Int. J. Oral Maxillofac. Surg. 2016; 45: 1545–1550
http://dx.doi.org/10.1016/j.ijom.2016.06.014, available online at http://www.sciencedirect.com

International Journal of Oral & Maxillofacial Surgery

Clinical Paper
TMJ Disorders

Temporomandibular joint involvement in patients with multiple myeloma—a retrospective study☆

W. Abboud[1], R. Yahalom[1], M. Leiba[2], G. Greenberg[3], N. Yarom[1,4]

[1]Department of Oral and Maxillofacial Surgery, Sheba Medical Center, Tel-Hashomer, Israel; [2]Department of Hemato-oncology, Sheba Medical Center, Tel-Hashomer, Israel; [3]Department of Diagnostic Imaging, Sheba Medical Center, Tel-Hashomer, Israel; [4]Department of Oral Pathology and Oral Medicine, School of Dental Medicine, Tel-Aviv University, Tel-Aviv, Israel

W. Abboud, R. Yahalom, M. Leiba, G. Greenberg, N. Yarom: Temporomandibular joint involvement in patients with multiple myeloma—a retrospective study. Int. J. Oral Maxillofac. Surg. 2016; 45: 1545–1550.

Abstract. Multiple myeloma (MM) is a common hematological malignancy that has widespread manifestations in multiple organs, including bones and joints. This retrospective study aimed to evaluate the involvement of the temporomandibular joint (TMJ) in patients with MM. Consecutive subjects with a diagnosis of MM who presented to the oral and maxillofacial surgery clinic for routine evaluation between 2008 and 2014 were identified. Patients who had a computed tomography (CT) scan of the TMJs as part of their MM staging were included in the study. Outcome variables were the presence of TMJ myelomatous changes on CT and the presence of TMJ symptoms. Of the 88 patients included in the study, 28 demonstrated TMJ myelomatous lesions on CT scans and 10 patients complained of TMJ pain or dysfunction. The CT scans of seven of the 10 symptomatic patients demonstrated myelomatous involvement of the TMJ area. Myelomatous involvement of the TMJ is common in MM patients and the majority of lesions are asymptomatic. An MM patient complaining of temporomandibular symptoms is relatively highly likely to having a lesion in the TMJ. Diagnosing the myelomatous lesions in the TMJ is important for accurate hemato-oncologic staging and providing treatment without delay.

Key words: temporomandibular joint; TMJ; temporomandibular disorder; multiple myeloma.

Accepted for publication 22 June 2016
Available online 1 July 2016

Multiple myeloma (MM) is a plasma cell malignancy that has a multicentric origin within bone. The disease accounts for 10–15% of all hematological malignancies and is the second most common among them after non-Hodgkin lymphoma.[1,2] If metastatic diseases were excluded, MM would account for nearly 50% of all malignancies that involve the bone.[3]

MM is characterized by the proliferation of abnormal plasma cells. The clinical features of the disease are due to this proliferation and to the subsequent replacement of normal bone marrow cells together with the resulting production of a paraprotein (M protein) and/or its polypeptide subunits (Bence Jones protein).[4] The manifestations of the disease are characterized by hypercalcemia, renal insufficiency, anemia, bone disease, and

☆ Sheba Medical Center is affiliated to Sackler School of Medicine, Tel-Aviv University, Israel.

0901-5027/01201545 + 06

recurrent infections.[5,6] Because of this tendency for widespread manifestations in multiple organs, MM is of interest to many medical specialists, including oral and maxillofacial surgeons.[7]

The typical radiographic findings in the skeleton are usually of focal osteolytic lesions with or without areas of diffuse osteoporosis.[4] The most commonly involved bones are the spine, skull, pelvis, and ribs. The radiolucent areas of the bone contain neoplastic plasma cell proliferations,[3] and a high tumor burden is associated with greater numbers of abnormal bony changes on imaging.[8]

There are only four research studies reported in the literature that have evaluated the presence of jaw lesions in MM patients.[4,7,9,10] All four utilized plain radiography rather than computed tomography (CT) as the imaging modality. No attempt was made to specify the exact location of the lesions; however, they all noted that the majority appeared in the mandibular body. There are no clinical research studies in the literature that have addressed the involvement of the temporomandibular joint (TMJ) in patients with MM. A search of the English language literature yielded only four case reports describing myelomatous involvement of the TMJ.[11–14] This study was performed to address the topic of TMJ involvement in MM.

The aim of the present study was to evaluate patients with MM both clinically and radiologically for any TMJ involvement, to determine whether there is a correlation between the radiographic findings and the clinical TMJ symptoms, and to examine whether a longer duration of MM disease correlates with a greater number of TMJ lesions and symptoms.

Patients and methods

A retrospective analysis of the medical records and CT scans of patients with MM was performed. They had been evaluated in the outpatient clinic of a department of oral and maxillofacial surgery over a 5.5-year period (December 2008 to May 2014). A total of 115 patients were examined; 88 of them had CT scans that demonstrated the TMJ area and were included in the study. The patients were referred to the clinic from the department of hemato-oncology at the same institute. The purpose of the referral was varied and included regular dental check-ups before the initiation of bisphosphonate therapy, dental complaints, osteonecrosis of the jaws, oral mucosa-related complaints, and temporomandibular pain and dysfunction.

CT scans were obtained as routine periodic head and cervical spine studies in MM patients, and were taken at different time points depending on the hematological status of the patient and the decision of the treating hemato-oncologist. The CT scans were not ordered due to TMJ-related disease and were performed in the axial plane. Reformatted coronal and sagittal oblique images were obtained. The imaging of the patients was evaluated by a radiologist who specializes in head and neck radiology. Any alteration of the TMJ area that was considered to be myelomatous in origin was identified and documented.

The differentiation between a small punched-out lesion of myelomatous origin and a large subchondral cyst as a manifestation of degenerative joint disease was given special attention. A lesion was considered to be a subchondral cyst rather than a myelomatous alteration if it was located adjacent to the articular cortex and accompanied by other degenerative changes, such as flattening of the articular surfaces, erosion of the articular cortex, sclerosis of the subchondral bone, presence of osteophytes, narrowing of the joint cavity, or resorption of the articular surfaces.

The data obtained from the medical records included demographic characteristics, co-morbidities, duration of MM at the time the CT scan was performed, and any complaints of pain or dysfunction in the TMJ area as reported by the patient.

The duration of MM was defined as the length of time that had elapsed since the date of MM diagnosis and the first appearance of any TMJ lesions on CT imaging. The duration of disease for the patients with no TMJ lesions was measured from the time of MM diagnosis to the time the last CT scan was performed.

For statistical analysis, differences between sexes for continuous variables were tested using the *t*-test. Differences between involved and non-involved joints for continuous variables were also tested using the *t*-test. Associations between sex, TMJ involvement, and categorical variables were tested by χ^2 test or Fisher's exact test. The statistical software program used was IBM SPSS Statistics version 23.0 (IBM Corp., Armonk, NY, USA).

The study was approved by the institutional ethics review board, which waived informed consent. The study conformed to the guidelines of the Declaration of Helsinki.

Results

The 88 patients who had CT scans that demonstrated the TMJ area were included in the study. There were 45 males and 43 females, whose mean age was 64.0 ± 8.5 years. The reason for the referral was for a regular dental check-up before the initiation of bisphosphonate therapy in 31 patients, dental complaints in 18 patients, osteonecrosis or suspected osteonecrosis of the jaws in 16 patients, oral mucosa-related complaints in 13 patients, and temporomandibular pain or dysfunction in 10 patients.

The primary outcome variable was the presence or absence of myelomatous alterations in the TMJ area as evidenced on CT scans. The CT scans of 32% of the study population (28 of 88 patients) demonstrated lesions that were compatible with myelomatous changes in one or both TMJs. The CT scans of the remaining 60 patients did not demonstrate any changes in the TMJs that could be attributed to MM. The group of patients with TMJ lesions did not differ from the rest of the study population with regard to sex, age, or duration of MM (Table 1). Myelomatous alterations appeared either as solitary myelomas (focal osteolytic lesions) or in the form of myelomatosis pattern (multiple well-circumscribed lytic bone lesions) (Figs 1 and 2).

The secondary outcome variable was the presence or absence of TMJ symptoms. Ten patients presented with a complaint of pain and/or dysfunction in the TMJ area. The rest of the study population did not report any masticatory dysfunction or temporomandibular pain when presenting to the clinic. The two groups of symptomatic and asymptomatic patients did not differ from the rest of the study population with regard to sex, age, or duration of MM (Table 2).

The clinical signs and symptoms mimicked the most common intra-articular temporomandibular disorders, and the clinical presentation was not suggestive of bone pain secondary to bony lesions. The diagnosis of the MM lesions was made after evaluation of the CT scans. The main complaint reported by the patients was inability or difficulty chewing hard foods. Two patients also reported a subjective feeling of malocclusion. The primary finding on clinical examination was localized tenderness in the pre-auricular area. The tenderness was elicited either by palpation or by passive mouth opening/stretching by the examiner. In addition, three patients suffered from limited mouth opening. The symptoms were on the same side as the lesion (Table 3).

The primary and secondary outcome variables were compared in order to

Table 1. Primary outcome variable: TMJ involvement as evidenced on CT scans.

	TMJ involvement 28 patients (32%)	No TMJ involvement 60 patients (68%)	*P*-value
Age, years, mean ± SD	64.3 ± 8.9	64.0 ± 8.4	0.905
Sex, M/F	16/12	29/31	0.497
Duration of MM, years, mean ± SD	6.7 ± 4.2	6.8 ± 4.9	0.935
TMJ symptoms, *n* (%)	7 (25%)	3 (5%)	0.01

TMJ, temporomandibular joint; CT, computed tomography; SD, standard deviation; M, male; F, female; MM, multiple myeloma.

examine whether there was any correlation between TMJ lesions on imaging and TMJ symptoms. Of the 10 patients with TMJ symptoms, seven (70%) had TMJ myelomatous lesions on imaging, whereas only 21 of the 78 asymptomatic patients (27%) demonstrated TMJ lesions on CT (Table 2). This difference was found to be statistically significant ($P = 0.01$). From a different perspective, seven of the 28 patients (25%) with TMJ lesions on CT had initially presented to the clinic with a complaint of pain and/or dysfunction in the TMJ area, compared to only three of the 60 patients (5%) with no TMJ lesions on CT (Table 1). This difference was also statistically significant ($P = 0.01$).

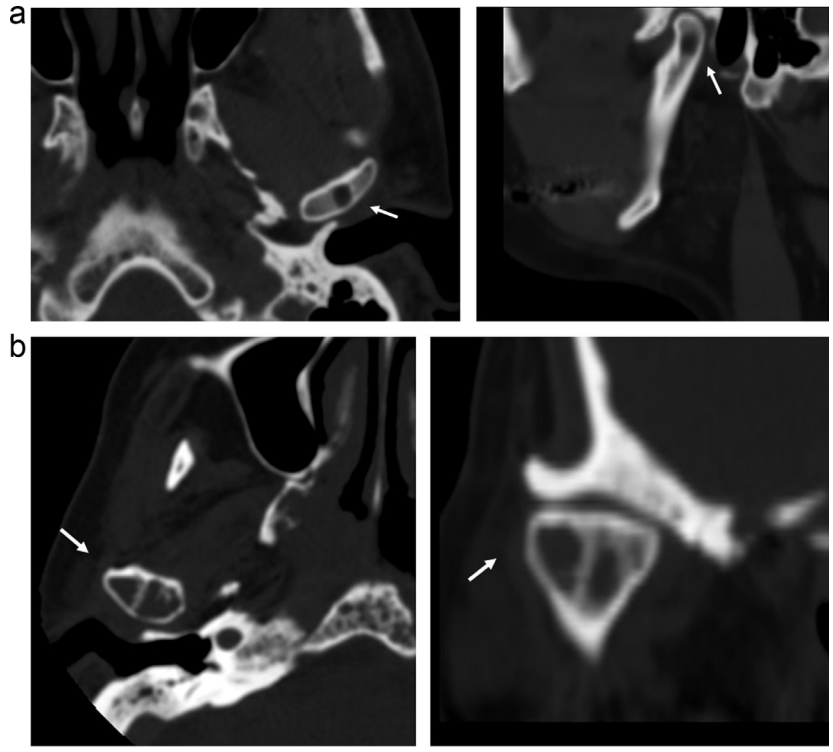

Fig. 1. Examples of focal osteolytic lesions (solitary myelomas) involving the condylar head. (A) Axial and sagittal CT scans demonstrating a focal osteolytic lesion (white arrow) of the left condylar head. Note the intact articular cortex and the normal contour of the articular surfaces. The osteolytic lesion lies at a considerable distance from the cortical surface, as opposed to subchondral cysts which lie subjacent to the cortex. (B) Axial and coronal CT scans demonstrating focal osteolytic lesions (white arrow) occupying most of the right condylar head. Although there is significant narrowing of the joint cavity, the articular cortex of the condyle and fossa are intact with no erosions or osteophytes.

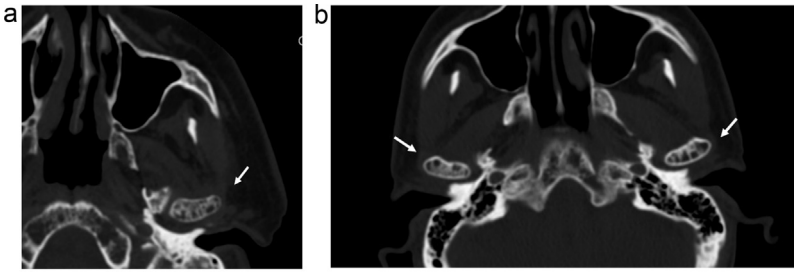

Fig. 2. Examples of the myelomatosis pattern. (A) Axial CT scan demonstrating multiple well-circumscribed lytic bone lesions (white arrow) of the left condylar head. (B) Axial CT scan demonstrating bilateral involvement of condylar heads with multiple well-circumscribed lytic bone lesions (white arrows).

The seven symptomatic patients with evidence of TMJ involvement on imaging were referred to the department of hemato-oncology for further management. A decision was made regarding treatment, depending on the stage of the disease and the systemic condition of the patient, in the form of palliative focal radiotherapy, the addition of bisphosphonates, or chemotherapy. The latter was restarted, continued, or modified. The three symptomatic patients with no evidence of MM involvement were treated by conservative therapy consisting of a soft diet, analgesics, physiotherapy, and occlusal splints, with various degrees of improvement.

None of the lesions reported in this study were biopsied because none appeared as the first sign of MM.

Discussion

The present study evaluated the involvement of the TMJ in patients with MM. It was found that TMJ myelomatous lesions are quite common among patients with MM, with an occurrence of 32%. The majority of patients, however, were asymptomatic, with only 25% (7/28) of those with radiographically confirmed involvement of the TMJ having presented with signs and symptoms of TMJ pain and dysfunction. On the other hand, the results clearly showed that an MM patient who complained of temporomandibular symptoms had an increased likelihood (70%) of having a myelomatous involvement of the TMJ area.

There are four case reports published in the English language literature that have documented the occurrence of myelomatous lesions in the TMJ area.[11–14] All four reported symptomatic patients with TMJ pain and dysfunction that mimicked the more commonly encountered intra-articular disorders. In addition, there are

Table 2. Secondary outcome variable: TMJ symptoms on clinical assessment.

	Symptomatic 10 patients (11%)	Asymptomatic 78 patients (89%)	*P*-value
Age, years, mean ± SD	64.5 ± 8.6	63.9 ± 8.4	0.832
Sex, M/F	4/6	41/37	0.517
Duration of MM, years, mean ± SD	6.8 ± 4.7	6.8 ± 4.5	0.99
TMJ lesions on CT, *n* (%)	7 (70%)	21 (27%)	0.01

TMJ, temporomandibular joint; SD, standard deviation; M, male; F, female; MM, multiple myeloma; CT, computed tomography.

four research articles on jaw lesions in general occurring concomitantly with MM.[4,7,9,10] These studies used plain X-rays and not CT scans for imaging studies. The reported incidence of jaw myelomatous lesions ranged from 5% to 15%, a much lower proportion than that found in the current study. Moreover, although no attempt was made to specify the exact location of the lesions, all four articles noted that almost all the lesions occurred in the mandible, and that the majority appeared in the mandibular body area. One reason for the lower incidence of lesions in general, and the lower incidence in the TMJ area in particular, may be at least partly related to the inadequate thoroughness of the radiographic survey used in the previously published studies, i.e., using less sensitive X-rays for diagnosing pathologies and alterations in lieu of CT studies. The latter drawback is further emphasized in the TMJ area.

A longer duration of MM disease did not correlate with more myelomatous alterations in the TMJ area, as one may intuitively assume. This is somewhat different from what is known about other areas in the skeleton (e.g., spine, skull, pelvis, and ribs), where a longer duration of the disease manifests with more bony involvement and subsequently with more symptoms.[8,15–18] This could be explained by the fact that the present study was retrospective. The CT scans were not performed at regular intervals, but rather on an individual basis depending on the patient's hematological status, which prevents the predictable outcome variable 'duration of MM' from being fully reliable.

Oral and maxillofacial surgeons are more acquainted with pain associated with osteonecrosis of the jaw, the etiology of which is bisphosphonate therapy, not MM by itself. The present study dealt with MM pain associated with bone destruction, evidenced as osteolytic lesions or areas of osteoporosis. While the treatment of osteonecrosis includes discontinuation of the bisphosphonates (in addition to antibiotics, mouth rinses, and surgery ranging from limited debridement to resections),[19–21] the treatment of the osteolytic painful bony lesions includes the administration of bisphosphonates (in addition to palliative radiotherapy and the usual pharmaco-oncologic therapies and bone marrow transplantation).[2,16,22,23]

This study has a number of strengths: the uniformity of radiological interpretation, the relatively large cohort, and the availability of the full medical records from the department of hemato-oncology.

The lack of histopathological confirmation raises a risk of decreased specificity in diagnosing the osteolytic bone lesions. This was overcome by having the CT scans evaluated by a radiologist who is a specialist in head and neck radiology and is experienced in both TMJ pathology and myelomatous lesions. Only lesions that had a definite, characteristic myelomatous appearance were included in this group, and strict criteria were used to differentiate degenerative subchondral cysts from MM osteolytic lesions. The presence of any degenerative changes (e.g., flattening of the articular surfaces, erosion of the articular cortex, sclerosis of the subchondral bone, presence of osteophytes, narrowing of the joint cavity, or resorption of the articular surfaces) excluded the diagnosis of a myelomatous lesion. The other differential diagnoses of such localized hypodense lesions could be benign bone tumors and fibro-osseous lesions, which are so rare in the condylar area that the chances of increasing the false-positive results and causing over-diagnosis are very low.

Ten of the 88 patients (11%) included in the study cohort presented to the oral and

Table 3. Patients with temporomandibular symptoms.

	Age, years	Sex	Duration of disease, years	Side of lesion	Temporomandibular signs and symptoms	Side of symptoms
1	67	F	12	R	Pre-auricular tenderness Subjective feeling of malocclusion	R
2	57	M	11	L	Pre-auricular tenderness Subjective feeling of malocclusion	L
3	42	F	3	L	Pre-auricular tenderness Limited mouth opening 35 mm Avoiding hard foods	L
4	61	M	3.5	R	Pre-auricular tenderness Limited mouth opening 30 mm Avoiding hard foods	R
5	56	M	3	L	Pre-auricular tenderness Avoiding hard foods	L
6	68.5	F	1	R and L	Pre-auricular tenderness Avoiding hard foods	R and L
7	83	F	3	R	Pre-auricular tenderness Limited mouth opening 25 mm	R
8	59	F	6	–	Pre-auricular tenderness Avoiding hard foods	L
9	85	M	1	–	Avoiding hard foods Pre-auricular pain upon yawning	R and L
10	67	F	6	–	Avoiding hard foods	R

F, female; M, male; R, right; L, left.

maxillofacial surgery clinic with a complaint of temporomandibular pain or dysfunction. This is a significantly higher proportion of TMJ-related complaints than is seen in the general population. Several large-scale studies have shown that approximately 2% of the general population seeks treatment for a TMJ-related symptom.[24–26] The high percentage of temporomandibular complaints encountered in the present study was correlated to the myelomatous involvement of the TMJ area. Bone destruction causing osteolytic lesions and bone pain is a well-defined feature of MM.[27] As the myeloma burden increases, an imbalance between osteoblast and osteoclast activities ensues, with suppression of bone formation by osteoblasts and uncoupled activation of osteoclasts.[28–30] In fact, bone pain represents one of the four classical symptoms of MM (the others being anemia, hypercalcemia, and renal failure), and approximately 60% of patients will present with bone pain at the time of diagnosis.[31] The pain is usually localized to sites of osteopenia or lytic bone lesions. Bisphosphonates can palliate pain and prevent bone-related complications; however, large osteolytic lesions often necessitate local radiotherapy.[32,33] As much as half of MM patients are expected to receive palliative radiation therapy over the course of their illness.[23,27] Seven of the 10 symptomatic patients in the present study were found to have MM lesions in the TMJ. From a different perspective, seven of the 28 patients with TMJ lesions on CT had initially presented to the clinic with a temporomandibular complaint, compared to only three of the 60 patients with no TMJ lesions on CT. This difference was statistically significant. Combining these findings with the high rate of temporomandibular complaints encountered in the present study (11%), the occurrence of temporomandibular symptoms on the same side as the lesions, and the fact that CT interpretation narrowed down the differential diagnosis, one can confidently conclude that at least the majority of TMJ pain in the present study was MM-related.

Of importance was the fact that history and clinical examination did not raise a suspicion of MM involvement of the affected joint. Only after evaluating the CT scans were the lesions detected. No specific signs and symptoms related to MM bony lesions in the TMJ were found, and the patients could easily have been misdiagnosed as suffering from intra-articular derangement or degeneration disorders. In addition, the four previously published case reports dealing with myelomatous TMJ involvement concluded that the clinical findings were non-specific and that proper imaging was essential for lesion detection and diagnosis.[11–14] This is further emphasized by the recommendation of the European Society for Medical Oncology (ESMO) regarding MM, that proper imaging should be performed to detect new bone lesions in any area of the skeleton presenting with bone pain.[16]

The oral and maxillofacial surgeon should be aware that the clinical signs and symptoms of temporomandibular involvement associated with MM are non-specific, and the establishment of an accurate diagnosis without appropriate imaging can be a diagnostic challenge.[34,35] Early diagnosis of these lesions will prevent unnecessary and unsuitable treatments. The appearance of new bone lesions, as in any other area of the skeleton, has implications for diagnosis, staging, and therapy. After the detection of TMJ lesions, the patient should be referred to the department of hemato-oncology. Depending on the stage of the disease and the systemic condition of the patient, a consideration is made by the hemato-oncologist regarding oncologic staging and treatment. Early referral will ensure that the patient receives the appropriate care. Symptomatic patients who do not demonstrate MM involvement of the TMJ should be treated with the appropriate temporomandibular therapies and followed up closely.

The clinician should practice a high level of suspicion when examining an MM patient who complains of temporomandibular symptoms, because a relatively high proportion of patients (70% in this study) will have myelomatous lesions in the TMJ area. It is recommended that the patient's clinical evaluation be supplemented with a CT scan of that region, and that the patient be referred immediately to the treating hemato-oncologist in the case of positive radiographic findings.

Funding

None.

Competing interests

None.

Ethical approval

Approval for the analysis of data was confirmed by the Institutional Review Board of Sheba Medical Center (ethical approval number 2486-15-SMC).

Patient consent

Not required.

References

1. Beider K, Bitner H, Leiba M, Gutwein O, Koren-Michowitz M, Ostrovsky O, et al. Multiple myeloma cells recruit tumor-supportive macrophages through the CXCR4/CXCL12 axis and promote their polarization toward the M2 phenotype. *Oncotarget* 2014;**5**: 11283–96.
2. Leiba M, Kedmi M, Duek A, Freidman T, Weiss M, Leiba R, et al. Bortezomib–cyclophosphamide–dexamethasone (VCD) versus bortezomib–thalidomide–dexamethasone (VTD)-based regimens as induction therapies in newly diagnosed transplant eligible patients with multiple myeloma: a meta-analysis. *Br J Haematol* 2014;**166**:702–10. http://dx.doi.org/10.1111/bjh.12946.
3. Neville B, Damm D, Allen C, Bouqout J. Hematologic disorders. In: Neville B, Damm D, Allen C, Bouqout J, editors. *Oral and maxillofacial pathology*. third ed. St. Louis: Saunders Elsevier; 2009 . p. 604–6. http://dx.doi.org/10.1016/B978-1-4557-0082-0.00020-X.
4. Epstein JB, Voss NJ, Stevenson-Moore P. Maxillofacial manifestations of multiple myeloma. *Oral Surg Oral Med Oral Pathol* 1984;**57**:267–71. http://dx.doi.org/10.1016/0030-4220(84)90182-8.
5. Mesguich C, Fardanesh R, Tanenbaum L, Chari A, Jagannath S, Kostakoglu L. State of the art imaging of multiple myeloma: comparative review of FDG PET/CT imaging in various clinical settings. *Eur J Radiol* 2014;**83**:2203–23. http://dx.doi.org/10.1016/j.ejrad.2014.09.012.
6. Leiba M, Jakubikova J, Klippel S, Mitsiades CS, Hideshima T, Tai YT, et al. Halofuginone inhibits multiple myeloma growth in vitro and in vivo and enhances cytotoxicity of conventional and novel agents. *Br J Haematol* 2012;**157**:718–31. http://dx.doi.org/10.1111/j. 1365-2141.2012.09120.x.
7. Witt C, Borges AC, Klein K, Neumann HJ. Radiographic manifestations of multiple myeloma in the mandible: a retrospective study of 77 patients. *J Oral Maxillofac Surg* 1997;**55**:450–3. discussion 454–5.
8. Dimopoulos MA, Hillengass J, Usmani S, Zamagni E, Lentzsch S, Davies FE, et al. Role of magnetic resonance imaging in the management of patients with multiple myeloma: a consensus statement. *J Clin Oncol* 2015;**33**:657–64. http://dx.doi.org/10.1200/JCO.2014.57.9961.
9. Lambertenghi-Deliliers G, Bruno E, Cortelezzi A, Fumagalli L, Morosini A. Incidence of jaw lesions in 193 patients with multiple myeloma. *Oral Surg Oral Med Oral Pathol* 1988;**65**:533–7.
10. Bruce KW, Royer RQ. Multiple myeloma occurring in the jaws; a study of 17 cases.

Oral Surg Oral Med Oral Pathol 1953;**6**:729–44.
11. Cohen B, Meyers H. Multiple myeloma involving the temporomandibular joint. *Oral Surg Oral Med Oral Pathol* 1956;**9**:1274–80.
12. Halpern KL, Calhoun NR. Pathological fracture of mandibular condyloid process associated with multiple myeloma: report of case. *J Oral Surg* 1978;**36**:560–1.
13. González J, Elizondo J, Trull JM, De Torres I. Plasma-cell tumours of the condyle. *Br J Oral Maxillofac Surg* 1991;**29**:274–6. http://dx.doi.org/10.1016/0266-4356(91)90197-D.
14. Jagger RG, Helkimo M, Carlsson GE. Multiple myeloma involving the temporomandibular joint: report of case. *J Oral Surg* 1978;**36**:557–9.
15. Dimopoulos M, Terpos E, Comenzo RL, Tosi P, Beksac M, Sezer O, et al. IMWG International myeloma working group consensus statement and guidelines regarding the current role of imaging techniques in the diagnosis and monitoring of multiple myeloma. *Leukemia* 2009;**23**:1545–56. http://dx.doi.org/10.1038/leu.2009.89.
16. Harousseau JL, Dreyling M. Multiple myeloma: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. *Ann Oncol* 2010;**21**(Suppl. 5):v155–7. http://dx.doi.org/10.1093/annonc/mdq178.
17. Hillengass J, Fechtner K, Weber MA, Bäuerle T, Ayyaz S, Heiss C, et al. Prognostic significance of focal lesions in whole-body magnetic resonance imaging in patients with asymptomatic multiple myeloma. *J Clin Oncol* 2010;**28**:1606–10. http://dx.doi.org/10.1200/JCO.2009.25.5356.
18. Song IC, Kim JN, Choi YS, Ryu H, Lee MW, Lee HJ, et al. Diagnostic and prognostic implications of spine magnetic resonance imaging at diagnosis in patients with multiple myeloma. *Cancer Res Treat* 2015;**47**:465–72.
19. Khan AA, Sándor GK, Dore E, Morrison AD, Alsahli M, Amin F, et al. Canadian consensus practice guidelines for bisphosphonate associated osteonecrosis of the jaw. *J Rheumatol* 2008;**35**:1391–7.
20. Jabbour Z, El-Hakim M, Mesbah-Ardakani P, Henderson JE, Albuquerque Jr R. The outcomes of conservative and surgical treatment of stage 2 bisphosphonate-related osteonecrosis of the jaws: a case series. *Int J Oral Maxillofac Surg* 2012;**41**:1404–9.
21. Fliefel R, Troltzsch M, Kuhnisch J, Ehrenfeld M, Otto S. Treatment strategies and outcomes of bisphosphonate-related osteonecrosis of the jaw (BRONJ) with characterization of patients: a systematic review. *Int J Oral Maxillofac Surg* 2015;**44**:568–85. http://dx.doi.org/10.1016/j.ijom.2015.01.026.
22. Krstevska S, Sotirova T, Balkanov T, Genadieva-Stavric S. Treatment approach of non-transplant patients with multiple myeloma. *Mater Sociomed* 2014;**26**:348–51. http://dx.doi.org/10.5455/msm.2014.26. 348-351.
23. Featherstone C, Delaney G, Jacob S, Barton M. Estimating the optimal utilization rates of radiotherapy for hematologic malignancies from a review of the evidence: part II—leukemia and myeloma. *Cancer* 2005;**103**:393–401.
24. De Kanter RJ, Käyser AF, Battistuzzi PG, Truin GJ, Van't Hof MA. Demand and need for treatment of craniomandibular dysfunction in the Dutch adult population. *J Dent Res* 1992;**71**:1607–12.
25. Goulet JP, Lavigne GJ, Lund JP. Jaw pain prevalence among French-speaking Canadians in Québec and related symptoms of temporomandibular disorders. *J Dent Res* 1995;**74**:1738–44.
26. Fletcher MC, Piecuch JF, Lieblich SE. Anatomy and pathophysiology of the temporomandibular joint. In: Miloro M, Ghali GE, Larsen P, Waite P, editors. *Peterson's principles of oral and maxillofacial surgery*. second ed. London: BC Decker; 2004. p. 933–48. http://dx.doi.org/10.1007/978-1-60761-459-3.
27. O'Donnell E, Cottini F, Raje N, Anderson K. Myeloma. In: Kaushansky K, Lichtman MA, Prchal JT, Levi MM, Press OW, Burns LJ, Caligiuri MA, editors. *Williams hematology*. 9th ed. McGraw-Hill Medical; 2015. p. 1709–60.
28. Bataille R, Chappard D, Marcelli C, Dessauw P, Baldet P, Sany J, et al. Recruitment of new osteoblasts and osteoclasts is the earliest critical event in the pathogenesis of human multiple myeloma. *J Clin Invest* 1991;**88**:62–6.
29. Taube T, Beneton MN, McCloskey EV, Rogers S, Greaves M, Kanis JA. Abnormal bone remodelling in patients with myelomatosis and normal biochemical indices of bone resorption. *Eur J Haematol* 1992;**49**:192–8.
30. Raje N, Roodman GD. Advances in the biology and treatment of bone disease in multiple myeloma. *Clin Cancer Res* 2011;**17**:1278–86.
31. Kyle RA, Gertz MA, Witzig TE, Lust JA, Lacy MQ, Dispenzieri A, et al. Review of 1027 patients with newly diagnosed multiple myeloma. *Mayo Clin Proc* 2003;**78**:21–33.
32. 8 Gy single fraction radiotherapy for the treatment of metastatic skeletal pain: randomised comparison with a multifraction schedule over 12 months of patient follow-up. Bone Pain Trial Working Party. *Radiother Oncol* 1999;**52**:111–21.
33. Wernicke AG, Sabbas A, Kulidzhanov F, Shamis M, Golster Y, Niesvizky R, et al. A single-dose conformal delivery of radiotherapy following osteoplasty: a novel approach to treatment of osteolytic metastasis in the setting of multiple myeloma. *HSS J* 2012;**8**:169–74. http://dx.doi.org/10.1007/s11420-011-9213-4.
34. Abboud W, Givol N, Yahalom R. Arthroscopic lysis and lavage for internal derangement of the temporomandibular joint. *Ann Maxillofac Surg* 2015;**5**:158–62. http://dx.doi.org/10.1053/joms.2001.21002.
35. Abboud W, Yahalom R, Givol N. Treatment of intermittent locking of the jaw in Wilkes stage II derangement by arthroscopic lysis and lavage. *J Oral Maxillofac Surg* 2015;**73**:1466–72. http://dx.doi.org/10.1016/j.joms.2015.02.027.

Address:
Waseem Abboud
PO Box 111
Shfar-Am 20200
Israel
Tel: +972 526657050;
Fax: +972 49502322
E-mail: waseem.abboud@gmail.com