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The Maxillofacial Region May Have the First Manifestation of Multiple Myeloma

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Abstract

Objective: this article aims to identify, through an integrative review, the primary manifestations of Multiple myeloma (MM) in the maxillofacial complex. **Material and Methods:** this integrative review was performed using the PubMed and Scopus databases, and included articles that reported the first manifestations of MM in the maxillofacial region. The search was performed using the descriptors "oral manifestation" and "multiple myeloma". **Results:** this integrative review describes 28 cases of MM reported in the literature where the first manifestations were in the maxillofacial region, emphasizing the importance of a complete oral clinical exam due to the highly variable clinical manifestations and radiographic or other imaging features, since multiple myeloma can be diagnosed at earlier stages. **Conclusion:** thus, it is essential that the healthcare professional has knowledge for the correct diagnosis and agility in this urgent treatment, in order to preserve the dental organ in the oral cavity for a longer time.

Keywords: Multiple myeloma; Oral manifestations; Clinical diagnosis; Maxillofacial pathology; Jaw.

Introduction

Multiple myeloma (MM) is a hematological neoplasm characterized by an abnormal proliferation of plasma cells originating from the bone marrow and the atypical production of monoclonal immunoglobulins. Plasma cells are the main cells responsible for this dyscrasia.[1-4] MM corresponds to 10% of hematological tumors, and 1% of all tumors in general.[3,5] It is most commonly diagnosed in patients aged 60 years and over,[6,7] with a male predominance of 3:2 and a black racial predominance of 2:1.[3,8-10]

The involvement of the maxillofacial bones occurs in approximately 14% of patients with MM,[4,5] with the mandible being more frequently affected than the maxilla.[1,5,11] Oral manifestations of MM include swelling, gingival bleeding, dental mobility, hyperplasias,[3,6] pathological fractures, and paresthesia. The diagnosis of MM is based on a combination of clinical, laboratory, anatomopathological, and imaging presentations.[3,12]

Although late oral maxillofacial involvement is common in cases of MM,[6,11] primary manifestations in this region are rare, and correspond to only 12–15% of the cases.[2,5,7,11,13-15] Given the lack of published studies, we considered it important to perform an integrative review of MM cases in which the diagnosis was based exclusively on oral features. Moreover, we also wanted to emphasize to healthcare professionals, the importance of paying attention to the first signs and symptoms of MM in the maxillofacial region.[6]

This article aims to identify, through an integrative review, the primary manifestations of MM in the maxillofacial complex.

Material and Methods

This integrative review was performed using the PubMed and Scopus databases, and included articles that reported the first manifestations of MM in the maxillofacial region. The research was conducted in April 2018. Articles from the previous 30 years were selected, which included case reports and a case series published in English with their full text available on the internet. The search was performed using the descriptors "oral manifestation" and "multiple myeloma".

A single researcher collected the articles through the following steps: I) duplicate articles were excluded; II) each title was read; III) each summary was read; IV) checking the availability of the article; V) the language in which each article was written was checked; and VI) the final inclusion was made after reading each article in its entirety.

The data were collected and organized using Microsoft Excel for Windows 10. The following variables were considered: year, country of publication, age, sex, site, extraoral signs, intraoral signs, symptoms, imaging findings, histopathological findings, treatment, and outcome.

Results

Out of the 237 articles found in the databases, 70 were duplicates. Further, 74 and 51 articles were excluded after reading the title and abstract, respectively. The full text of 38 of the 42 remaining articles was available. We selected 23 articles after applying our inclusion and exclusion criteria, which included 26 reported cases (Table 1). Figure 1 shows the flowchart for retrieving the articles.

Table 1. Demographic, diagnostic and treatment data collected of primary manifestations of multiple myeloma in maxillofacial complex over the literature.

Study (Country)	Age (Sex)	Location	Extraoral Signs	Intraoral Signs	Symptoms	Imaging Exam	Imaging Findings	Histopathological Findings	Ihc	Treatment	Outcome
Senn JS *et al*. (1984 - Canada)[16]	30 (M)	Mand (R and L)	Swelling	Soft-tissue lesion	Pain / Paresthesia / Facial palsy / Tongue deviation	PERI + PAN + CT	Apical radiolucencies	Plasma cells with pleomorphism	-	MELP + PRED + RT + CP + DOXO + CARM	Death (general bleeding)
Gonzáles J. *et al*. (1991 - Spain) - Case 1[17]	70 (M)	Mand (R)	Mouth opening limitation	Normal	Pain	PAN	Expansive osteolytic lesion	Plasma cell tummor	-	CHT NS + RT	Death (2-year follow-up)
Gonzáles J. *et al*. (1991 - Spain) - Case 2[17]	41 (F)	Mand (R)	Asymmetry / Swelling / Sounds in TMJ / Mouth opening limitation	NR	Pain	PAN	Osteolytic lesion	Proliferation of plasma cells (FNAC)	-	CHT NS	NR
Lee S-H. *et al*. (1996 - Taiwan) - Case 1[18]	55 (M)	Mand (R and L)	Swelling	Paresthesia / Mass / Ulcer	Pain / Paresthesia	PAN + LAT	Extensive radiolucent lesion / Multiple "punched out" lesions	Diffuse plasma cell aggregation with eccentric nuclei	-	MELP + PRED + RT	New lesion in Max (10-month follow-up) / Death from sepsis
Lee S-H. *et al*. (1996 - Taiwan) - Case 2[18]	53 (F)	Mand (L)	NR	Mass / Swelling / Mand expansion	Pain	PAN + PA	Multiple "punched out" lesions / Root resorption	Diffuse infiltration of plasma cells with eccentric nuclei	-	VINC + DOXO + DEXA + MELP + PRED + RT	Progression of the disease (multiple bone fractures)
Reboiras López MD. *et al*. (2001 - Spain)[19]	60 (F)	Mand (R)	NR	Dental mobility / Sensitivity to percussion test	Paresthesia	PAN + CT + NMR	Expansive radiolucent lesion / Cortical bone rupture	Numerous plasma cells with eccentric nuclei (FNAC)	-	MELP	NR
Mozaffari E. *et al*. (2002 - USA)[20]	55 (M)	Mand (L)	Swelling	Swelling / Erythematous mucosa / Signs of hemorrhage	NR	PAN + PA	Extensive radiolucent lesion / Ill-defined borders / Multiple radiolucent lesions	NR	-	NR	Lost to follow-up
Sugawara Y. *et al*. (2003 - Japan)[21]	62 (F)	Mand (L)	Swelling	Swelling / Non-vital tooth	Paresthesia	PERI + PAN + PA + CT + NMR	Extensive and expansive osteolytic lesion / Cortical bone rupture / Multiple "punched out" lesions	Diffuse proliferation of atypical plasmacytoid cells	-	NR	NR
Pinto LS. *et al*. (2007 - Brazil)[8]	65 (F)	Max (L)	NR	Swelling	Pain	PAN + PERI + LAT	Diffuse radiolucency	Sheets of atypical plasma cells	Positive for EMA e kappa chain	CP + PRED	Regression of lesion / Death (9-month follow-up)
Segundo AVL. *et al*. (2008 - Brazil)[7]	81 (M)	Mand (symphysis)	Increased volume	Normal mucosa	Paresthesia	LAT + PAN + CT	Extensive osteolytic lesion / Ill-defined borders / Cortical bone rupture / Multiple radiolucent lesions	Plasmacytoid cells with eccentric nuclei	-	NR	Death (9-month follow-up)

Amirchaghmaghi M. *et al*. (2010 - Iran)[22]	58 (F)	Mand (R)	Swelling	Swelling / Ulcer	Pain	PAN + SKULL	Multiple "punched out" lesions	Malignant plasma cells with eccentric nucleus	Positive for kappa chain	MELP + PAMI (BP) + PRED + RT	Under medical care (2-year follow-up)
Santos PSS. *et al*. (2012 - Brazil)[23]	73 (M)	Mand (R)	NR	Mass	Pain	PAN + CT	"Punched out" lesion	Proliferation of plasmacytoid cells	Positive for kappa chain	RT (3600cGy) + BORTE + MELP + PRED + DEXA	Death (6-month follow-up)
Jain S. *et al*. (2013 - India)[14]	58 (M)	Generalized gingival hyperplasia	NR	Gingival enlargement / Spontaneous bleeding / Purulent discharge / Dental mobility	Asymptomatic	PAN + SKULL	Severe bone loss	Sheets of plasma cells	-	THALI	Normal gingiva after CHT
Vinayachandran D; Sankarapandian S. (2013 - India)[24]	72 (M)	Mand (R and L)	Swelling	Dental mobility / Swelling	Asymptomatic	OCCL + PAN + CT	Multilocular radiolucent lesion / Dental displacement / Root resorption	Cellular neoplasm composed of plasma cells	Positive for CD138 and lambda chain	CHT NS	NR
Dengra S. *et al*. (2014 - India)[6]	56 (M)	Mand (R)	Increase of volume	Gingival bleeding / Cortical plate expansion / Mass / Bleeding on provocation	Pain / Paresthesia	PAN + LAT	Extensive osteolytic lesion / Ill-defined borders / Cortical bone rupture	Plasmacytoid cells with eccentric nuclei	Positive for CD138 lambda chain	NR	Death
Pushpanshu, K. *et al*. (2014 - India)[25]	67 (M)	Mand (R)	Swelling	Mass / Ulcer	Pain / Difficulty to feed	PAN + CT	Extensive osteolytic lesion / Multiple "punched out" lesions	Sheets of plasma cells with nuclear pleomorphism	-	RT + BORTE + MELP + PRED	NR
Romano A. *et al*. (2014 - Italy) - Case A[1]	72 (M)	Mand (L)	Normal	Mass / Ulcer	Pain / Difficulty to feed	PAN + FDG-PET + NMR	PET-CT poorly + in Mand	Poorly differentiated plasma cell neoplasm	Positive for CD138, CD38, EMA, vimentine and CD79a	BORTE + DEXA + THALI	Death (pneumonia)
Romano A. *et al*. (2014 - Italy) - Case B[1]	63 (M)	Max (L)	Swelling	Mass / Normal mucosa	NR	CT + NMR	Osteolytic lesion	Well-differentiated plasma cells	Positive for lambda-light-chain	LENA + DEXA	Partial remission
Troeltzsch M. *et al*. (2014 - Germany)[26]	67 (M)	Mand (R and L)	Swelling	Dental mobility / Non-vital tooth	Asymptomatic	PERI + PAN + CT + PET-CT	Extensive osteolytic lesion / Multiple osteolytic lesions / Root resorption	Infiltration by clonal plasma cells	Positive for CD138	BORTE + DEXA + MELP + ASCT + IBAN (BP)	Free of disease recurrence (3-year follow-up)
Zhao XJ. *et al*. (2014 - China)[11]	69 (M)	Max (L)	Swelling / Mouth opening limitation	Mass / Ulcer / Hemorrhage	Pain	CT + NMR	Bone destruction	Sheets of atypical plasma	Positive for CD138, Vs38c, EMA, and lambda chain	THALI + DEXA + BORTE + MITOX + ASCT	Remission
Goetze E. *et al*. (2015 - Germany)[13]	76 (F)	Mand (R)	Swelling / Mouth opening limitation / Laterotrusion	Tumor / Normal mucosa	Pain	PAN + CT	Radiolucent unilocular lesion / Ill-defined borders / Erosion of condylar process	Plasma cell tumor	Positive for CD138 and slight detection of kappa-light-chain	VINC + DOXO + DEXA	Stable with radiographic image unchanged (2-year follow-up)

Jhamb T. *et al*. (2015 - USA)[27]	63 (F)	Mand (L)	NR	No expansion	Paresthesia	CT	Low-density lesion / Ill-defined border / Cortical bone rupture	Sheets of plasma cells	-	CHT NS	NR
Kasamatsu, A. *et al*. (2015 - Japan)[2]	33 (M)	Max (R)	Swelling	Mass / Dental mobility	Asymptomatic	PAN + CT + NMR	Osteolytic lesion / Ill-defined borders / Reabsorption of the maxillary sinus floor	Atypical plasma cells	Positive for CD138	BORTE + DEXA	Good tolerability to CHT
Ramaiah KK. *et al*. (2015 - India)[15]	50 (M)	Max (L)	Swelling	Swelling/ Mass / Dental mobility	Pain	PAN + PA + CT	Osteolytic lesion / Ill-defined borders / Multiple "punched out" lesions	Atypical plasma cells with large hyperchromatic nuclei	Positive for CD138	DEXA + THALI	Patient is doing well
Thomas AE. *et al*. (2015 - India)[28]	58 (F)	Mand (L)	Swelling / Mouth opening limitation	Normal mucosa	NR	PAN + CT + USG + PET-CT	Osteolytic and destructive lesion / Ill-defined borders / Multiple radiolucent lesions	Aggregates of binucleated and multinucleated plasma cells (FNAC)	-	RT (3000cGy) + CP + BORTE + DEXA	Scheduled for HSCTa
Nayak A. *et al*. (2016 - India)[29]	40 (M)	Max (L) and Mand (L)	Skin pallor	Erythema / Overgrowth	NR	LAT + CT + NMR	Multiple radiolucent lesions	Sheets of neoplastic plasmacytoid cells (narrow biopsy)	-	BORTE + DEXA + THALI	Lost to follow-up
Crowley M. *et al*. (2016 - Ireland)[30]	69 (F)	Mand (L)	Swelling	Swelling	Pain / Inability to wear denture / Difficulty to feed	PERI + LAT + PAN	Lytic lesion / Ill-defined borders / Several well-circumscribed, radiolucent Lesions ("pepper-pot skull")	Sheets of plasmacytoid cells	Positive por kappa chain	NS BP	Swelling reduced greatly
Benjelloun L. *et al*. (2017 - Morocco)[31]	55 (M)	Mand (L)	Swelling	Swelling / Normal mucosa / Non-vital teeth / Dental mobility	Pain	PAN + CT	Extensive radiolucent lesion / Ill-defined borders / Cortical bone rupture / Root resorption	Sheets of plasma cells with nuclear pleomorphism	Positive for CD79a and CD138	THALI + DEXA + CP + ZOL (BP)	Intraoral swelling disappeared (6-month follow-up)
Ali IK. *et al*. (2018 - India)[32]	46 (M)	Mand (L)	Normal	Mass	NR	CBCT + LAT	Osteolytic lesion / Ill-defined borders / Multiple "punched out" lesions / Cortical bone rupture	Plasmocytoma	Positive for CD138 and kappa light chain	BORTE + CP + DEXA + RT	Complete response to the treatment

Subtitles: AP – Anteroposterior radiograph of the skull; ASCT – Autologous stem cell transplant; BORTE – Bortezomib; BP – Bisphosphonate; CARM – Carmustine; CBCT - Cone beam computed tomography; cGy – Centigray; CHT – Chemotherapy; CP – Cyclophosphamide; CT – Computed tomography; DEXA – Dexamethasone; DOXO – Doxorubicin; F – Female; FDG-PET - Fluorodeoxyglucose positron emission tomography; FNAC – Fine needle aspiration cytology; IBAN – Ibandronate sodium; L – Left; LAT - Lateral radiograph of the skull; LENA – Lenalidomide; M – Male; Mand – Mandible; Max – Maxilla; MELP – Melphalan; MITOX – Mitoxantrone; NMR – Nuclear magnetic resonance; NR – Not reported; NS - Not specified; OCCL – Occlusal radiograph; PA - Posteroanterior radiograph of the skull; PAMI - Pamidronate disodium; PAN – Panoramic radiograph; PERI – Periapical radiograph; PET-CT – Positron emission tomography - computed tomography; PRED – Prednisone; R – Right; RT – Radiotherapy; SKULL – Skull radiograph; THALI – Thalidomide; TMJ – Temporomandibular joint; USA – United States of America; USG – Ultrasonography; VINC – Vincristine; ZOL – Zoledronic acid.

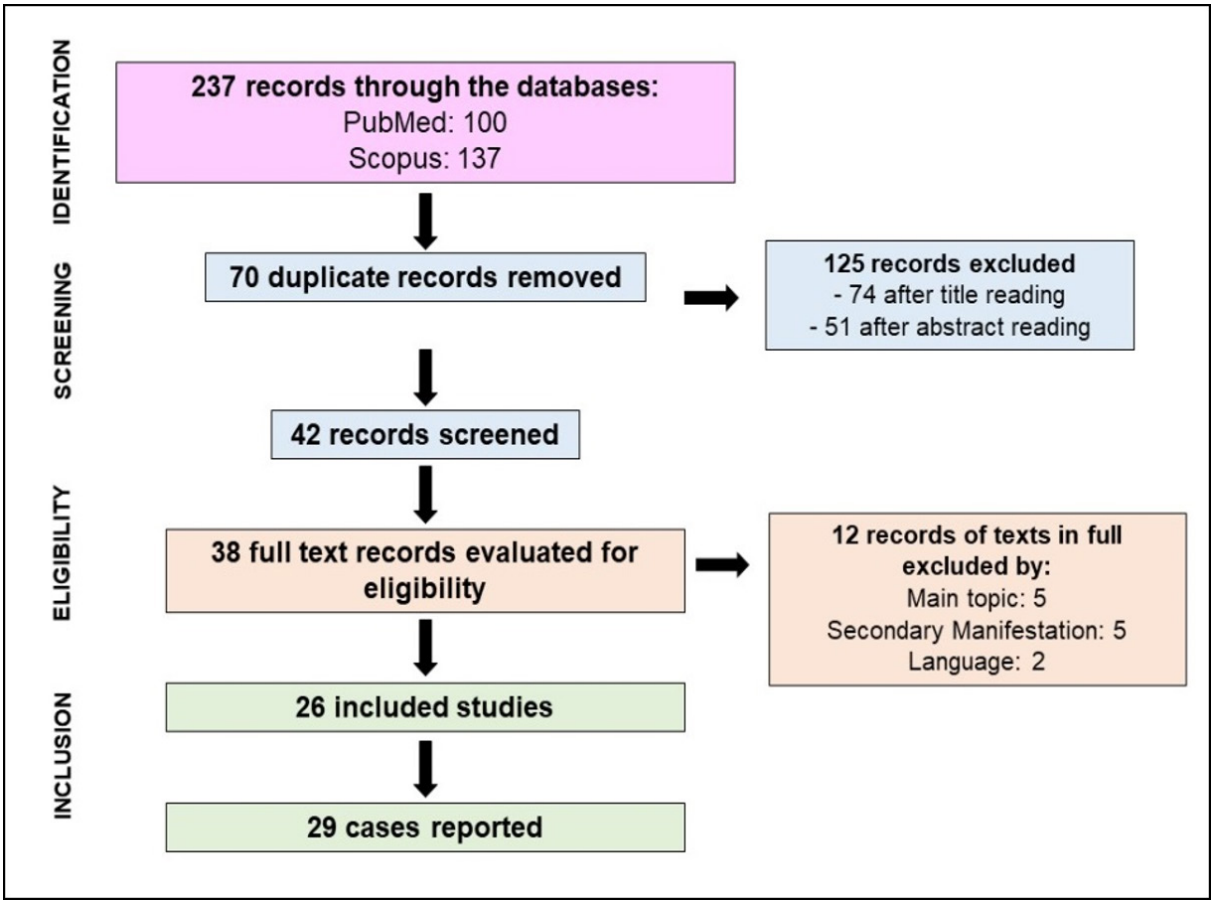

Figure 1. Flowchart for obtaining the articles

Discussion

The manifestations of MM may vary greatly, but oral maxillofacial lesions are usually present. Although rare, oral maxillofacial lesions can manifest as an early sign of the disease, and their detection warrants greater attention from clinical practitioners.[3,10] Once the diagnosis is established, therapy may be promptly initiated, contributing to a more favorable disease prognosis.

Epidemiological profile

The mean age at MM diagnosis was 60 years (ranging from 33 years[2] to 81 years).[7] Most patients (82.76%) were older than 50 years of age. Moreover, we observed a male predominance of 1.9:1.

Our analysis of ethnicities was hampered by lack of information. However, the highest number of reported cases originated from India,[6,14,15,24,25,28,29,32] followed by Brazil.[7,8,23] Furthermore, there were other reports from Europe, Asia, Africa, and North America, which showed the extreme geographic diversity of this disease.

Site of involvement

The most commonly affected oral maxillofacial site in MM was the mandible in isolation, which accounted for three quarters of the cases,[1,2,6-8,14-18,20-26,28,30,32] unilaterally,[1,2,6,8,14,15,17,18,20-23,25,28,30,32] or bilaterally.[16,17,24,26] The maxilla was also a common site, not only in isolation[11,13,18,19,29] but also concomitantly with the mandible.[27] These findings highlight the importance of a thorough and detailed physical examination.

Oral manifestation

The most common clinical manifestation noted via an extraoral physical examination was facial edema.[1,2,6,7,11,13,17,18,20-22,24,25,26,28,30-32] Other findings included trismus,[11,13,17,28] facial asymmetry,[17,32] temporomandibular joint clicking[17] and pallor.[29]

The most frequent manifestations observed on intraoral physical examination were the appearance of a mass or soft lesion in the oral cavity,[1,2,6,11,15,18,23,25,29,32] edema,[6,8,13,16,18,20-22,24,30,31] dental mobility,[2,14,15,19,24,26,31] ulceration,[1,11,18,22,25] bleeding,[6,11,14,20] non-vital teeth[21,26,31] and gingival enlargement.[14] Cortical plate expansion,[22] erythema,[29] purulent secretion[14] and sensitivity to percussion[19] have also been reported.

Symptoms

The patients commonly presented with pain as the main symptom.[1,6,8,11,13,15,16,17,18,23,25,30,31] However, there are cases that

reported paresthesia or numbness,[6,16,18,19,21,27,30] difficulty in feeding,[1,25,30] difficulty in wearing dentures, facial palsy, and even tongue deviation as the main symptom/s.

However, extraoral and intraoral symptoms and clinical manifestations may be absent in some cases.[2,7,14,17,24,25] Unfortunately, not all the published reports specified whether there were oral manifestations or symptoms.[1,8,14,16-20,23,27-29]

Complementary exams

The most frequently requested tests for complementary diagnosis were panoramic radiography,[1,10,12,18,20,26,28,30,31] volumetric and cone beam computed tomography[1,2,7,11,13,15,16,19,21,23-28,31,32] and skull radiographs (lateral, posteroanterior, and non-specified).[1,6,7,14,15,18,20,21,22,29,30,32] Other examinations included nuclear magnetic resonance,[1,2,11,19,21] periapical radiographs,[1,8,16,21,26,30] positron-emission tomography,[26] ultrasonography,[28] occlusal radiography[24] and fluorodeoxyglucose positron-emission tomography.[1]

Imaging findings

Imaging findings of the oral manifestations of MM may range from the appearance of an extensive radiolucent and/or osteolytic lesion[1,2,6,7,8,13,15,17-21,24-28,30-32] to multiple radiolucent lesions known as "punched-out" lesions.[7,15,16,18,20,21-23,25,26,28,29,32] Destruction of the cortical bone,[6,7,11,19,21,27,31] tooth displacement[24] and absence of imaging changes[1] may also be observed.

Histological and immunohistochemical characteristics

Incisional or excisional biopsies of the lesions in the mouth followed by fine needle aspiration cytology[17,19] were performed in most cases.[1-18,20-23,25-27,29-32]These results confirmed the presence of atypical plasma cells with hyperchromatic nuclei, binucleation, and large cytoplasm, characteristic of MM. Immunohistochemistry was also an option, complementary to the biopsy, which primarily searched for CD138 (Sindecam 1)[1,2,6,11,13,15,31,32] and kappa chain markers.[8,13,22,23,32] Positive expression was also found in the lambda chain,[6,11,31] epithelial membrane antigen,[1,8,11] CD79a (B-cell antigen receptor complex-associated protein alpha chain and MB-1 membrane glycoprotein),[1,31] vimentin,[1] and VS38c.[11]

Treatment of MM

Once the diagnosis of MM is confirmed, various treatment options are available, depending primarily on the disease staging and systemic conditions. The standard treatment is high-dose chemotherapy, followed by autologous stem cell transplantation for transplant-eligible patients, after the completion of induction therapy. Transplantation can induce significant remission, prolong patient survival, and should be considered early in all eligible patients.

Induction therapy usually consists of a combination of three drugs and is mainly administered to newly diagnosed and transplant-eligible patients. According to the International Myeloma Foundation, in the United States, treatment mainly consists of the administration of a combination of bortezomib, lenalidomide, and low-dose dexamethasone. Other combinations employed include bortezomib, cyclophosphamide, and dexamethasone; bortezomib, thalidomide, and dexamethasone; lenalidomide and dexamethasone; bortezomib and dexamethasone; as well as a reduced dose and modified schedule of bortezomib, lenalidomide, and dexamethasone.[1,2,11,14,15,28,29,31,32,33]

Treatment for patients not eligible for transplantation may include melphalan and prednisone, combined with bortezomib, thalidomide or lenalidomide, and a lower dose of dexamethasone.[8,16,18,19,22,23,25,26,34]

Considering the low number of articles reporting transplantations,[11,26] we concluded that the eligibility for transplantation may be uncertain. In addition, information about the treatment performed had not been provided in many cases.[6,7,20,21] Considering that these studies are case reports of recent and primary diagnoses, a lack of information is expected.

Outcomes

Some patients were lost to follow-up after diagnosis or referral for treatment,[3,20,29] making it impossible to determine the clinical outcomes and if treatment was adequate.

The clinical outcomes included partial or total remission of the mouth lesions,[1,8,11,14,18,26,31] disease recurrence,[18] and death.[1,6-8,17,18,23]

Conclusion

Considering that manifestations of MM may affect the oral maxillofacial region in the initial stages of the disease, it is important for clinical practitioners to be familiar with these manifestations, especially since a wide variety of signs, symptoms, and imaging findings may be observed.

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References

1. Romano A, Marescalco MS, Liardo C, Villari L, Vetro C, Conticello C, *et al*. Oral lesion as unusual first manifestation of multiple myeloma: case reports and review of the literature. Case Rep Hematol. 2014;2014:529452.
2. Kasamatsu A, Kimura Y, Tsujimura H, Kanazawa H, Koide N, Miyamoto I, *et al*. Maxillary Swelling as the First Evidence of Multiple Myeloma. Case Rep Dent. 2015;2015:439536.
3. Cardoso RC, Gerngross PJ, Hofstede TM, Weber DM, Chambers MS. The multiple oral presentations of multiple myeloma. Support Care Cancer. 2014;22(1):259-67.
4. Shah A, Ali A, Latoo S, Ahmad I. Multiple Myeloma presenting as Gingival mass. J Maxillofac Oral Surg. 2010;9(2):209-12.
5. Adeyemo TA, Adeyemo WL, Adediran A, Akinbami AA, Akanmu AS. Orofacial manifestation of hematological disorders: Hemato-oncologic and immuno-deficiency disorders. Indian J Dent Res. 2011;22(5):688-97.
6. Dengra S, Sharma N, Tiwari V. Oral manifestation of multiple myeloma as plasmacytoma: A case report. J Oral Maxillofac Surg Med Pathol. 2013;26(3), 421–3.
7. Segundo AVL, Lima-Falcão MF, Correia-Lins Filho R, Marques Soares MS, López López J, Chimenos Küstner E. Multiple Myeloma with primary manifestation in the mandible: A case report. Med Oral Patol Oral Cir Bucal. 2008;13(4):E232-4.
8. Pinto LSS, Campagnoli EB, Leon JE, Lopez MA, Jorge J. Maxillary lesion presenting as a first signo f multiple myeloma: Case report. Med Oral Patol Oral Cir Bucal. 2007;12(5):E344-7.
9. Mehdi G, Ansari HA, Haider N. Cytological diagnosis of multiple myeloma presenting as a jaw swelling. J Cytol. 2009;26(2):80-2.
10. Tanaka AKO, Ferreira GZ, Coracin FL, Santos PSS. Diagnosis and Management of Oral manifestations of Multiple Myeloma. In Steve Holt. (Org.). Multiple Myeloma: Risk factors, diagnosis and treatment. New York: Nova Biomedical; 2014. P.111-8.
11. Zhao XJ, Sun J, Wang YD, Wang L. Maxillary pain is the first indication of the presence of multiple myeloma: A case report. Mol Clin Oncol. 2014;2(1):59-64.
12. Patil PB, Kamarthi N, Taneja N, Patil N. Multiple Myeloma Presenting as an Intra-Oral Alveolar Mass - A Case Report and Brief Review. Int J Oral-Med Sci. 2010;8(3):162-6.
13. leeze E, Walter C, Kämmerer PW. Osseous Plasma Cell Neoplasm of the Mandible for Initial Diagnosis of Multiple Myeloma: Case Report and Literature Review. J Maxillofac. Oral Surg. 2015;14(Suppl 1):S469-S474.
14. Jain S, Kaur H, Kansal G, Gupta P. Multiple Myeloma presenting as gingival hyperplasia. J Indian Soc Periodontol. 2013;17(3):391-3.
15. Ramaiah KK, Joshi V, Thayi SR, Sathyanarayana P, Patil P, Ahmed Z. Multiple myeloma presenting with a maxillary lesion as the first sign. Imaging Sci Dent. 2015;45(1):55-60.
16. Senn JS, Stoneman DW, Cheng G, Kassel EE, Main JH. Multiple myeloma with initial presentation in the jaw: a clinical-pathologic discussion. J Oral Pathol. 1985;14(4):282-8.
17. Gonzalez J, Elizondo J, Trull JM, De Torres I. Plasma-cell tumours of the condyle. Brit J Oral Max Surg. 1991;29:274-6.
18. Lee SH, Huang JJ, Pan WL, Chan CP. Gingival mass as the primary manifestation of multiple myeloma: report of two cases. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 1996;82(1):75-9.
19. Reboiras López MD, García García A, Antúnez López J, Blanco Carrión A, Gándara Vila P, Gándara Rey JM. Anaesthesia of the right lower hemilip as a first manifestation of multiple myeloma. Presentation of a clinical case. Med Oral. 2001;6(3):168-72.
20. Mozaffari E, Mupparapu M, Otis L. Undiagnosed multiple myeloma causing extensive dental bleeding: report of a case and review. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2002;94(4):448-53.
21.Sugawara Y, Marumo M, Sasano T. Paresthesia of the left lower lip as a first manifestation of multiple myeloma - A case report. Oral Radiol. 2003;19(2):56-64.
22. Amirchaghmaghi M, Pakfetrat A, Mozafari PM, Saghafi S. Mandibular Swelling as the First Manifestation of Multiple Myeloma. Iran J Med Sci. 2010;35(4):331-4.
23. Santos, PSS, Klingbeil MFG, Abrahão AC, Gallottini M, de Souza, SCOM. Multiple myeloma with primary manifestation in mandibular area. Oral Surg. 2012;5:26-9.
24. Vinayachandran D, Sankarapandian S. Multiple osteolytic lesions. J Clin Imaging Sci. 2013;3(Suppl 1):6.
25. Pushpanshu K, Punyani S, Kaushik R. Mandibular mass as the primary manifestation of multiple myeloma. Braz J Otorhinolaryngol. 2014;80(3):266-7.
26. Troeltzsch M, Oduncu F Mayr D, Ehrenfeld M, Pautke C, Otto S.
Root resorption caused by jaw infiltration of multiple myeloma: report of a case and literature review. J Endod. 2014;40(8):1260-4.
27. Jhamb T, Syed AZ, Baur D. Recognizing Oral Manifestations of Multiple Myeloma. J Mass Dent Soc. 2015;64(1):18-9.
28. Thomas AE, Kurup S, Jose R, Soman C. Facial Swelling as a Primary manifestation of Multiple Myeloma. Case Rep Dent. 2015;2015:319231.
29. Nayak A, Nayak MT. Multiple myeloma with an unusual oral presentation. J Exp Ther Oncol. 2016;11(3):199-206.
30. Crowley M, Cronin O, Sleeman D, McKenna J. Multiple myeloma presenting as mandibular pain. J Ir Dent Assoc. 2016;62(5):276-8
31. Benjelloun L, Dghoughi S, Taleb B. A mandibular lesion revealing multiple myeloma. Oral Surg. 2018;11:157-62.
32. Ali IK, Parate AR, Kasat VO, Dora A. Multiple Myeloma with Primary Manifestation in the Mandible. Cureus. 2018;10(3): e2265.
33. Brian GM, Durie MD. Concise Review of the Disease and Treatment Options. International Myeloma Foundation, Los Angeles. 2018.
34. Ramasamy K, Dhanasiri S, Thom H, Buchanan V, Robinson S, D'Souza VK, *et al*. Relative efficacy of treatment options in transplant-ineligible newly diagnosed multiple myeloma: results from a systematic literature review and network meta-analysis. Leuk Lymphoma. 2019;61:(3):668-79.

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