MULTIPLE MYELOMA OF MANDIBLE : REPORT OF A CASE

*Dept. of Oral & Maxillofacial Surgery, Kangnam General Hospital, Public Corporation
**Dept. of Oral & Maxillofacial Surgery, Medical service battlion, 17th Division, Korean Army

Hyun-Seok Jang* · Gi-Cheol Lee**

하악골에 발생한 다발성골수종의 증례보고

*장현석 · **이기철

*지방공사 강남병원 구강악안면외과
**육군 17사단 의무대 치과

다발성 골수종은 다양한 증세를 보이는 형질세포로부터 기원하는 악성종양으로 40세이상의 남성에서 호발되며 alkylating agent 단독, 혹은 corticosteroid와 병용하는 항암제 치료로 생존율이 크게 증가되기는 하였지만 치료후 평균생존기간이 20개월 내외로 완치율이 그다지 높지않은 형편이다. 악골에서의 발생은 극히 드물고 대개 늑골, 편평골, 척추, 골반, 두개골 등에 광범위한 patchy destruction의 형태로 나타나는데 악골에 발생할 경우 임상증상은 장기적인 무통성 종창이 가장 흔하며 때로는 동통, 악골의 팽창, 감각이상, 치아의 동요, 악골골절등을 보이기도 한다. 전신적증상으로 무력감, 체중감소, 빈혈, 신부전, hypercalcemia, hyperiviscosity syndrome을 나타내기도 하는데 약 10%의 환자에서 전신적인 amyloidosis를 보인다. 진단은 골수생검상 골수의 plasmacytosis가 10% 이상이면서 혈장이나 뇨전기영동법에서 monoclonal globulin peak이 있을때 가능하다. 여러 학자들은 처음에는 독립적인 고립성 병소로 나타났다가 장기적으로 다발성골수종으로 이행됨을 주장하면서 장기적인 추적을 권하고 있지만 골내 고립성 형질세포종(solitary plasmacytoma in bone), 수질외 형질세포종(extramedullary plasmacytoma) 등은 다발성골수종과는 다른 질환이라 주장하는 등 아직 많은 논란이 있는 형편이다. 치료는 4000~6000 rad의 방사선치료와 여러가지 약제의 복합적인 항암요법이 사용되고 있으며 국소적인 병소의 경우 외과적 절제술이 추천되기도 한다.

저자들은 59세 여자환자에서 하악골에 발생된 다발성골수종을 치험하였기에 문헌고찰과 함께 보고하는 바이다.

주요어 ; 다발성골수종, 형질세포, 항암요법

I. INTRODUCTION

Multiple myeloma or plasma cell myeloma is a malignancy of plasma cells with many disease manifestations, and it is one kind of plasma cell neoplasms which are derived from bone marrow stem cells of B lymphocyte lineage which are functionally differentiated to produce and secrete immunoglobulin. Because these tumors are derived from a single neoplastic clone, they are associated with the production of monoclonal immunoglobulin components, with the immunoglobulin light chain restricted to either the kappa or the lambda type. These tumors may present in soft tissue as extramedullary plasmacytoma, in bone as a solitary lytic lesion known as a plasmacytoma of bone, or most commonly, as part of the multifocal disseminated disease multiple myeloma. Multiple myeloma is a disease of the hematopoietic marrow-bearing bone of the skeleton, but 70~95% of these patients have also had radiographic involvement of the bones of the maxilla or mandible.

This is a report of a case about 59-year-old female patient with multiple myeloma treated by chemotherapy and radiation therapy. We obtained the poor treatment result, so I represents the case with literatural reviews.

II. CASE REPORT

The patient was 59 years old and had received an operation due to colon carcinoma(Adenocarcinoma) 3 years ago and she had been diagnosed as multiple myeloma by hyperglobulinemia in that time. So she had been treated with combined chemotherapy using VBAP (#2 cycle) and VAD(#16 cycle) from August, 1992 to June, 1995. She visited emergency room of Seoul national university hospital because of constant postoperative bleeding since the left mandibular second molar was extracted in a local dental clinic dut to pain and mobility 2 days ago. In that time, chief complaints were pain and swelling, local heat, tenderness in left mandibular angle area. Left mandibular first molar showed mobility(++) and positive response on percussion(++). In laboratory finding, PT was 103%, BT was 3min, RBC was 3.93 and BUN was 8. Although she had received combined chemotherapy for 3 years, multiple myeloma was slowly progressive and didn't response well to chemotherapeutic agents. During the chemotherapy, copression frature occured in thoracic and lumbar vertebare(T11-L4) and received radiation therapy in that area(3000Gy) conservatively. She had Cushing syndrome with adrenal insufficiency by long-term steroid therapy with prednisolone because of bronchial asthma since December, 1994 and she showed moon face(Fig 1).

In skull P-A and panoramic views, there was wide radiolucent bone destruction in left mandibular body and angle area, and left mandibular first molar was in floating state by

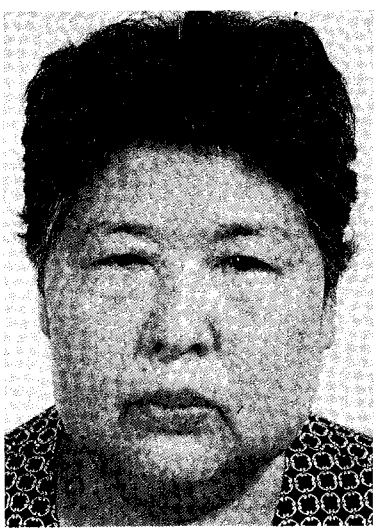

Fig 1. Facial photo : Swelling on left mandibular angle area, and moon face.

extended surrounding alveolar bone destruction and showed partial external root resorption(Fig 2 & Fig 3)

In MRI finding, left mandible was being destroyed by the mass(4×2.5cm) in angle area, and showed isosignal intensity in proton and T1, T2 axial image and the mass wasn't enhanced. There was local area in central mass which showed high signal in proton and T2W1, low signal in T1W1 with uncertain border, and it seemed to be focal high vascularity(Fig 4). In ultrasonographic finding, there was no abnormal lymphadenopathy in both submandibular, submental and internal jugular vein area.

The patient was discharged after conservative treatment in extraction area. During the follow-up in out-patient department, multiple frature occured in right femur and left tibia and fibula due to fall down on Octorber, 19th in 1995 and she was operated in department of orthopedic surgery on Novenber 4th, but she expired because of postoperative massive bleeding, disseminated intravascular coagula-

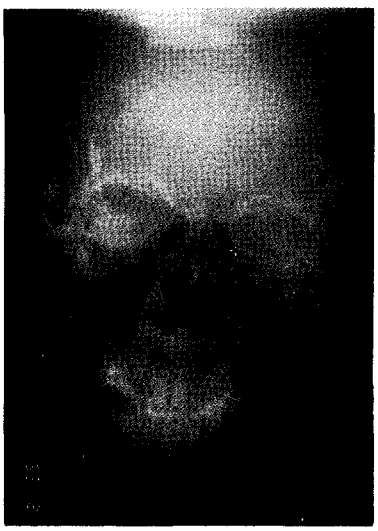

Fig 2. Skull P-A : Wide radiolucent bone destruction in left mandibular body and angle area.

Fig 3. Orthopantomogram : Floating of left mandibular first molar by extended surrounding alveolar bone destruction, and partial external root resorption.

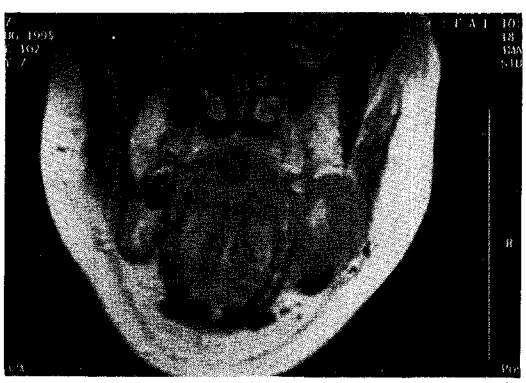

Fig 4. MRI : Bony destruction by the mass(4×2.5cm) in mandibular angle area.

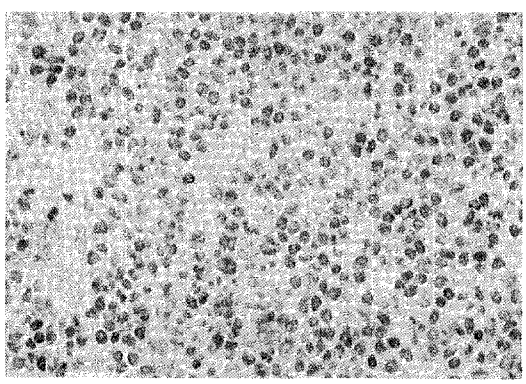

Fig 5. Histopathologic finding : Monotonous proliferation of pure plasma cells

tion and sepsis on December 4th.

III. DISCUSSION & SUMMARY

Multiple myeloma or plasma cell myeloma represenets a spectrum of disease which originates from a primary dyscrasia of plasma cell origin. It is generally felt that solitary myeloma of bone, extramedullary plasmacytoma, most frequently, multiple myeloma are different manifestations of the same basic process [1]. In 2~10% of patients, the disease is first manifested as a solitary lesion. Most will eventually develope multiple myeloma ; however, their course is often quite protracted, and patients may live for many years without evidence of dissemination. In the extramedullary plastomacytomas, 80% of patients have the lesion in the head and neck area such as the nasopharynx, nasal cavity, paranasal sinuses, and tonsils. They can be also found in gingivam palate, floor of the mouth, and tongue. Solitary plasmacytoma of bone is rare in the mandible and maxilla : it is generally found in the ribs, flat bones, vertebrae, pelvis and skull, where it produces extensive areas of patchy destruction.

Multiple myeloma can be rarely seen before fifth decade, and appears at a mean age of 63 years, and there is a slight male predomince[2]. It can involve the jaws asymptomatically or may produce pain, swelling, expansion, numbness, mobility of teeth, or pathologic fracture. Weakness, weight loss, anemia, and hyperviscosity syndromes can be developed in some patients. Roughly 10% of patients with multiple myeloma develope systemic amyloidosis. 85% of patients with multiple myeloma show an abnormal bony radiographic examination. Although the remaining patients have an apparently normal radiographic series, they demonstrate plasmacytosis on marrow aspirate or biopsy[2].

The most reliable diagnostic finding is bone marrow plasmacytosis exceeding 10%, in association with a monoclonal globulin peak on serum or urine electrophoresis. By serum protein elctrophoresis, most patients with myeloma have a decreased quantity of normal Ig and an abnormal monoclonal Ig protein peak known as an M spike[3]. The Ig is usually of the IgG or IgA class, with a monoclonal light chain component. Some plasma cell neoplasms may secrete only a monoclonal light chain. These monoclonal Ig components can be demonstrated by immunoelectrophoresis of both serum and urine in 91~97% of patients with myeloma. Urinary monoclonal light chains, so called Bence Jones proteinuria, may be detected by a less sensitive heat test in roughly half of myeloma patients. 2% of myeloma cases are non-secretory, although monoclonal Ig may be demonstrated within plasma cell cytoplasm by the immunoperoxidase method[2,4].

Radiographically, there are multiple sharply punched-out patchy destruction[5] but non-corticated radiolucency of bone destruction typically in multiple myeloma. Plasma cell tumors in the jaws may be expansile and on rare occasions may be osteosclerotic. The finding of a solitary plasma cell tumor in the jaws is more often a manifestation of systemic disease than is a solitary plasmacytoma of bone.

Histopathologically, all kind of plasma cell tumors have similar findings. Tumors are composed of a monotonous proliferation of pure plasma cells. The neoplastic plasma cells may have a wide range of differentiation, from mature-appearing plasma cells to less differentiated forms resembling immunoblastic large cell lymphomas. The abundant plasma cells within bone marrow can be distinguished from plasma cells of a chronic osteomyelitis or periapi-

cal grauloma by the associated proliferation of small vessels and fibroblasts with admixed neutrophils and macrophages in the reactive lesions. In addition, with the immunoperoxidase technigue, a monoclonal intracytoplasmic Ig light chain can be demonstrated in nearly all plasma cell neoplasms, whereas reactive plasma cell infiltrates are uniformly polyclonal.

Although there is a characteristic punched-out bony destruction, multiple myeloma should be differentially diagnosed with other malignancies of the maxilla and mandible such as metastatic carcinoma, lymphoma, idiopathic histiocytosis. So an accurate diagnosis is possible only with tissue biopsy or aspirate. In histopathologic finding, very poorly differentiated plasma cell neoplasm is similar with relatively undifferentiated malignant neoplasm such as lymphoma, leukemia, undifferentiated carcinoma, metastatic malignant melanoma, neuroblastoma, but lymphoma and leukemia can be differentially diagnosed by leukocyte common Ag on immunoperoxidase detection, carcinoma can be differentially diagnosed by cytokeratin, melanoma can be differentially diagnosed by S-100 protein and melanoma-associated Ag, and neuroblastoma by neuron-specific enolase.

Most patients of myeloma die of inection and, less commonly, of renal failure, disseminated myeloma, cardiac complications, and hematologic complications of hemorrhage or thrombosis. Since the availability of effective chemotherapy with alkylating agents, either alone or combination with corticosteroids, the survival time of patients with this disease has lengthened significantly. Local radiation directed to painful bone lesions can be used with chemotherapy. The overall mean survival is 20 months, with only 18% of patients surviving 5 years[1]. Indicators of poor prognosis are severe azotemia, hypercalcemia, and anemia[3,6]. It is known that 85% of patients of multiple myeloma have anemia[6]. Prognosis of chemotherapy has been known to be closely related with serum protein level, so the survival and remission times were longer for patients with only lambda chains in comparison with patients producing only kappa light chains[4]. Prognosis is not related with age, sex, race and the size of tumor mass. Because there is high recurrence rate in case of radiation therapy under 3000rad, it is recommended to use 4000~6000 rad of radiation by Meyer[1]. Serum protein leval(continued or increased paraprotein peak is considered as recurrence or progression of disease), Ig level (production of abnormal protein means lowering of normal Ig level), Bence Jones Protein level in urine(1mg/cc^3 or greater means recurrence) give an important information about recurrence of disease[7].

Solitary plasmacytoma of bone appeared in male adult, mainly in fourth decade. It rarely can be seen in mandible and maxilla, it can developed mainly in mandibular angle area[8]. It can be diagnosed when there is no plasmacytosis on bone marrow aspirate or biopsy in other area[6]. But it is known that 32~75% of the patients of solitary plasmacytoma of bone become the patients of multiple myeloma. Similarly with multiple myeloma, clinically solitary plasmacytoma of bone shows pain, swelling, pathologic fracture. It shows well-defined lytic lesion with occasional multilocular state similarly with central giant cell granuloma, but it can destroy surrounding cortical bone and extend to surrounding soft tissue. Differently from multiple myeloma, solitary plasmacytoma of bone has normal peripheral blood picture and differential chemistry. About 17~25% of patients have monoclonal Ig in serum or urine. Histopathologic finding of solitary plasmacytoma of bone is simi-

lar with multiple myeloma. Primarily the treatment of choice is local radiotherapy, surgical excision is recommended if possible[9]. Recurrence rate is about 10~15%, and mean survival time is 10 year, comparable to 20 months of multiple myeloma. So solitary plasmacytoma is considered as a biologically low-grade, slowly progressive form of multiple myeloma[1,10,11]. But there are a number of different opinions about this disease progression[12], and they recommend long term follow-up[1,10,11].

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