Clinical manifestations and diagnostic approach to metastatic cancer of the condyle

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(Received Sep 12, 2017; Revised version received Oct 11, 2017; Accepted Oct 11, 2017)

ABSTRACT

Metastatic malignancy on the mandibular condyle is a very rare, but life-threatening condition that is frequently misdiagnosed as temporomandibular joint disorder (TMD) and other dental diseases. The researchers report on a patient who was referred with an initial diagnosis of TMD, due to symptoms resembling TMD, such as limited mouth opening with pain on the temporomandibular joint (TMJ) and mandibular deviation during mouth opening. However, the final diagnosis was malignant condylar metastasis. The researchers reviewed available literature on malignant condylar metastatic cases focusing on initially misdiagnosed cases to find additional diagnostic information. The analysis revealed that some aspects of malignant condylar metastasis were overlooked, which frequently led to misdiagnosis and incorrect treatment. Further understanding of condylar metastasis might lead to early detection of occult primary cancer, possibly preventing further metastasis.

KEY WORDS: Mandibular condyle, Neoplasm metastasis, Neoplasms

Introduction

Metastatic bone cancer in the stomatognathic system is infrequent, comprising less than 1% of all bony metastasis [1, 2]. Reports of involvement of the mandibular condyle have been extremely rare [3] since the first case report in 1947 [4]. Though clinical symptoms of condylar metastasis vary, depending on the severity of metastatic involvement and properties of the primary cancer, the common symptoms in approximately half of these cases include click, crepitation, deviation during opening, limited opening and lateral movement, tenderness to palpation, and pain in function [5], which are similar to those seen in temporomandibular disorders (TMD) [6]. Considering that radiographic changes may be minimal or absent in early stages of the disease [5] and TMD-mimicking symptoms

may be the first sign of a malignant tumor [1, 7], it is sometimes difficult to differentiate clinically between TMD and metastatic involvement of the condyle. Moreover, many patients with condylar metastasis are misdiagnosed and receive improper treatment, resulting in effective treatment delay. Therefore, the exact diagnosis of condylar metastasis is challenging for many dentists.

In this article, we report on a patient with metastasis to the mandibular condyle who presented with TMD-like symptoms and bony resorption on the mandibular condyle. We reviewed the related literature, analyzing the clinical manifestations of condylar metastases to assist clinicians in differentiating them from TMD and other orofacial diseases.

Case Report

In October 2011, a 75-year old female patient was referred to the department of Oral Medicine, Kyungpook National University Dental Hospital by a local dental clinic for pain in the right temporomandibular joint (TMJ)

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region with restricted mouth opening. The symptoms had begun one month prior without any traumatic event. The pain was centered in the region of the right TMJ and was accentuated with jaw opening. On clinical examination, the patient exhibited restricted mouth opening with 35 mm maximum jaw opening capacity, accompanied by pain on the right TMJ. Mild tenderness over the region around the

right TMJ was observed on palpation.

The patient's past medical history included squamous cell carcinoma of the right neck, treated by radical neck dissection in October 2008. In 2009, metastasis to the lung had been observed on a periodic follow-up exam, and radiotherapy and chemotherapy had been administered. The patient reported that there were no remarkable findings

Fig. 1. Panoramic radiograph (A) and four panoramic transcranial views (B) show ill-defined, diffuse osteolytic radiolucency on the right condylar area.

Fig. 2. Contrast-enhanced CT images (A-D) show an ill-defined bony destruction together with round mass on the right condylar area.

supporting any metastasis on positron emission tomography/computed tomography (PET/CT) taken in April 2011.

A panoramic and four panoramic transcranial views, acquired using an Orthopantomograph HOP 100D (Instrumentarium Imaging, Tuusula, Finland), showed an ill-defined bony destruction on the right condyle, suggestive of possible metastasis of the malignant tumor (Fig. 1). The patient was subsequently transferred to the department of Oral and Maxillofacial Surgery for further treatment. Contrast-enhanced CT (Lightspeed Ultra, GE Healthcare, Milwaukee, WI, USA) revealed an ill-defined enhanced mass on the right condylar head area accompanied by bony destruction (Fig. 2) and thickening of the enhanced lateral pterygoid muscle. These findings strongly supported the possibility of a metastatic lesion. Scintigraphy with Technetium-99m tagged to hydroxymethylene diphosphonate (Tc 99m HDP) was performed using Infinia (GE Healthcare, Milwaukee, Wisconsin, USA) to rule out further metastasis. Apparent focal tracer uptake was observed on the right TMJ and the left seventh rib, and the upper portion of the sacrum (Fig. 3). An 18F-fluorodeoxyglucose (FDG) PET/CT scan combined PET/CT unit (Reveal RTHiRez CTIMI, Knoxville, TN; a six slice CT scanner) showed a hypermetabolic mass on the right condylar area (Fig. 4) and intense FDG uptake on the upper lobe of the left lung and lower lobe of the right lung. Based on the past medical history and imaging information, the patient was finally diagnosed with metastasis to the right condyle, although a biopsy was not performed. Given the patient's poor health status and advanced metastatic disease, surgical

Fig. 3. The whole body bone scan with Tc 99m HDP reveals an increased radiotracer uptake in the right TMJ, the left seventh rib, and the upper portion of the sacrum.

cal removal of the metastatic tumor was not performed. Therefore, the patient was transferred to the department of hemato-oncology for palliative radiotherapy and chemotherapy.

The patient was alive without any sign or symptom of tumor recurrence or additional metastasis at the most recent visit 14 months after the original presentation. She is being followed-up by the oncological service for one year.

Fig. 4. Positron emission tomography CT scans reveal hypermetabolic masses on the right condyle (A) and the left lung (B).

Discussion

Metastasis to the TMJ is a very rare but life-threatening condition. When searching the PubMed database (up to August 2017) and references for other literature, we found that only 62 cases, including the current case, have been published in English. In PubMed, the search was performed repeatedly using the keywords “condyle” (or “condylar”), “metastasis” (or “metastatic”), and “malignant”. Secondary searches were performed among references cited in the articles initially found. Sixty two cases including this one were identified through this process [2-4, 6, 8-58]. Analysis of various clinical data was performed in these cases. In addition, because two cases showed involvement in both TMJs with different radiographic appearances, radiographic analysis was based on each lesion.

In our review, patient age ranged from 15 to 85 years, with an average age of 56.5 years. All cases except two had unilateral involvement, with left condylar involvement in 33 cases and right condylar involvement in 27 cases (64 lesions). Gender distribution showed that the incidence of condylar metastasis is slightly higher in females than males, with 35 female and 26 male patients (Table 1). These findings differ in age and gender distribution from TMD, the most frequent TMJ disease, characterized with a definite predilection for the young female [59].

The most common primary tumor site was breast (16 cases), followed by prostate (six cases), lung (six cases), colorectum (five cases), bronchus (three cases), kidney (two cases), liver (three cases), and others (eleven cases). Primary tumor site obviously differs between male and female. In this review, breast cancer was the most com-

mon origin for metastatic oral cancer in females, while in males, prostate cancer followed by lung cancer was most frequent. Such a gender difference is attributed to difference in incidence of primary malignancy by gender. Histologically, the most common type of primary tumor was adenocarcinoma, and there were less common primary tumors such as chordoma, cystosarcoma, melanoma, neuroblastoma, osteosarcoma and testicular classic seminoma.

Regarding clinical manifestations, 71% of cases had pain around the TMJ, 59.7% presented with swelling, 40.3% had decreased opening range from 1 mm to 35 mm, 17.7% had tenderness on palpation on TMJ, 14.5% had paresthesia on the orofacial area, 11.3% had change in occlusion, 9.7% showed limitation of lateral movement, and 8.1% reported joint sound. Other symptoms included mass formation, discomfort, and dysphagia (Table 2). Many clinical manifestations are similar to those of TMD including pain [44], joint sound during mandibular movement [22], tenderness to palpation [49], occlusal change [40], and abnormal mandibular movements, including deviation at the opening, limited opening, and lateral movement [53]. However, many patients presented with atypical symptoms different from typical TMD, such as preauricular tender swelling (59.7%) [50], and facial paresthesia (14.5%) [60]. Additionally, some patients with typical symptoms of mouth opening limitation showed extremely restricted mouth opening range of ≤ 20 mm, rare in patients with TMD (Table 3). Therefore, metastatic condylar malignancy should be considered as a more likely diagnosis for patients with unusual clinical manifestations such as swelling, paresthesia, and severe limitation of mouth opening.

Radiographic appearance of metastatic lesions was char-

Table 1. Age and gender distribution

Age	Male (%)	Female (%)	Total (%)
10 - 19	0 (0.0)	1 (1.6)	1 (1.6)
20 - 29	0 (0.0)	1 (1.6)	1 (1.6)
30 - 39	2 (3.2)	1 (1.6)	3 (4.8)
40 - 49	4 (6.4)	7 (11.3)	11 (17.7)
50 - 59	5 (8.1)	13 (21.0)	18 (29.0)
60 - 69	8 (12.9)	9 (14.5)	16 (27.4)
70 - 79	6 (9.7)	3 (4.8)	8 (14.5)
80 - 89	1 (1.6)	0 (0.0)	1 (1.6)
Total	26 (41.9)	35 (56.5)	61 (98.4)

The gender of a 42-year-old patient was not stated.

Table 2. Clinical manifestations in patients with metastatic condylar lesion

Clinical features	Cases (%)
Pain	44 (71.0)
Swelling	37 (59.7)
Limitation of mouth opening	25 (40.3)
Tenderness	11 (17.7)
Paresthesia	9 (14.5)
Change of occlusion	7 (11.3)
Limitation of jaw movement	6 (9.7)
Joint noise	5 (8.1)
Others*	14 (22.6)

*Others include mass (3), deviation (2), discomfort (2), asymmetrical prognathism, dislocation, dysfunction, dysphagia, facial asymmetry, fullness, stiffness, and TMD syndrome.

Table 3. Mouth opening range in patients with opening limitation

Mouth opening range	Cases (%)
≤ 10 mm	4 (6.5)
10 mm<, ≤ 20 mm	6 (9.7)
20 mm<, ≤ 30 mm	4 (6.5)
> 30 mm	1 (1.6)

Mean range of mouth opening in 15 patients was 17.03 mm (1 - 35 mm).

acterized by destruction of the mandibular condyle such as condylar erosion and osteolysis in 34 lesions (53.1%) including our case. However, some metastatic lesions may present with an osteosclerotic, or osteoblastic appearance (4.7%), or mixed-density appearance (9.4%) of osteolytic and osteoblastic areas. In addition, subtle bony changes or normal radiographic appearance were also found in 11 lesions (17.2%), most likely representing the initial stage of the disease (Table 4) [27]. Radiographic manifestation on the initial stage is due to the fact that 30~50% of mineral content must be lost before the radiograph can reveal a lytic lesion, implying that initial radiographs may appear normal even if some resorption had already occurred [61]. As described above, the radiographic findings may be nonspecific and varied despite the predominant osteolytic appearance.

Misdiagnoses were initially made in 16 (25.8%) of 62 patients as TMD and other diseases at a local dental clinic, as in the present case. Lack of specific radiographic and clinical findings lead to misdiagnosis and unnecessary treatment such as tooth extraction [14], pharmacotherapy [18], and oral appliance therapy [24, 31, 45]. Our review revealed that five of 11 lesions (45.5%) with normal radiographic findings had been initially misdiagnosed (Table 4) and, subsequently, maltreated. Among various radiographic findings, misdiagnosis was most often made in lesions with normal radiographic appearance. This implied that dentists were likely to overlook the fact that condylar metastasis at an initial stage might appear normal on routine radiography. Consequently, various imaging procedures including CT, MRI, and bone scan should be considered for patients presenting with unusual clinical symptoms, even if their routine radiographs display normal appearance or subtle TMJ changes.

In our review of the applied treatment modalities, radiotherapy (58.1%) was most common, followed by surgery (40.3%), chemotherapy (37.1%), palliative or hormone therapy (9.7%) and no treatment (1.6%) (Table 5). The

Table 4. Rate of initial misdiagnosis according to radiographic manifestation

Radiographic manifestation	Misdiagnosis		
	Yes (%)	No (%)	Total
Osteolytic (pathologic fracture; 7)	7 (10.9)	27 (42.2)	34 (53.1)
Normal	5 (7.8)	6 (9.4)	11 (17.2)
Mixed (pathologic fracture; 7)	1 (1.6)	5 (7.8)	6 (9.4)
Sclerotic	2 (3.1)	1 (1.6)	3 (4.7)
Non-stated	2 (3.1)	8 (12.5)	10 (15.6)
Total	17 (26.6)	47 (73.4)	64 (100)

Table 5. Treatment of metastatic lesion

Treatment	Cases (%)
Radiotherapy	36 (58.1)
Surgery	25 (40.3)
Chemotherapy	23 (37.1)
Palliative or hormone treatment	8 (12.9)
No treatment	1 (1.6)
Not-stated	3 (4.8)

selection of the treatment modality depends on the patient's general condition and type of tumor. For patients with a solitary metastatic lesion and the primary disease, surgical treatment is indicated to enable patients to speak and eat normally. While 25 patients could undergo more active surgical procedures, seven patients could take only palliative treatments and even no treatment, probably due to poor general condition and widespread metastasis. Therefore, early detection of cancer may affect choice of treatment modalities and furthermore, provide better quality of life.

Prognosis of condylar metastasis is usually poor [21, 27, 49, 62]. Most patients died within one year after diagnosis of metastasis of serious complications resulting from disease deterioration [62]. Medium life expectancy is approximately five months, with a survival time range from two weeks to four years [63]. Loss of critical time for treatment due to misdiagnosis and subsequent incorrect treatment results in delay of proper treatment and worsening of patients' remaining quality and quantity of life. Therefore, the accuracy and promptness in diagnosis and treatment are of utmost importance for substantial improvement in the disease prognosis.

The medical history of malignancy preceded the onset of TMD-like symptoms in more than half of the cases. However, 27 cases (43.5%) presented with TMD-like

symptoms as the first indication of primary and metastatic malignancy. This percentage is higher than in reports of one-third to one-fifth of patients in previous reviews [64-66]. Such a proportion indicates that thorough examination is necessary to detect the presence of undisclosed cancers even in patients without any cancer history and that the dentist is in a position to notice unusual symptoms implying the presence of primary malignant lesions. This places considerable responsibility upon dentists. Twenty seven patients presented with clinical symptoms as the first indication of malignancy and 7 patients were unfortunately misdiagnosed as a problem of dental origin, TMD, or osteomyelitis and subsequently treated inadequately, including physiotherapy [9, 12], related pharmacotherapy [12, 23, 50], and oral appliance therapy [9, 24]. When compared to the misdiagnosis rate in cases where the clinician was aware of the history of cancer, it was interesting to note that this important information made only a slight difference. This indicates that previous cancer history was not considered in the diagnosis of malignant condylar metastasis by many clinicians. Therefore, clinicians should pay more attention to the previous cancer history and consider that TMD-like symptoms could be caused by malignant condylar metastasis instead of TMD. In conclusion, inaccurate diagnosis and treatment of metastatic condylar lesions may cause not only inadequate treatment results but also a malpractice suit against the clinician. Tremendous care should be taken to obtain detailed medical and dental histories and perform thorough physical and radiographic exams, especially in patients with atypical manifestations such as swelling, paresthesia, severe mouth opening limitation, and poor treatment response together with previous cancer history.

In summary, we present a case of metastatic condylar cancer with TMD-like symptoms, initially misdiagnosed as TMD at a local dental clinic. While our analysis of 60 malignant condylar metastatic cases suggested that condylar metastasis should be considered for patients presenting with swelling in the TMJ area, facial paresthesia, extremely limited mouth opening, osteolytic lesion, and previous cancer history, we found diverse clinical and radiographic manifestations, ranging from normal or subtle to distinctive. Consequently, condylar metastasis cannot be defined by a single disease profile. Therefore, to diagnose it accurately, it is essential to gain a deeper understanding of the diversity of its clinical and radiographic manifestations.

Acknowledgements

This study was supported by the National Research Foundation of Korea (NRF) grant funded by the Korean government (MEST) (NRF-2015R1D1A1A01060821). This study was supported by a National Research Foundation of Korea (NRF) grant funded by the Korean Government (NRF-2015R1C1A2A01055438).

Conflict of Interest

The authors declare that they have no competing interests.

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