruckmayer et al^[33] conducted a major retrospective study of 763 patients with nonspecific pain in the mandible, and only 9 patients (1.2%) had mandibular metastases. They projected the pain as an important marker in the study^[33]. Most of the cases we collected also reported pain or other symptoms, such as

lost teeth and numbness of the skin. However, the patient in our case did not experience any discomfort. This may also be a factor in the discovery of metastases after 21 years of partial thyroidectomy. The period of thyroid cancer metastasis may be relatively long. In addition to our case, the period of thyroid cancer metastasis in the case reported by Kahnet al^[34] was for 32 years and that in the other case reported by Liu et al^[35] was for 22 years. Although this is rare, these facts are also consistent with the indolent process of well-differentiated thyroid carcinoma. This also raises the question of whether the follow-up of thyroid cancer patients should be extended for at least 40 years.

This rare case highlights the importance of a clinical maxillofacial malignancy that is likely to metastasize from other sites and the need for follow-up of patients with malignancy. As thyroidists, we should follow patients with thyroid follicular carcinoma for at least 40 years, and the follow-up should include the maxillofacial area. As otolaryngology and stomatology physicians, it is important to carefully review the patient's history and pay attention to the entire case history of thyroid lumps when diagnosing maxillofacial masses, especially in women. When maxillofacial masses cannot be diagnosed, careful clinical examination combined with radiological, histological, and immunohistochemical assessments can lead to early detection of the primary tumor, more appropriate treatment, and a better prognosis for these patients.

Conclusion

Because of the rare occurrence of oral and facial metastatic tumors and deceptive clinical and histopathological features, it is often difficult to diagnose this disease. The diagnosis is more challenging when oral and facial metastases are the first manifestations of distant, undetected malignancy. Some highlights of the current case are as follows: (1) this is first reported case of solitary thyroid cancer metastatic to the ascending ramus region of the mandible in nearly 30 years; (2) the period of metastasis was relatively long; (3) the patient reported facial swelling without pain and other special clinical manifestations; and (4) the anatomical location of metastatic carcinoma makes the diagnosis and operation difficult. Although this is a rare occurrence, practitioners should always be highly suspicious when diagnosing patients with oral-facial metastases. The ascending ramus region of the mandible should also be examined in the follow-up period and the time of follow-up should be prolonged.

Abbreviations

FTC	Follicular thyroid carcinoma
EBRT	external beam radiotherapy
BM	bone metasis
MRI	magnetic resonance imaging
BMI	body mass index
CT	computed tomography
TTF-1	thyroid transcription factor-1
PAX-8	paired box gene-8
CK7	cytokeratin-7
CK19	cytokeratin-19
CD56	cluster differentiation-56
TSH	thyroid-stimulating hormone
PTC	papillary thyroid carcinoma
NIS	sodium iodide symporter
TC	thyroid carcinoma
NCCN	National Comprehensive Cancer Network
ND	Not described

Declarations

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Author information

Authors' contributions

All authors have contributed significantly: DZ and SZ designed the study; DZ, SZ, and QS analyzed and interpreted data; DZ, SZ, and QS wrote and/or reviewed the manuscript; all authors discussed the results, commented on the manuscript, and saw and approved this manuscript.

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Ethics declarations

Ethics approval and consent to participate

The case study and treatment plan were approved by the Institutional Review Board and Ethics Committee of The China-Japan Union Hospital of Jilin University.

Consent for publication

Written informed consent was obtained from the patient according to the federal and institutional guidelines.

Competing interests

The authors declare that they have no competing interests.

Availability of data and materials

Data sharing not applicable to this article as no datasets were generated or analysed during the current study.

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Figures

Figure 1

Computed tomography angiography of the carotid showed marked bony destruction in the involved mandible (A), the size of the space-occupying lesions at the right parotid region (B) and angiography (C and D).

Figure 2
Hematoxylin and eosin staining of the biopsy at 40X (A) and 100X (B); images show infiltrating tumor cells. Immunohistochemical analysis of nodule revealed TTF1 (C) and thyroglobulin (D) positivity; CK7 (E), PAX-8 (G) and galectin-3 (H) staining showed positivity; and the Ki67 index was 5% (F).

Figure 3

Pathology image (A) shows gross macroscopic pictures of the excised specimen; (B) the tissue specimen was cut lengthwise to reveal its interior; (C) the operative cavity after removal of the tumor.

Figure 4

Hematoxylin and eosin staining at 40X (A) and 100X (B) depicting tumor cells infiltrating and destroying the mandibular bone after the operation. Immunohistochemical analysis of the nodule revealed TTF1 (C) and thyroglobulin (D) positivity; CK-19 (E) showed positivity; and the Ki67 index was 5% (F).