CASE REPORT

Multiple myeloma presenting as plasmacytoma of the jaws showing prominent bone formation during chemotherapy

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A 65-year-old female visited our hospital complaining of a swelling on the left cheek area of 2 years' duration. A panoramic radiograph revealed an ill-defined osteolytic radiolucent bony lesion involving the left mandibular angle, ascending ramus, coronoid process and condylar process. Histological examination showed the mandibular lesion to be a plasmacytoma, and a systemic work-up was obtained to rule out multiple myeloma. Contrast-enhanced CT images showed a well-defined and slightly enhanced round mass on the left ramal area, accompanied by the destruction of the left ramus and posterior maxilla. An ¹⁸F-fluorodeoxyglucose positron emission tomography CT (¹⁸F-FDG PET/CT) scan revealed a hypermetabolic mass extending from the left mandible to the left maxillary sinus. The patient had M-protein in serum and urine, plasma cells up to 36.5% on bone marrow biopsy and anaemia as a clinical complication. The patient was diagnosed with multiple myeloma and received chemotherapy with thalidomide, cyclophosphamide and dexamethasone. A PET/CT scan taken 6 months later revealed that the hypermetabolic mass had disappeared and there was remarkable bone formation on the left mandible compared with a previous PET/CT scan. A panoramic radiograph taken 8 months later also demonstrated a prominent bone formation of the affected site. To the best of our knowledge, the current case is the first report of multiple myeloma presenting as plasmacytoma of the mandible with an FDG PET/CT scan. The lesion was solitary at diagnosis, and remarkable bone formation was newly observed on the radiographic examination during chemotherapy.

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Case report

A 65-year-old female visited our hospital complaining of a swelling on the left cheek area for 2 years. The extraoral examination revealed an asymptomatic expansion on the left cheek area. Intraorally, the involved area showed a soft to fluctuant consistency and was covered by locally ulcerated mucosa. There was no complaint of paraesthesia or anaesthesia. A panoramic

radiograph was acquired using an Orthopantomograph[®] OP 100D (Instrumentarium Imaging, Tuusula, Finland) and revealed an ill-defined osteolytic radiolucent bony lesion involving the left mandibular angle, ascending ramus, coronoid process and condylar process (Figure 1). It also demonstrated a loss of the inferior border of the left zygomatic process of the maxilla and a soft-tissue shadow around the affected area. The lesion contained septum-like residual bone at the angle of the mandible. An incisional biopsy of the left anterior ramal area was performed under local anaesthesia, during which intra-oral bleeding was not noted. A histopathological examination of the specimen

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Figure 1 Panoramic radiograph shows an ill-defined osteolytic radiolucency on the left mandibular angle-ramus-condyle-coronoid process area. It also reveals a loss of the inferior border of the left zygomatic process of the maxilla and a septum-like residual bone at the angle of the mandible

revealed a solid proliferation of plasmacytoid cells with eccentric nuclei and basophilic cytoplasm, partially showing atypia on haematoxylin and eosin staining, which was indicative of plasmacytoma (Figure 2).

The patient was referred to haemato-oncology and a systemic work-up for the final diagnosis was performed to differentiate the solitary plasmacytoma of bone and multiple myeloma. A skeletal radiographic survey including posteroanterior and lateral skull views was performed and showed no additional osteolytic lesion. Contrast-enhanced CT (LightSpeed Ultra; GE Healthcare, Milwaukee, WI) showed a well-defined and slightly enhanced round mass on the left ramal area, accompanied by the destruction of the left ramus and

Figure 2 A histopathological examination of the specimen reveals a solid proliferation of plasmacytoid cells with eccentric nuclei and basophilic cytoplasm, partially showing atypia (haematoxylin and eosin stain; original magnification $\times 400$)

Figure 3 Contrast-enhanced CT image shows a well-defined, slightly enhanced round mass on the left mandibular ramal area and the destruction of the left ramus and the posterior maxilla

posterior maxilla (Figure 3). An ^{18}F -fluorodeoxyglucose positron emission tomography CT (^{18}F -FDG PET/CT) scan combined PET/CT unit (Reveal RT-HiRez CTIMI; Knoxville, TN: a six-slice CT scanner) revealed a hypermetabolic mass extending from the left mandible to the left maxillary sinus (Figure 4).

Laboratory analysis showed an M-protein [immunoglobulin (IgG) κ type] on serum and urine electrophoresis and a mildly reversed albumin/globulin ratio; however, any other finding such as renal failure or hypercalcaemia was not found. A bone marrow biopsy showed increased plasma cells up to 36.5% of the absolute neutrophil count, which were slightly immature. The plasma cells had eccentric nuclei and showed multinuclearity. The red cells and the granulocytic series were hypoplastic. The final diagnosis was multiple myeloma.

The patient was recommended for multiagent chemotherapy and prescribed thalidomide, cyclophosphamide and dexamethasone. An ^{18}F -FDG PET/CT scan taken 6 months later revealed the disappearance of the hypermetabolic mass and a remarkable bone formation on the left mandible compared with the previous ^{18}F -FDG PET/CT scan (Figure 5). A panoramic radiograph taken 8 months later also demonstrated a prominent bone formation and cortical outlines of the affected mandible and the inferior alveolar canal (Figure 6). Deformity was noted on the newly formed left condyle. An ill-defined osteolytic lesion of the right mandibular canine area was suspected that had not been revealed on the ^{18}F -FDG PET/CT scan 2 months previously. A new diffuse bone marrow defect could not be excluded. The patient had tolerated the chemotherapy well until now.

Figure 4 A positron emission tomography CT scan reveals a hypermetabolic mass extending from the left mandible to the left maxillary sinus

Discussion

Multiple myeloma is a malignant neoplasm of plasma cells. It is characterized by a proliferation of a single clone of abnormal immunoglobulin-secreting plasma cells. Plasma cell neoplasms are broadly categorized into three groups: multiple myeloma, which is the commonest; solitary plasmacytoma of bone; and extra-medullary plasmacytoma.^{1,2}

Diagnostic criteria for multiple myeloma have varied over time. According to the 2008 World Health Organization classification,³ a diagnosis of the present case was confirmed as symptomatic myeloma because the patient had M-protein in serum and urine, bone marrow plasma cells up to 36.5%, plasmacytoma on tissue biopsy and anaemia as a clinical complication. The patient did not have typical complications, such as skeletal destruction with osteolytic lesions, pathological fractures, bone pain, hypercalcaemia and renal insufficiency. Some patients with undiagnosed multiple myeloma may present with initial signs or symptoms in the jaw bones and oral cavity and a systemic work-up should be obtained early after diagnosis of the lesion to rule out the existence of systemic disease.^{2,4-7} In the present case, the laboratory examination was essential to differentiate

solitary plasmacytoma of bone from multiple myeloma owing to a lack of characteristic clinical complications or end-organ/tissue damage, especially osteolytic lesion.

The radiographic features of multiple myeloma vary from normal to diffuse osteosclerosis; however, multiple radiolucent bone lesions are most common.^{1,8,9} Solitary plasmacytoma of the mandible also has various radiographic findings: “punched-out” appearance, ill-defined destructive radiolucencies and appearance of a multi-loculated lesion.^{4,10-14} In the present case, no additional osteolytic lesions were caused by multiple myeloma; however the left posterior mandible and ramal area were associated with plasmacytoma demonstrating ill-defined destructive radiolucencies. Early myeloma may not reveal observable changes on plain radiographs. Other imaging techniques show evidence of active myeloma in approximately 20% of patients with negative radiographs.^{15,16} The Durie/Salmon PLUS staging system includes new imaging techniques, such as MRI, whole-body FDG-PET scanning and whole-body CT (combined with PET directly or by fusion), offering anatomical and functional information.¹⁷ PET and PET/CT with ¹⁸F-FDG are insensitive to diffuse bone marrow infiltration; however, this technique may help to detect new non-suspected lesions overstaging the

Figure 5 A positron emission tomography CT scan 6 months later showing the disappearance of the hypermetabolic mass and remarkable bone formation on the left mandible

disease, with important implications in treatment, and to assess treatment response in solitary or multiple solid plasma cell tumours which have a high FDG uptake before treatment.^{18–25} To the best of our knowledge, the current case is the first report of solitary plasmacytoma of the mandible with an ^{18}F -FDG PET/CT scan. The initial PET/CT scan confirmed that the lesion was solitary with a maximum standardized uptake value of 3.1. Follow-up PET/CT scans revealed decreased FDG uptake and decreased mass and the reappearance of the cortical outline on the left ramal area.

Differential diagnosis of a current panoramic image showing aggressive bone destruction and extensive soft-tissue mass included primary or metastatic malignant tumour. Various malignant conditions were considered owing to its location, such as malignant tumour of neural origin, histiocytoma, fibrosarcoma and rhabdomyosarcoma. However, histiocytoma and sarcoma arise typically in younger patients and there was no known primary lesion suggestive of metastatic lesion. Although CT images demonstrated a well-defined round mass centred on the left ramal area and a mild homogeneous enhancement pattern different from a malignant lesion, the possibility of malignant tumour could not be excluded because of the aggressive appearance of the lesion.

On histological examination, a final diagnosis was confirmed as plasmacytoma.

The release of paracrine factors by myeloma leads to increasing bone demineralization and hypercalcaemia by activation of osteoclasts.²⁶ Bisphosphonates inhibit bone resorption by being selectively taken up and adsorbed to mineral surfaces in bone, where they interfere with the action of the bone-resorbing osteoclasts.²⁷ In

Figure 6 A panoramic radiograph, taken 8 months later, demonstrates a prominent bone formation and discontinuous cortical outlines of the affected mandible and the inferior alveolar canal. It shows a decrease in the ramal width and a deformity of the left condyle

the current case, the patient took zoledronic acid (Zometa®; Novartis Pharmaceuticals Corp, East Hanover, NJ) for preventing skeletal fractures from multiple myeloma. It is possible that residual osteoblasts of the left ramal area, despite severe initial bone loss, could induce bone formation because osteoclastic activity was suppressed by zoledronic acid.

In the case of advanced stage or symptomatic myeloma, melphalan–prednisone plus either thalidomide or bortezomib are the new standards in Europe for elderly patients.²⁸ Thalidomide kills malignant plasma cells directly, and also has antiangiogenic properties and other effects on the bone marrow microenvironment that may synergize with chemotherapy to induce apoptosis.^{29,30} Cyclophosphamide, thalidomide and dexamethasone provide higher response rates than melphalan–prednisone in patients with newly diagnosed multiple myeloma who are ineligible for intensive therapy and autologous stem cell transplantation.³¹

An early diagnosis of solitary plasmacytoma of bone is essential to overall patient survival. It may represent the

first manifestation of multiple myeloma, with conversion to multiple myeloma occurring in approximately 70% of cases at an average of 20.7 months after initial diagnosis.^{8,10,25,32} The 5-year survival rate of solitary plasmacytoma of bone is 60%; however, it goes down to 5.7% when progression to multiple lesions occurs.³³ In the present case, we could not exclude the possibility of conversion from solitary plasmacytoma of bone to multiple myeloma. The swelling had persisted for 2 years at diagnosis, and laboratory analyses were also close to the initial stage rather than the typical findings of multiple myeloma, which generally show renal insufficiency and hypercalcaemia.

In conclusion, we have reported a case of multiple myeloma presenting as plasmacytoma showing an ill-defined osteolytic radiolucency on the left mandibular angle–ramus–condyle–coronoid process area as a first sign of the disease. No additional bony lesions were found in initial the ¹⁸F-DG PET/CT scan and prominent bone formation was remarkable on both plain radiographs and an ¹⁸F-DG PET/CT scan during chemotherapy.

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