Temporomandibular disorders associated with metastases to the temporomandibular joint: a review of the literature and 3 additional cases

Astrid L.D. Kruse, MD, DMD,[a] Heinz-Theo Luebbers, MD, DMD,[a]
Joachim A. Obwegeser, MD, DMD,[b] Lars Edelmann, MD,[c] and Klaus W. Graetz, MD, DMD,[d]
Zurich, Switzerland
UNIVERSITY OF ZURICH

Introduction. Metastases involving the oral cavity account for 1% to 8% of all malignancies in the oral cavity Involvement of the temporomandibular joint (TMJ) is uncommon.
Method and results. We conducted a review of the literature between 1954 and 2008 regarding metastases to the TMJ. In total, 48 patients were found and in 28 patients a previous history of malignant neoplasm was known. The primary tumor was most commonly found in the breast (34%), followed by the lung (21%). Adenocarcinoma was predominant (72.97%).

Three new patients with TMJ pain as a first symptom for a disseminated tumor are also examined here.
Conclusion. Establishing an exact diagnosis of metastatic lesions in the TMJ can provide a diagnostic challenge. Clinicians should include the suspicion of cancer in the differential diagnosis, in particular when patients have a previous history of malignant neoplasm or do not respond to treatment appropriately. **(Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2010;110:e21-e28)**

Temporomandibular joint (TMJ) disorders, including myoarthropathy, disc luxation, and arthritis are common, but the probability of a metastasis to the mandibular condyle is low. Because of this rarity, diagnosing a metastatic lesion in the condyle is a challenge to all clinicians dealing with patients with TMJ disorders, and it should always be considered as a differential diagnosis for this patient group.

In general, metastases to the oral cavity are uncommon, accounting for 1% to 8% of all oral malignancies.[1] Metastatic spread to the condyle is even more uncommon, and no statistics concerning the number of instances are present in the literature. It is assumed that the number is probably higher than previously thought because patients who died of their metastasized neoplasm may have had unrealized metastasis in the TMJ. However, the exact incidence has remained elusive. Hirshberg et al.[2] performed the most comprehensive review to date on tumors metastasized to the oral cavity, but this study did not look at particular localizations in the lower jaw like the condyle. Very few studies have dealt with this entity. Therefore, the aim of this literature review, in comparison with the presentation of 3 new cases, was to collect clinical features, including primary symptoms, and regarding the primary tumor over a period of 55 years. Further, we examined whether TMJ metastasis appeared as a first hint of the neoplasm or if this patient group had a previous history of malignancy.

MATERIALS AND METHODS

For the literature review, electronic databases (Medline and Cochrane) were searched using a set of predetermined keywords: "metastasis," "temporomandibular," "TMJ," "condyle," "neoplasm," "malignant," "tumor," and "cancer." The search strategy was initially developed and implemented for PubMed but revised appropriately to suit the other database. A combination of free text terms with boolean operators and truncation were used. No restriction was placed on the year or language of publication.

The citations retrieved from each database were exported into EndNote bibliometric management software. Duplicates and summarized papers without attribution to information of the individual cases were discarded. The titles and abstracts were screened by 2 of the authors who are maxillofacial surgeons. The

[a]Consultant, Department of Craniomaxillofacial and Oral Surgery, University of Zurich, Switzerland.
[b]Vize-director, Department of Craniomaxillofacial and Oral Surgery, University of Zurich, Switzerland.
[c]Medical Student, Department of Craniomaxillofacial and Oral Surgery, University of Zurich, Switzerland.
[d]Professor and Head, Department of Craniomaxillofacial and Oral Surgery, University of Zurich, Switzerland.
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search strategy was devised in consultation with a senior librarian. Hard copies of all potentially relevant articles were retrieved. The results of the literature review were evaluated concerning primary symptoms, site of the primary tumor, and histological type of the metastasis. These parameters were compared with 3 cases of metastasis to the TMJ that were treated in the Department of Craniomaxillofacial and Oral Surgery, University Hospital, Zurich, between January 2007 and June 2009.

RESULTS

Age and gender

In the literature review, accounts were found of 48 patients all together with a slight female predominance (27 female, 19 male, 2 unknown gender) in the 55 years between 1954 and 2008 (Table I). Most metastatic tumors to the TMJ were found in patients in their fifth to seventh decade. The mean age in female patients was 56 years (range, 32 to 78 years) and in male patients 60.2 years (range, 48-74 years). The distribution of age was identical in all locations of primary neoplasm with a slight tendency for higher age (68-74 years) in patients suffering from prostate tumors (Fig. 1).

Clinical presentation

Local pain in the area of the TMJ or surrounding structures was mentioned in 21 of the 48 cases as a main symptom, followed by swelling in 15 cases. TMJ dysfunction was described in 11 cases, trismus in 10, and malocclusion in 2 cases. In only 1 case, a pathological fracture was found (Table II).

Adenocarcinoma was the predominant histology that occurred in TMJ metastases (72.97%) (Fig. 2).

Primary site

The most common site for the primary tumor was the breast (34%), followed by the lung (21%) (Fig. 3). In 28 (58.3%) cases the TMJ metastasis was diagnosed in the presence of known malignant neoplasm.

Primary tumors of the liver (2), stomach (2), and colon (1) were found in male patients only and 59.3% of the female patients with known primary tumor had a primary breast tumor. The most common site in male patients was the prostate (36.8% of the known primary tumors).

Patients

Patient 1. A 73-year-old male farmer was referred to the Department of Craniomaxillofacial and Oral Surgery, University Hospital, Zurich, because of a progressive painful swelling of the left periauricular region 2 months after trauma from a horse's head. He had no history of malignancy, and 3 months previously a bronchoscopy had been performed because of hemoptysis, resulting in a diagnosis of chronic inflammation without malignancy. His family history did not present outstanding problems, and there was no history of malignancy. Physical examination revealed a hard swelling without signs of inflammation from the left preauricular region to the temporal region. On palpation and on mouth opening, the swelling was painful. No pathological lymph nodes were assessed. The mouth opening was limited to 28 mm. Because of the clinical aspect, conventional radiology was skipped and decision for magnetic resonance imaging (MRI) was made, presenting a tumor mass in the left TMJ with involvement of the temporal muscle, and osteolysis of the left TMJ. In frame of staging, an 18F-fluoro-deoxyglucose positron emission tomography (18F-FDG PET) scan (Fig. 4) was performed, revealing active tumors in the lung, right acetabulum, kidneys, and bilateral lymph nodes mediastinal. The metastasis pattern indicated a possible primary tumor in the lung, and a supporting biopsy from the left TMJ region revealed a low-differentiated carcinoma. The patient was referred for palliative chemotherapy to the Department of Oncology and died 4 weeks later.

Patient 2. A 75-year-old female patient was referred, complaining of 3 weeks of progressively worsening pain in the right preauricular region, accompanied by difficulty opening her mouth. She had no history of malignancy. Her medical and family histories were not contributory to this problem.

Physical examination revealed a slight swelling in the right temporomandibular region. Clinically no palpable lymph nodes were detectable in any level of the neck, there was no clicking in the TMJ, and the masseter and temporalis muscles were without pain. Intraorally, the patient had a full denture in the lower and upper jaw; the mouth opening was 30 mm with a deviation to the right side. Laterotrusion to the left was 2 mm and to the right side, 6 mm. Initial radiological examination that included a panoramic film did not reveal any suspicious lesions (Fig. 5). The initial impression was anterior disc luxation without reposition, and the patient received diclofenac, soft food, and physiotherapy. Two weeks later when the pain was unchanged, an MRI scan was performed (Fig. 6), revealing a tumor mass in the right TMJ with a necrotic lymph node in the right parotid gland. A fine needle punction was performed, which revealed an adenocarcinoma. The PET–computed tomography (PET-CT) showed, besides the enhancement of the bronchus of the left upper lung, mediastinal lymph nodes and bone metastases of the left scapula, including a pathological fracture of the left scapula, liver metastases, and a cerebellum metastasis. The patient died 2 weeks later.

Table I. List of all published metastases in the TMJ between 1954 and 2008

Author(s)	*Year*	*Primary tumor*	*Diagnosis*	*History of previous malignancy*	*Sex*	*Age, y*	*Symptoms*
Thoma[3]	1954	Toe	Melanosarcoma	yes	ns	ns	ns
Thoma[3]	1954	Unknown	Adenocarcinoma	no	M	48	TMJ dysfunction
Thoma[3]	1954	Unknown	Transitional cell carcinoma	no	F	51	TMJ dysfunction
Salman & Langel[4]	1954	Uterus	ns	diagnosed 1 month earlier	F	54	Swelling preauricular
Blackwood[5]	1956	Breast	Polygonal cell carcinoma	diagnosed 3 months earlier	F	46	Pain left maxilla / preauricular
Worth[6]	1966	Rectum	Adenocarcinoma	no	M	ns	TMJ dysfunction
Epker et al.[7]	1969	Breast	ns	diagnosed 5 years earlier	F	45	Pain, swelling
Hartman et al.[8]	1973	Breast	Intraductal carcinoma	diagnosed 5 months earlier	F	52	Pain and trismus
Agerberg & Soderstrom[9]	1974	Breast	Ductal carcinoma	diagnosed 2 years earlier	F	46	Preauricular pain
Mace[10]	1978	Breast	Adenocarcinoma	diagnosed 3 years earlier	F	54	Limitation in opening, paresthesia mental
Mizukawa et al.[11]	1980	Breast	Adenocarcinoma	1 year earlier	F	32	TMJ pain
Wolujewicz[12]	1980	Prostate	Adenocarcinoma	no	M	74	Swelling preauricular
Compere et al.[13]	1981	Lung	Squamous cell carcinoma	no	M	48	Swelling preauricular, trismus
Compere et al.[13]	1981	Pancreas	ns	no	F	73	Swelling preauricular, trismus
Compere et al.[13]	1981	Breast	Adenocarcinoma	6 months earlier	F	65	Pain, TMJ dysfunction
Peron et al.[14]	1981	Unknown	Adenocarcinoma	no	M	55	Ear pain, trismus
Peron et al.[14]	1981	Lung	Epidermoid Ca	no	M	74	Pain, swelling
Peron et al.[14]	1981	Unknown	Not clear	time unknown	F	39	Pain TMJ dysfunction
Peacock & Fleet[15]	1982	Lung	Squamous cell carcinoma	no	M	53	Right facial swelling, pain, limitation of jaw movements
Gerlach et al.[16]	1982	Lung	Squamous cell carcinoma	diagnosed 13 months earlier	M	42	Swelling, pain, trismus
Giles & McDonald[17]	1982	Rectum	Adenocarcinoma	diagnosed 6 years earlier	F	55	Pathological fracture, malocclusion
Sailer & Makek[18]	1985	Breast	Adenocarcinoma	Diagnosed 7 years earlier	F	56	Pain
DeBoom et al.[19]	1985	Prostate	Adenocarcinoma	No	M	68	Pathological fracture
Hecker et al.[20]	1985	Unknown	Adenocarcinoma	ns	F	63	Trismus
Owen & Stelling[21]	1985	Lung	Adenocarcinoma	No	M	68	TMJ disorder
Sokolov et al.[22]	1986	Breast	Adenocarcinoma	Diagnosed 6 years earlier	F	52	Pain, trismus
Sokolov et al.[22]	1986	Breast	Adenocarcinoma	Diagnosed 12 years earlier	F	54	Pain, trismus
Thatcher et al.[23]	1986	Prostate	Adenocarcinoma	No	M	68	TMJ disorder
Löwicke & Teuber[24]	1987	Kidney	ns	yes	ns	ns	ns
Cuttino & Steadman[25]	1988	Breast	Adenocarcinoma	Diagnosed 2 years earlier	F	62	TMJ disorder
Webster[26]	1988	Breast	Adenocarcinoma	4 years earlier	F	52	TMJ disorder
Rubin et al.[27]	1989	Unknown	Adenocarcinoma	ns	F	67	TMJ disorder
Rutsatz et al.[28]	1990	Lung	Adenocarcinoma	Yes	F	76	Swelling preauricular
Stavropoulos & Ord[29]	1993	Breast	Adenocarcinoma	7 years earlier diagnosed	F	55	Malocclusion
Johal et al.[30]	1994	Kidney	Malignant clear cell	No	F	65	Pain TMJ
Yoshimura et al.[31]	1997	Liver	no	ns	M	61	Painful swelling
Beck-Mannagetta et al.[32]	1997	Lung	Adenocarcinoma	1 year earlier	F	67	Swelling
Cohen & Rosenheck[33]	1998	Prostate	ns	Yes	M	66	ns
Kolk et al.[34]	2003	Stomach	Adenocarcinoma	4 years earlier	M	51	Preauricular swelling, limited mouth opening
Kaufmann et al.[35]	2005	Lung	Adenocarcinoma	1 months earlier	M	48	Pain
Smolka et al.[36]	2004	Stomach	Adenocarcinoma	Diagnosed 2 years earlier	M	67	Swelling
Mason et al.[37]	2005	Colon	Adenocarcinoma	No	M	73	Swelling
Duker[38]	2006	Breast	ns	Yes	F	60	Pain
Miles et al.[1]	2006	Breast	Adenocarcinoma	Diagnosed 19 years previously	F	78	Pain, trismus
Boniello et al.[39]	2008	Lung	ns	No	M	60	TMJ pain
Menezes et al.[40]	2008	Breast	Adenocarcinoma	No	F	42	Pain, swelling
Schulze[41]	2008	Lung	ns	No	F	52	TMJ dysfunction
Kamatani et al.[42]	2008	Liver	Hepatocellular carcinoma	Diagnosed 3 years earlier	M	59	Preauricular swelling

F, female; *M,* male; *ns,* not specified; *TMJ,* temporomandibular joint.

Patient 3. An 85-year-old male patient had fallen 6 months previously, at which time he was admitted to the hospital. Four weeks later, he felt a malocclusion and was seen by a dental practitioner. A panoramic film showed osteolysis, including a fracture in the left TMJ. Nine years before, the patient had been treated surgically for prostate carcinoma. Clinically, the patient also revealed a hypoesthesia on the left mental region.

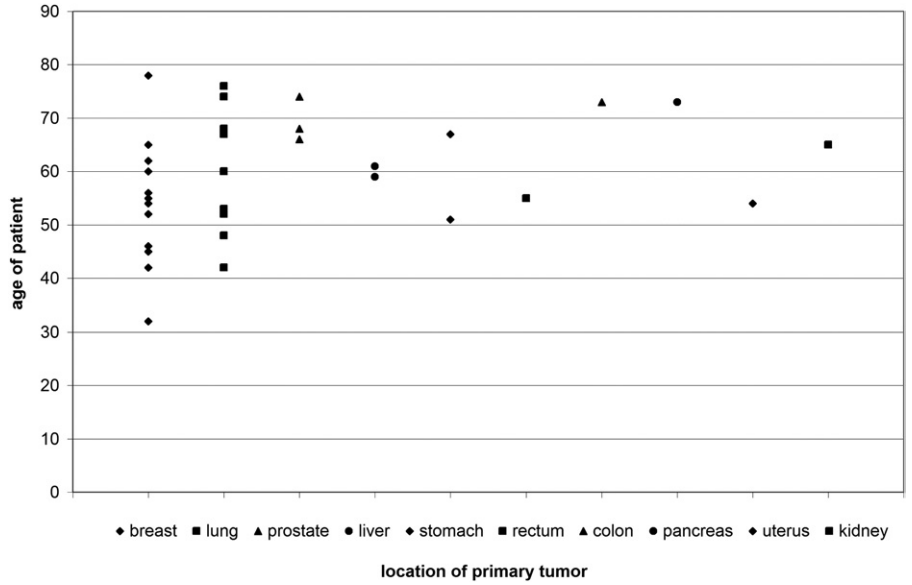

Fig. 1. Distribution of primary malignant tumor.

Table II. Summary of the 3 presented patients

Age	*Sex*	*Primary tumor*	*Diagnosis*	*History of previous malignancy*	*Symptoms*
73	M	Lung	Low differentiated carcinoma	No	Swelling/pain
75	F	Lung	Adenocarcinoma	No	Pain, limited mouth opening
85	M	Thyroid gland?	Unclear	Prostate carcinoma 9 years before	Dysocclusion

F, female; *M,* male.

Mouth opening was 51 mm with deviation to the left side. The PET-CT (Fig. 7) scans revealed an enhanced tumor in the left TMJ with pathological fracture; furthermore, there were 18F-FDG active tumors in the thyroid gland, mediastinum, peribronchial lymph nodes, colon ascendens, mesenterial, and retroperitoneal. The 18F-FDG active tumor pattern indicated a possible primary tumor of the thyroid gland. The patient and the relatives rejected further diagnostics, including a fine-needle aspiration, so that the location of the primary tumor and the histological diagnosis of the TMJ metastasis is still unclear.

DISCUSSION

Metastases involving the oral cavity account for 1% of all neoplasms in the oral cavity,[43] and most oral metastases involve the bone, in particular the mandible, with the most common location being in the molar and premolar regions.[44] The literature review indicates that the incidence of cancer metastasis to the jaw is low, relative to the overall incidence of metastasis to skeletal bone. Solitary metastasis in the TMJ is extremely rare, and in most cases, TMJ involvement is associated with generalized skeletal metastases in the final stage of malignant disease.[36] Metastasis seems to be more common in the corpus part of the mandible. The most comprehensive review to our knowledge, done by Hirshberg et al.,[45] revealed 390 jawbone metastases, also with a slight female predominance (52%). One reason for the lower incidence in the condyle could be the relative lack of marrow in comparison with the corpus part of the mandible. Most of the red marrow is located in the mandibular third molar region, and this is the region most often involved in metastatic disease.[8] Soft tissue involvement was reported for one third of the metastases.[2,43] The reason for the localization of the metastases in the TMJ seems to be hematogenous dissemination of the primary tumor. Different explanations have been discussed in the literature: Henriques[46] assumes that for head and neck involvement, the hematogenous spread is caused by the valveless paravertebral venous plexus, whereas Thoma[3] mentioned the separate blood supply for the TMJ (derived from the circular penetrating branches of the maxillary artery and superficial temporal artery), and yet another reason is seen in the slow circulation.[6]

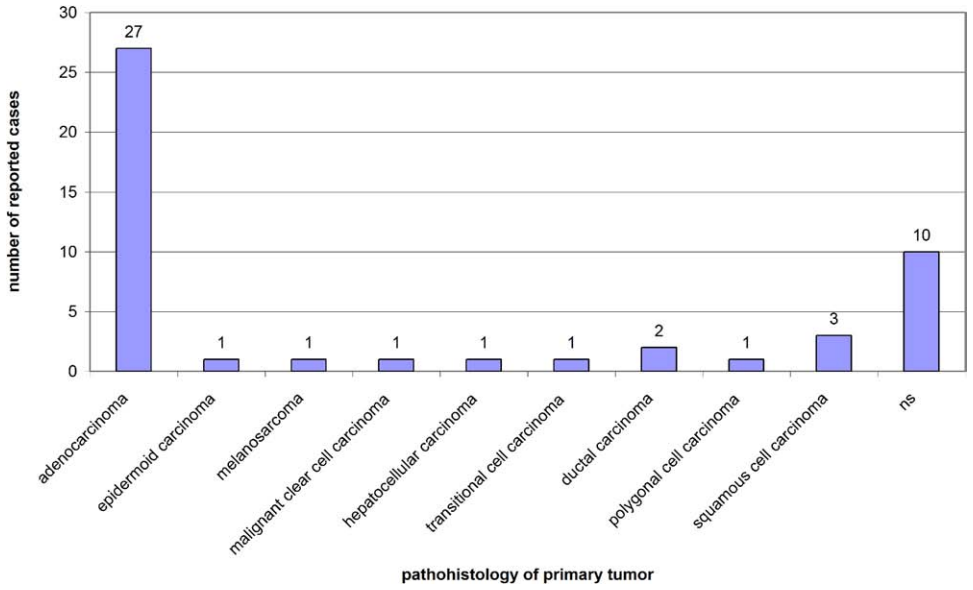

Fig. 2. Distribution of pathohistology of primary tumor.

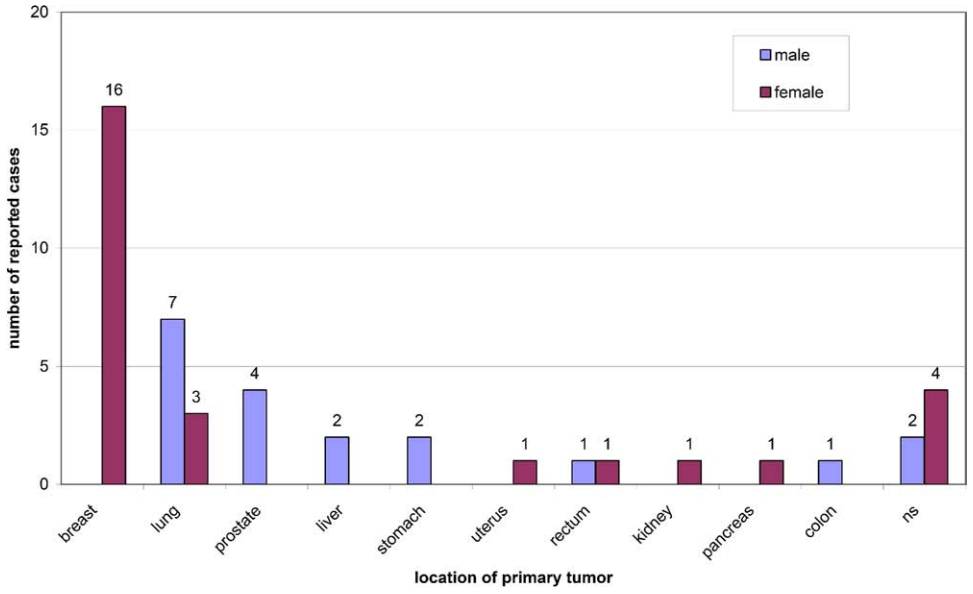

Fig. 3. Distribution of primary tumor site.

Clinical symptoms in only the TMJ as the first clinical manifestation of a distant tumor are extremely rare. Most of the 48 published cases between 1954 and 2008 suffer from a lack of exact data, such as exact information on clinical examination/symptoms or on other information that might have led the attending physician to the rare diagnosis of metastasis lesion in the TMJ. However, these symptoms of metastatic disease to the condyle are variable, but included in the published cases are pain, paresthesia, swelling, limited mouth opening, pathological fracture, and malocclusion. These symptoms usually do not draw attention to a potential underlying malignancy at the time of initial presentation. Pruckmayer et al.[47] presented 9 cases in which mandibular pain was the leading clinical symptom for metastatic disease. This result is supported by our study, followed by swelling as another main symptom. Also in the 3 new cases (Table II), TMJ pain as a

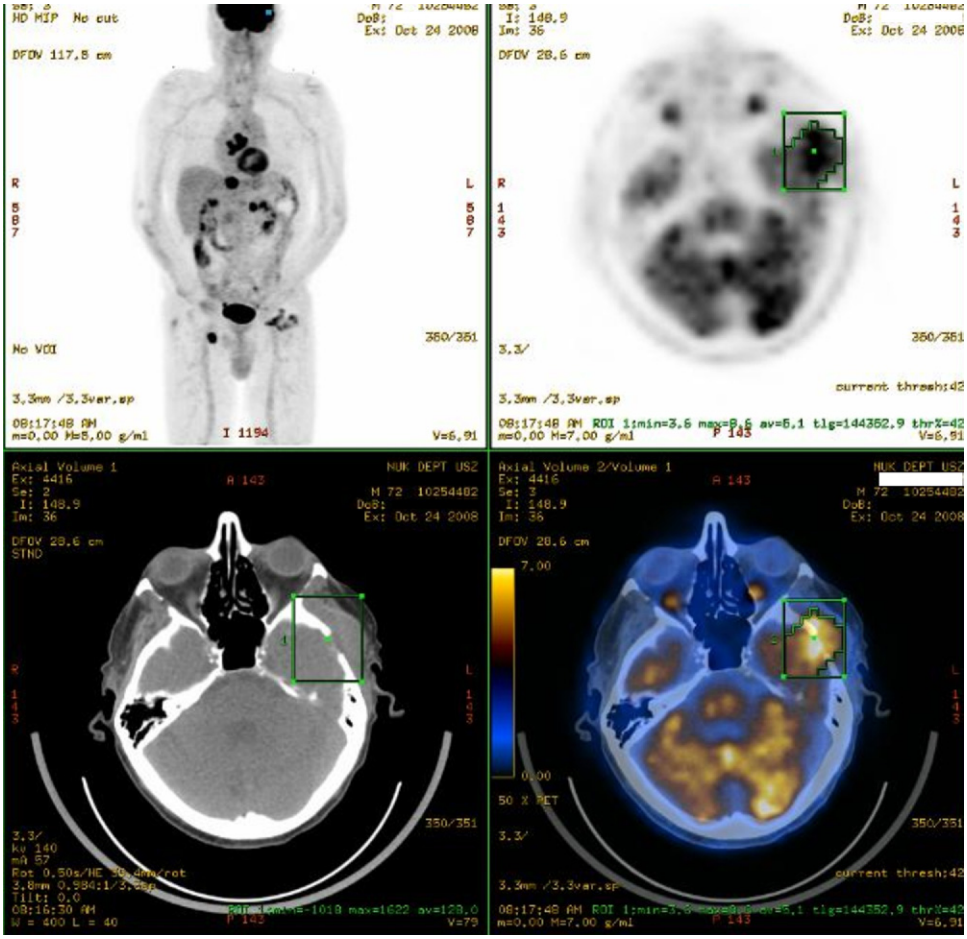

Fig. 4. PET scan presenting the metastases (patient 1).

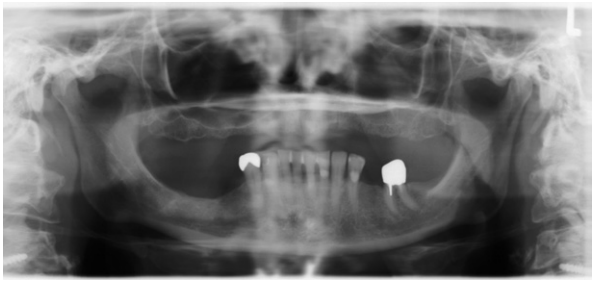

Fig. 5. Panoramic view not revealing any pathology at the right TMJ (patient 2).

first clinical sign was present for metastasis. Special attention should be paid in cases of known malignant neoplasm, in 28 of the studied 48 patients, a previous diagnosis of malignant neoplasm was known.

Concerning the radiographic diagnostics, it should be noted that most of the tumors produce osteolytic-type lesions, but several forms of carcinoma, including prostatic, breast, and lung cancer, are known to form osteoblastic or sclerotic lesions. In general, CT scans can recognize a bony metastatic lesion up to 6 months earlier than a conventional x-ray can.[48] Concerning TMJ, Mostafapour and Futran demonstrated in 6 cases that radiographic studies (CT or MRI) resulted in confirmation that the initial diagnosis was inadequate and suggested neoplastic proliferation.[49] In the presented patient 2, contrary to the panoramic x-ray, MRI scans revealed the neoplasm.

In the 3 cases presented here, besides the use of conventional x-ray at 2 levels (panoramic x-ray and Clementschitsch view), PET-CT was performed to exclude the rare possibility of a condylar primary or secondary malignancy within the differential diagnosis.

Although some authors do not believe there is a gender predilection,[1] a female predominance of 27:19 is striking, as is the younger age of female patients at 56 years. But one reason could be that breast cancer was the most common cancer for females, at 34%. In general, approximately 70% of patients examined in this

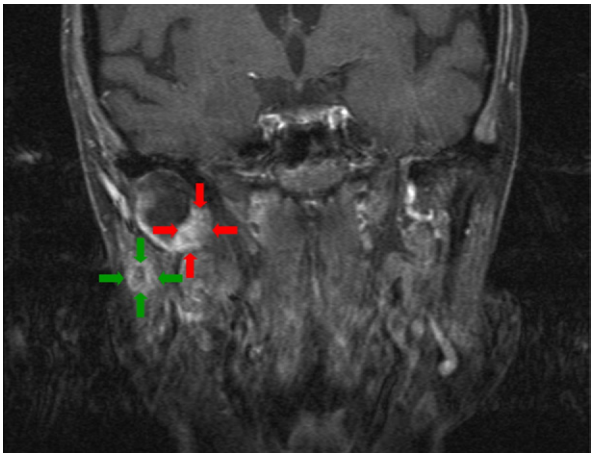

Fig. 6. MRI scan presenting the tumor mass in the right TMJ (*red arrows*) and necrotic lymph node in the parotid gland (*green arrows*) (patient 2).

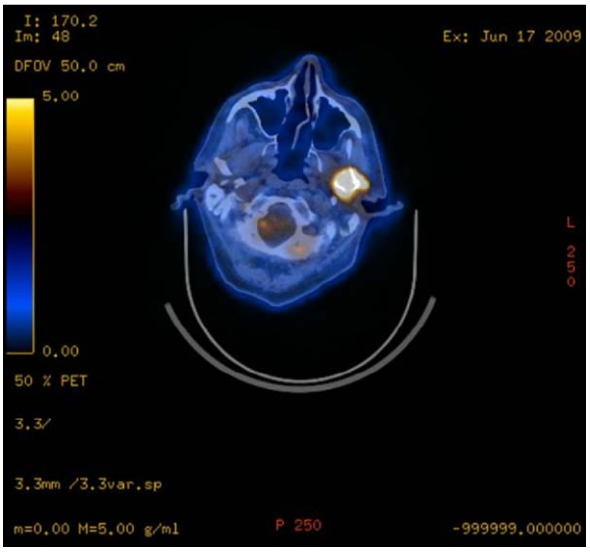

Fig. 7. PET scan of the tumor mass in the left TMJ (patient 3).

study were at least 40 years of age and greater than half were older than 50.[1]

Concerning dissemination patterns, 4 pathways have been discussed:[18] (1) tumor cells from the vena portae region (e.g., from the spleen, stomach, or bowel) via the liver to the TMJ region; (2) tumor cells from the vena cava (all regions except abdominal viscus, i.e., breast, kidney, prostate) via the lung to the TMJ region; (3) primary liver tumors via the lung; and (4) primary lung tumors to the TMJ region.

The treatment of the metastatic lesion depends on the location of the metastasis, the degree of dissemination, and the patient's general condition. Overall survival is reduced in this patient group, but prompt identification of the metastases can offer potential for quality of life with symptomatic relief, as in the presented patients.

The establishment of the exact diagnosis of metastatic lesions in the TMJ can provide a diagnostic challenge, because clinical appearance can mimic inflammation or dysfunction of the TMJ. Age can give a hint because TMJ disorders often occur in younger patients whereas malignancies are quite rare. But on the other hand, TMJ disorders in older patients are not too rare and, as shown in Fig. 1, breast cancer is an example of one of the more common primary lesions for TMJ metastasis even in relatively young patients.

Therefore, clinicians should include the suspicion of cancer in the differential diagnosis, in particular when patients show progressively worsening limitation and increasing pain and, finally, do not respond to treatment appropriately. In these cases and in cases of previous malignancy additional imaging measures like PET-CT should be immediately performed.

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Reprint requests:

Astrid Kruse, MD, DMD
University Hospital Zurich
Department of Craniomaxillofacial
Surgery
Frauenklinikstr. 24
CH-8091 Zurich
Switzerland
astrid.kruse@usz.ch