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CASE REPORT

Osseous Plasma Cell Neoplasm of the Mandible for Initial Diagnosis of Multiple Myeloma: Case Report and Literature Review

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Abstract
Purpose Plasmocytoma of the bone represents a variance of plasma cell neoplasms, which often gives hint for systemic affection. A case of a mandibular tumor as first manifestation of multiple myeloma (MM) is presented and discussed with the literature.
Materials and Methods A 76-year old female with pain and swelling of the right lower jaw was assigned to the hospital. Radiograph showed a lytic tumor at the mandibular condyle and histological analysis gave evidence of a plasma cell tumor with positivity to CD138. In further examinations, elevated immunoglobulin levels in serum and osseous plasma cell infiltration unveiled MM. PubMed-database was searched by "multiple myeloma primary lesion jaw", "multiple myeloma primary manifestation mandible" and "multiple myeloma mandibular lesion" within the last 30 years.
Results Together with the current case, 11 reports including 13 patients were found describing mandibular plasmocytoma as first sign for MM. Mean age was 59 years with slight female preference. Initial symptoms were mostly swelling episodes with or without pain. The main radiological presentation was a uni- or multilocular radiolucency. After a mean follow up time of 29 months (stated in 8 cases; standard deviation 50, min: 1, max: 151), 3/8 patients died and in 5/8 cases, signs of progress were seen.
Conclusion In rare cases, occurrence of plasmocytoma of the mandible is first sign for MM and should always lead to further investigations regarding systemic disease. Simple examinations such as panoramic X-rays can lead to early detection of MM and thereby better prognosis by earlier treatment.

Keywords Plasmocytoma · Multiple myeloma · Plasma cell tumor · Mandible · Lower jaw · Literature review

Introduction

Multiple myeloma (MM) is a systemic disease with abnormal intramedullary plasma cell proliferation and hyperproduction of monoclonal immunoglobulins. Affected population age has age predominance in the sixth decade of life. Preference of male patients is mostly described [1]. Long bones and vertebrae are commonly affected; involvement of the jaw is rare and mostly occurs in the posterior, bone marrow-richer parts of the mandible [1]. Affection of the jaws usually leads to pain and non-specific swelling of the bone [2]. Mucosal alterations, movement or loss of teeth, decrease in mouth opening capacity, numbness of the lower jaw or pathological fractures may be found. Diagnosis includes a radiograph and computer-tomography of the affected site. Typical radiological appearance is a well-defined radiolucent lesion, uni- or multilocular, eventually with trabecular patterns [3]. In the minority of cases, lytic features are seen [1]. Differential diagnoses are inflammatory diseases, metastatic

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lesions, odontogenic tumors such as ameloblastoma, odontogenic myxoma, keratocystic odontogenic tumor or non-odontogenic lesions such as giant cell granuloma, aneurysmal bone cyst or AV-malformation [2, 3]. Therefore, histological evidence is essential for diagnosis and fine needle aspiration or direct biopsy should be obtained. MM has to be treated by chemotherapeutic regime and bony lesions are to be treated in case of complications only.

In this article, we present a rare case of a mandibular plasma cell neoplasm as first manifestation of MM. Additionally, a systematic review of similar cases was conducted and discussed together with our case.

Case Report

In June 2011, a 76-year-old female consulted the Department of Oral, Maxillofacial and Plastic Surgery, University Medical Center Mainz, Germany, with a painful swelling of the right lower jaw in the pre-auricular region (Fig. 1) associated with impaired mouth-opening and laterotrusion. The patient stated that she noticed the first signs 3 months ago. A prior fine needle aspiration of the tumor, which was conducted elsewhere, did not reveal a diagnosis. The patient's medical history contained coronary heart disease with an electronic ablation because of ectopic atrial arrhythmia and prior removal of uterus and ovaries. In clinical examination, a tumor (about 8 × 7 cm) that was adjacent to the bone and covered with skin was seen. There was no secretion or mucosal change. Suspect lymphatic nodes were not found. Panoramic radiography showed a radiolucent mass in the region of the ascending ramus and temporo-mandibular joint. The lesion was unilocular with ill-defined and lytic edges and a complete erosion of the condylar process; a cortical reaction was absent (Fig. 2). Computed tomography showed a tissue-dense tumor with total erosion of the condylar process without visible invasion of the surrounding soft tissue (Fig. 3a, b). A biopsy was initiated via pre-auricular approach. Intraoperatively, the lesion presented as a dark-red and compact mass. Immediate histological examination revealed a plasma cell tumor (Fig. 4a, b). Further histological processing included a microscopical stain for plasma cell marker CD138 (Fig. 5) and slight detection of kappa-light-chain-restriction.

After surgery the patient was referred to the department of haemato-oncology for further diagnostics and treatment. Diagnosis procedures concerning MM were performed, including a serum/urine electrophoresis, a bone-marrow sample and serum calcium levels. The results gave evidence for a systemic disease with intramedullary plasma cell proliferation (>10 %) and further skeletal sites of the MM. Electrophoresis showed elevated IgG-globulines and kappa-light-chains. Final diagnosis was osseous plasma cell tumor of the jaw as first sign of MM. The patient was treated via chemotherapy in the haemato-oncology department with MM, Stage IIIa after Salmon/Durie. The chemotherapy consisted of 2 mg vincristine i.v., 40 mg/m^2 doxorubicin i.v. and 40 mg dexamethasone per os daily for 5 days. This regime was repeated six times every 4 weeks. The patient was seen in close clinical follow up and there has been a serological progress from January 2012. Currently, after a total follow up time of 24 months, the patient is in a stable condition. The lesion of the left condyle stayed radiologically unchanged during our follow-up examinations.

Review of the Literature

Search Strategy

A PubMed database literature search was performed with the aim of analysis of occurrence of a plasma cell tumor of

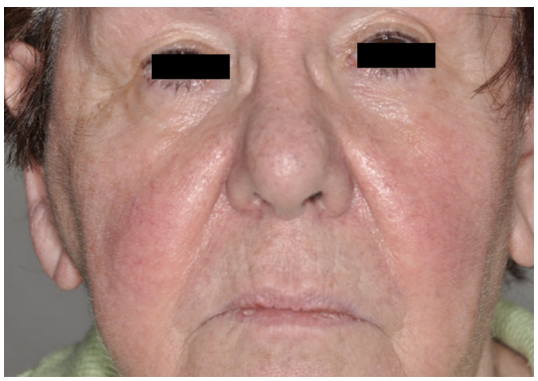

Fig. 1 From the frontal view, a distinct swelling in the right pre-auricular area is visible

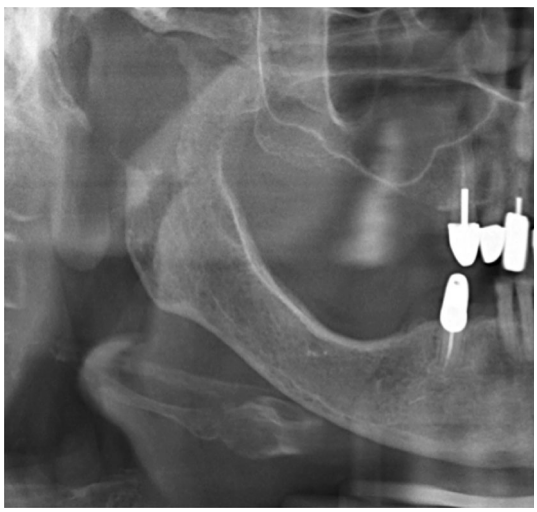

Fig. 2 Panoramic X-ray showing a radiolucent, lytic lesion of the condylar process of the mandible

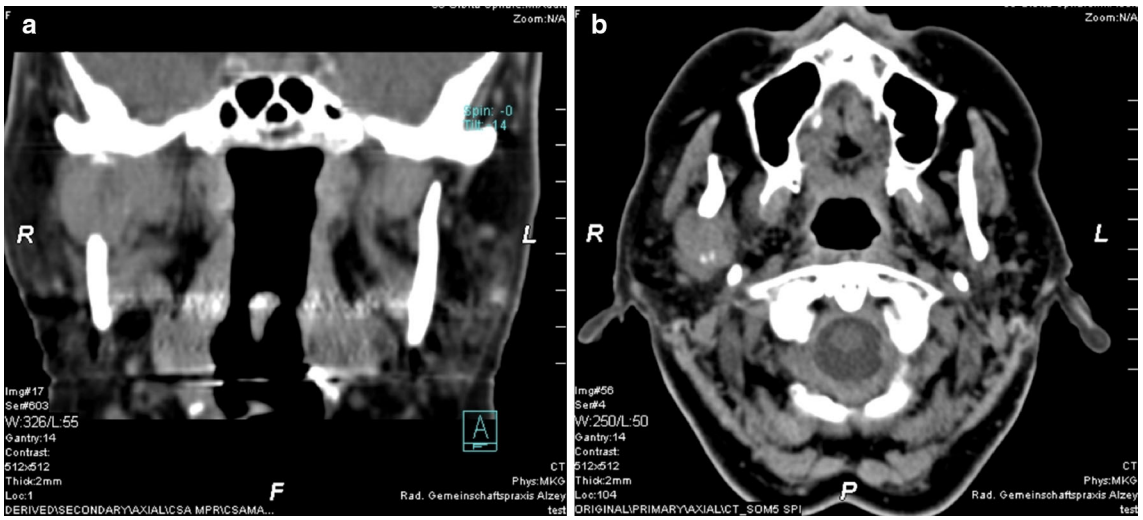

Fig. 3 CT of the head–neck-region: tumor formation at the right mandible with complete destruction of the condyle in coronar (**a**) and transversal (**b**) planes

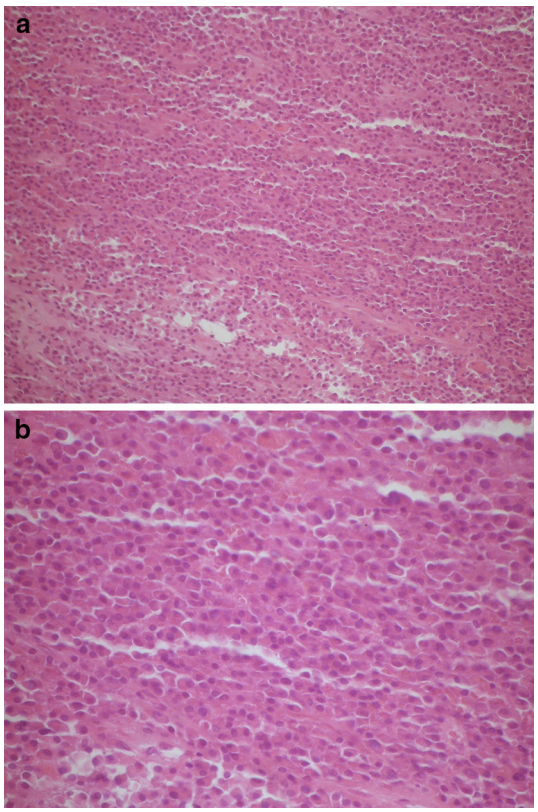

Fig. 4 HE-staining showing sheets of tumor cells resembling plasma cells (**a** original magnification ×200; **b** original magnification ×400)

the mandible as first sign for MM. Search strategy contained the keywords "multiple myeloma primary lesion jaw", "multiple myeloma primary manifestation mandible" and "multiple myeloma mandibular lesion". Results were limited to English and German language, for the last 30 years,

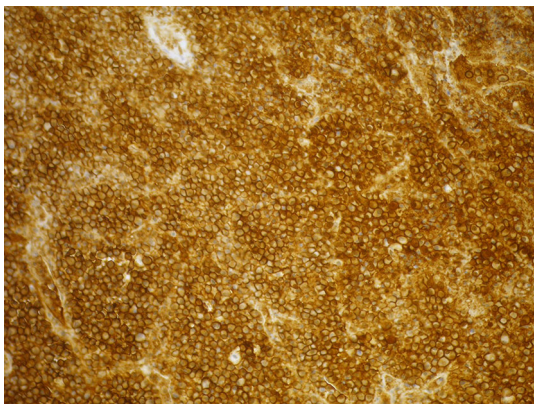

Fig. 5 Immunohistochemical staining showing positivity of cell to CD138 (original magnification ×200)

occurrence of plasmocytoma, mandibular sites and topics not linked to "jaw osteonecrosis" or "analytic methods". Out of the included articles, descriptions of patients' age, sex, initial symptoms, location, duration before diagnosis, radiographic features, laboratory findings, results of bone marrow aspirations, treatment and follow-up information were collected and compared with the current case.

Results

Together with the current report, a total of 11 articles describing 13 patients with mandibular plasmocytoma as initial diagnosis of MM were included [4–13] (Table 1). The mean age was 59.9 years (min: 22, max: 81); female patients (54 %) were affected slightly more often than males (46 %). Initial symptoms were unspecific such as swelling (69 %), pain (46 %), teeth problems (23 %) and

Table 1 Articles describing mandibular plasma cell tumor as initial diagnosis in course of multiple myeloma

Author	Year	Article	Patient (age, gender)	Initial symptom	Symptom duration before examination	Location	Radiographic features	Laboratory findings	Bone marrow aspiration	Other osteolytic lesions	Treatment	Follow up
[4]	2011	Review three patients included	37, male	Pain	3 months	Left MD	Lytic defect	IgG, IgA gammopathy	NA.	NA.	Irradiation 45 Gy	151 month: disease free
			57, male	Painful swelling, hyperesthesia	NA.	Body and alveolar ridge bilaterally	Multilocular radiolucency	Monoclonal gammopathy with IgG, Bence-Jones protein pos.	10 % plasma cell infiltration	Present	Chermotherapy (mephalan/ prednisone)	24 month: progress of disease
			68,female	Swelling	NA.	Left body and ridge	Multilocular radiolucency	IgA-α Gammopathy	5–10 % plasmacell infiltration	Left femur	NA.	NA.
[5]	2013	Case report	65, female	Swelling	2 years	Left mandibular angle, ramus, coronoid, condylar process	Ill-defined osteolytc radiolucent lesion	Anemia, M-protein in serum and uriene	36,5 % plasmacell infiltration	none	Chermotherapy (thalidomide/ cyclophosphamide/ dexamethasone)	Bone formation in MD after 8 month
[6]	2011	Case report	71, male	Pathological fracture	1 day	Right angle	Dislocated fracture in correspondence with extensive well-defined unilocular radiolucent osteolytic lesion	Anemia, erythropenia, monoclonal gammopathy for IgG lambda chain	50 % interstitial infiltration by plasma cells	NA.	Resection/ chemotherapy (thalidomide/ melphalan/ prednisone)	NA.
[7]	2009	Case report	70, male	Numbness of chin and lip, toothache, mobile tooth	NA.	Left corpus	Ill-defined multilocular radiolucent lesion	Monoclonal gammopathy for IgG lambda chain, proteinuria	NA.	Humerus, femur	Radiation (21 Gy bone/20 Gy oral)/ chemotherapy (thalidomide/ prednisone)	NA.
[8]	1999	Case report	22, male	Painless swelling	6 months	Right ramus	Osteolytic lesion	Monoclonal gammopathy for IgM and kappa light chain	Plasma cells infiltration, pos. for kappa light chain	No other lesions	Radiation (52 Gy)/ chemotherapy (melphalan/ prednisone), further treatment was refused	Relapse under chemotherapy than lost for follow up
[9]	2009	Case report	45, female	Swelling, dysphagia	2 months	Left ramus and body	Destructive, radiolucent lesion	Anemia, raised blood sedimentation time, Bence-Jones-protein pos.	NA.	Skull	NA.	NA.
[10]	1989	Case report	53, female	Loosening of premolar and molar teeth, local discomfort	4 months	Right corpus	Bi-lobulated, well-defined radiolucent lesion, root resorption of teeth	Increase in erythrocyte sedimentation time, monoclonal gammopathy for IgA with light kappa chains, Proteinuria	Plasma cell infiltration 19 %, some immature	Iliac crest	Resection/ chemotherapy (melphalan/ prednisone)	Bone formation in jaw after 9 months

Table 1 continued

Author	Year	Article	Patient (age, gender)	Initial symptom	Symptom duration before examination	Location	Radiographic features	Laboratory findings	Bone marrow aspiration	Other osteolytic lesions	Treatment	Follow up
[11]	1986	Case report	64, female	Painful swelling, kinesalgia of right upper arm	NA.	Right angle	NA.	NA.	Plasma cell infiltration 16,8 %, pos. for kappa light chain	Skull, humerus	Radiation (40 Gy)/ chemotherapy (5FU/MCNU/ interferon/ prednisone/ melphalan)	Death after 5.5 months
[12]	1988	Case report	70, female	Painful swelling and toothache	NA.	Right MD over to left MD including symphisis	Ill-defined lytic lesion	Anemia, monoclonal gammopathy with lambda light chain	NA.	No other lesions	None due to sudden death	None due to sudden death
[13]	2008	Case report	81, male	Painless swelling	7 months	Symphisis	Extensive ill-defined osteolytic lesion and multilocular round-shaped lesions	Anemia, leukocytosis, eosinophilia, lymphocytopenia	NA.	Scapula, clavicularibs	NA.	Death after 9 months
Own case	2014	Case report	76, female	Pain, swelling,impaired mouth opening	3 months	MD right ramus, condyle	Unilocular radiolucency	Monoclonal gammopathy (IgG kappa light chain)	No result	Rib	Chemotherapy	24 months

MD Mandible, *NA.* information not available

paresthesia (15 %). Furthermore, impaired mouth opening, dysphagia, ulceration as well as one pathological fracture were seen. In decreasing frequency, the mandibular body (54 %), the angle (31 %) and the ramus (23 %) were affected. Unilateral involvement was seen more often (75 %) than bilateral manifestations. Between the right and left side, cases were equally distributed. The mean reported time between first symptoms and clinical presentation was 6 months (min: 1 day, max: 24 months). Though, duration of symptoms had not been specified in nearly half of the cases. Radiologically, the lesions presented as uni- or multilocular radiolucencies, partly with osteolytic features. Laboratory examination showed bi-/monoclonal gammopathy in 62 % of cases [IgG: 38 %, IgA: 23 %; IgM: 8 %, kappa (15 %) and lambda (23 %) light chains]. Other findings were anemia (38 %) and positive Bence-Jones proteins (15 %). In one case, proteinuria, increased blood sedimentation and changes in leucocytes were observed. Plasma cell infiltration in bone marrow aspirates was seen in 8/13 cases (62 %), though, in 5/13 cases (38 %), no information considering this technique was given. In 9 cases, the respective treatment was given which included chemotherapy (n = 3), radiation + chemotherapy (n = 3), resection + chemotherapy (n = 2) as well as irradiation only (n = 1). After a mean follow up time of 29 months (stated in 8 cases; standard deviation 50, min: 1, max: 151), 3/8 patients died and in 5/8 cases, signs of progress were seen.

Discussion

We report a case of a condylar manifestation of MM that led to the diagnosis of the systemic disease. In general, mandibular involvement as initial presenting sign of MM is very rare and difficulties in correct diagnosis of such an entity have to be emphasized. Especially misdiagnoses as ameloblastoma, odontogenic or malignant tumor of inflammatory disease are common [4].

The patient in our case was female and in the eighth decade of life, neither gender nor age were typical for the occurrence of MM [4, 14]. The size of the primary lesion as well as the systemic manifestations may hypothesize an initial delay in diagnosis. In accordance, the median age at diagnosis for MM is 10 years after those for patients presenting non-systemic solitary plasmocytoma of the bone (SB) [4]. Analogue to this, Zachriades et al. [15] reported that SB may be the first manifestation of MM with a progression rate of 65–100 % in 15 years. As described by others, the clinical presentation with swelling, pain at the lower jaw as well as a decreased mouth opening is non-specific [4]. Features such as tooth loss or paresthesia may be found but could not be seen in our case. We observed a

non-common, extensive affection of the ramus with resorption of the condyle. Generally, MM of the jaw is found more often in the corpus and the angle of the mandible [4, 16]. The radiographic feature with a lytic process at the mandibular condyle fits usual schemes but is not the most common appearance with a well-defined uni- or multilocular radiolucent lesion [4] which may resemble other benign and malignant lesions. After confirming a plasma cell neoplasm of the mandible, further analysis could prove MM by expressed elevated monoclonal immunoglobulines and bone marrow infiltration.

In 2–70 %, the jaws are affected in MM and in 5–15 % of patients with MM the mandible is affected during the progression of the disease [4]. The affection of the jaws as primary site is rarely seen. Primary manifestation of MM in the lower jaw is mostly stated in case reports. Based on the rarity, an estimation of the prevalence is not possible. Details such as treatment, follow up and survival rates are not always given. Death was seen in nearly 38 % of the cases under examination and progress of the disease in about 63 %. This illustrates the importance of a profound analysis of indistinct lesions in the oral and maxillofacial area. An early diagnosis with subsequent interdisciplinary treatment may enhance the overall survival. All precautions should be taken in order to avoid the spreading of the disease as well as to delay the correct diagnosis with the respective treatment. In case of SB, which is seen to be a precursor lesion of MM by some authors, radiotherapy is the first line treatment. Primary surgery can be obtained especially in younger patients with isolated lesions and good prognostic factors [4]. In case of MM, chemotherapeutic treatment is necessary and bone lesions only are specifically treated in course of complications as excessive pain or fracture. If plasmocytoma is confirmed, follow up under monitoring of immunoglobulins and Bence-Jones proteins in urine is needed.

Conclusion

Even if the occurrence of plasmocytoma of the jaw as first sign for MM is rare, simple diagnostics such as panoramic x-ray are valuable tools for primary diagnosis of early as well as later stages of the systemic disease. For the dentist, oral and maxillofacial manifestations of SB or MM should be taken into consideration. Delays in correct diagnosis due to non-specific signs indicate the further need of an intralesional biopsy that will lead to a proper interdisciplinary treatment.

Conflict of interest The authors state that there is no conflict of interest.

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