Postoperative Radiation Therapy in Ameloblastoma of the Jaw

—Report of Two Cases—

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=Abstract=

Ameloblastoma is a rare epithelial tumor of the jaw, comprising approximately 1% of all tumors and cysts of odontogenic origin. The tumor has been the subject of much controversy and discussion. Ameloblastoma is slow growing, locally invasive, and has a high rate of local recurrence, but rarely metastasizes.

This neoplasm has been considered radioresistant, so it has been treated with surgery primarily except some cases.

Recently it is suggested that ameloblastoma is radiosensitive, so radiation therapy (RT) would be used in addition to or, in certain cases, in place of surgery.

We report these two cases which were referred to the Department of Therapeutic Radiology for deciding the need of postoperative RT, because ameloblastoma is rare and has been known to be radioresistant. Postoperative RT was given to one of these two patients.

Key Words : Ameloblastoma, Postoperative Radiation Therapy, Jaw

INTRODUCTION

Ameloblastoma is a rare epithelial tumor of the jaw, comprising approximately 1% of all tumors and cysts of odontogenic origin, and is slowly growing odontogenic tumor[1-3]. Although the first complete description of these lesions is credited to Falkson(1879), it was not until 1933 that Churchill coined the term "ameloblastoma"[4]. Since then, this tumor has been the subject of much controversy and discussion. The W.H.O. Monogragh on International Histologic Classification of Tumors defines benign and malignant ameloblastomas separately. These can be combined to state that an ameloblastoma is an invasive, potentially malignant neoplasm consisting of proliferating odontogenic epithelium supported by fibrous stroma[5].

The age range is 20 to 50 years with the average age being 27 years, the male-to-female ratio is roughly 1:1, and there is no racial predominance. Eighty percents of cases occur in the mandible with the molar-ramus area at the third molar tooth being the most common site[1-3].

The exact origin of ameloblastoma is still essentially unknown. Grossly this tumor can be solid, cystic, or solid and cystic[6,7]. It is generally considered to originate from the enamel organ, epithelium of dentigerous cyst(or other odontogenic cysts), surface epithelial basal cells or remnants of the dental lamina, or Hertwigs sheath[7]. It has plexiform, follicular and mixed histologic patterns with 50% of ameloblastomas being mixed[7]. It is slow growing, locally invasive, and has a high rate of local recurrence. Its malignant potential is well-documented[5,7,8].

The only prognostically significant histologic

factor is that unicystic or cystogenic types are less aggressive especially if associated with impacted molar teeth[7,9]. As this tumor recurs, it becomes more clinically aggressive than sarcomas causing massive local destruction and metastases[7]. Recent literature has emphasized that this tumor rarely metastasizes. The tumor metastasizes most frequently to the lungs(75%); lymph nodes and bone are less common sites for tumor spread[10-12].

The presenting symptoms include facial deformity, swelling(75%), pain(33%), loosening of teeth, malocclusion, ill-fitting dentures or bridges, periodontal disease, and ulceration[7]. The most common complaint is a slow-growing painless swelling(75%).

Radiographically this lesion can be unilocular (more often seen in the maxilla), or multilocular, consisting of fusiform expansile radiolucencies (predominantly in the mandible)[7,13]. Solid tumors are also seen. Typically, plane radiographs reveal a coarsely trabeculated core of osseous destruction. Computed tomography(CT) scans and/or MRIs define the extent of lesion more clearly.

Ameloblastoma has been considered radioresistant and therefore has been treated with surgery except some cases[3,5,7]. Our two cases are the patients who were referred to the Department of Therapeutic Radiology for deciding the need of postoperative RT. Postoperative RT was given to one of these two patients. This report presents two cases of ameloblastoma which were referred to the Department of Therapeutic Radiology for deciding the need of postoperative RT with a literature review of treatment modalities to this tumor and our diagnostic and therapeutic experiences at the Chosun University Hospital.

CASE REPORT

Case No. 1.

A 25-year-old male patient presented with a 4-month history of severe buccal gingival swelling at the left upper molar area and masticatory difficulty. On physical examination, there was evidence of tooth mobility of left upper first and second molar(#26, #27) teeth and buccal gingival fluctuation.

Orthopantomogram demonstrated destruction of left maxillary sinus wall, root resorption of left upper premolar, first molar and second molar root apex, and radiolucency of their root area. Water's view revealed complete destruction with increased radiopacity in the left maxillary sinus wall and impacted left upper third molar tooth. Also, the border of the lesion was not distinct.

Treatment involved a left Caldwell-Luc approach with removal of a tumor mass. The left orbital floor was intact. But the lateral wall of left maxillary sinus showed erosion by mass and posterior and medial walls were perforated by mass, so maxillary sinus communicated with pterygopalatine fissure and nasal cavity. Ethmoid sinus was also involved. Pathologic examination revealed maxillary ameloblastoma(follicular & plexiform type). Postoperatively the patient did well except oroantral fistula formation. Fistula was treated by buccal fat pad pedicled graft at 10 months after surgery. On follow-up at 22 months after surgery there was no evidence of tumor recurrence. Postoperatively he was consulted for RT. But RT was not done because he was young and it was benign ameloblastoma and the surgeon had a chance of reoperation in a case of recurrence. We planned to perform postoperative RT after resection in case of recurrence during forthcoming follow-ups.

Case No. 2.

A 41-year-old man was admitted with a history of swelling on buccal mucosa of right lower second molar region and discomfort during mastication. A hard round bony elevation was palpated. The roentgenogram showed a radiolucent lesion at the apical area of right lower second molar tooth(Fig. 1). He underwent en bloc resection of tumor with iliac bone graft, and the pathologic diagnosis was the ameloblastoma of

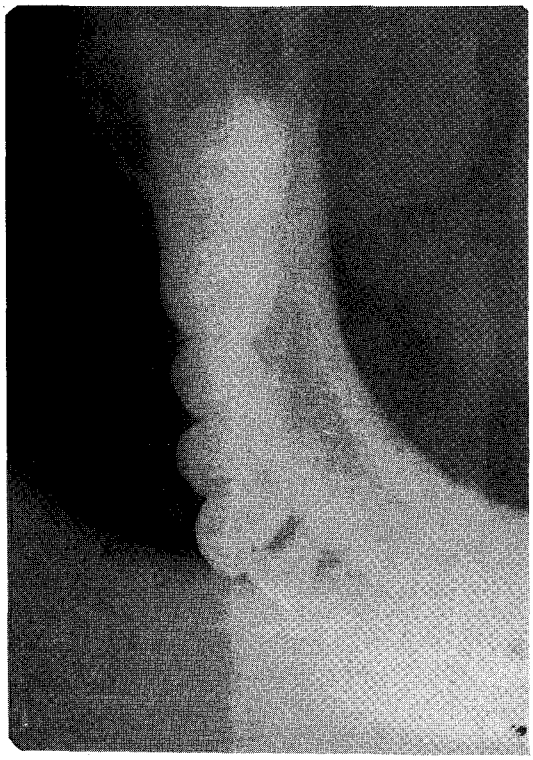

Fig. 1. Roentgenogram showing a radiolucent lesion at the apical area of right lower second molar tooth.

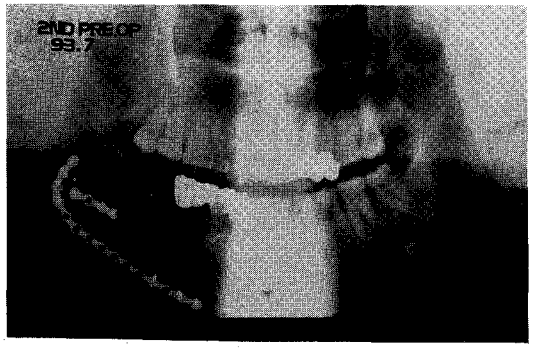

Fig. 2. Panoramic view revealing the radiolucent area at the previous operation site of right mandible diagnosed as the recurrence.

the mandible. Thereafter the follow-up was conducted regularly. Four years later, the follow-up panoramic view revealed the radiolucent area at

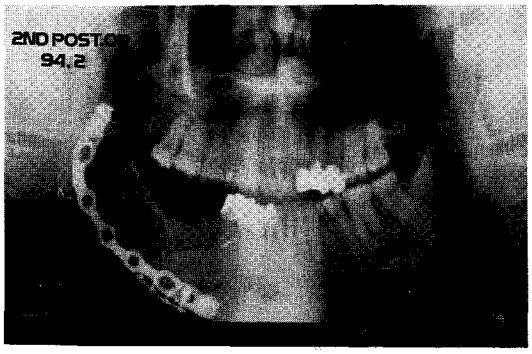

Fig. 3. Panoramic view at 3 months after the second operation and postoperative RT.

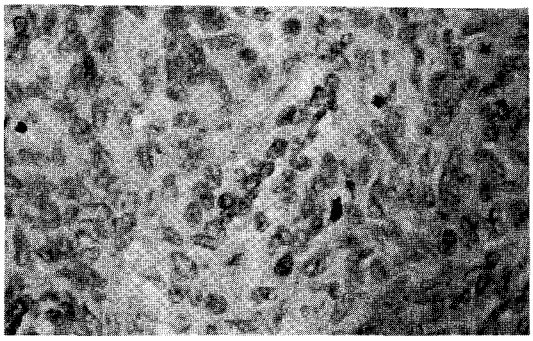

Fig. 4. Histologic section of malignant ameloblastoma showing cellular malignant changes.

the previous operation site of right mandible and diagnosed as the recurrence(Fig. 2). Subsequently he underwent the mandibulectomy and reconstruction with iliac bone marrow, resected autogenous autoclaved bone, and compression plate(Fig. 3). The biopsy was malignant ameloblastoma(Fig. 4). The ECOG(Eastern Cooperative Oncology Group) performance status was grade 1. He was referred for postoperative RT. Because the lesion was malignant and recurrent, postoperative RT was administered to the previous recurrent mass area using Co-60 teletherapy unit(Picker Company). RT started at post-op 7 weeks because of delayed wound healing from second extensive surgery. The left parotid gland was protected as much as possible. We used the 45° pair-wedged right lateral and anterior

fields with field size of 9×11cm (right lateral) and 8×10cm (anterior) with weighing for right lateral. After 3960cGy the spinal cord was shielded and the right lateral field was anteriorly angulated. The patient was treated with 1.8Gy/fraction to a total dose of 5040cGy/28 fractions in 38 days.

During treatment the patient developed a mucositis in the oral cavity at the dose of 2700cGy and a small ulcerative area(0.7cm) in the buccal mucosa near the right retromolar trigone at the dose of 4680cGy. The mucositis improved rapidly after the end of RT, and the small ulcerative lesion was also healed completely at 3 months after finishing RT. Since the second operation, no further tumor recurrence has been noted for 12 months.

DISCUSSION

Extensive review of the literature undertaken by Small and Waldron(1955) indicates that approximately 80% of the ameloblastomas are present in the mandible with 70% of them occurring in the region of molar ramus and 20% in the maxilla[3]. The biological behavior of this tumor is well known in that it is slow growing, locally invasive tumor with a high rate of recurrence if not removed adequately.

Our two cases are the patients who were referred to the Department of Therapeutic Radiology for deciding the need of postoperative RT. To know more about malignant ameloblastoma, following 'classification is presented. Elzay initially proposed classifying primary jaw intraosseous carcinomas as follows: type 1: arising ex odontogenic cyst; type 2: arising ex ameloblastoma(A) well differentiated(malignant ameloblastoma), (B) poorly differentiated (ameloblastic carcinoma): type 3: arising de novo (A) nonkeratinizing, (B) keratinizing[14-16].

Patients typically undergo surgical resection of primary tumor with no further treatment[7]. If recurrences or metastases occur, they often have multiple reoperations with the tumor becoming more aggressive after each resection[7]. The surgical approach has even recently advocated for treating metastatic disease. A recent paper by Laughlin stated that after reviewing 43 cases, surgical removal is preferred for treating metastasis[8]. But it should be noted that in their cases report the patient at one point was treated to the axilla(27Gy) and gluteal region(39.6 Gy) with external beam radiation. The axillary mass disappeared and the gluteal mass became less painful.

The surgical treatment of ameloblastoma has varied from time to time and from surgeon to surgeon from a conservative to a radical excision [5,6,17]. There is an increased tendency toward the radical resection[5,6]. This may be combined with a primary bone graft.

Sehdev et al. analyzed the results of various treatment modalities in 72 patients with ameloblastoma of the mandible and 20 patients with ameloblastoma of maxilla[5]. Controversial methods of treatment are discussed to arrive at a semblance of rational management. It was found that: 1. Curettage was followed by local recurrence in 90% of mandibular and all maxillary ameloblastoma; 2. Subsequent resection could control 80% of mandibular but only a fraction of maxillary recurrences; 3. Marginal resection, in a few selected cases, might control primary cases of mandibular ameloblastoma but is not a useful procedure for recurrent mandibular ameloblastoma; 4. External RT was ineffective in controlling ameloblastoma but did not seem to adversely affect prognosis even after subsequent resection; and 5. Distant metastases, although rare, occurred in 7 patients.

Advanced maxillary ameloblastoma is quite difficult to control due to the anatomical complexities of the maxilla and the invasive nature of the tumor.

A review of the literature about maxillary ameloblastoma demonstrates that many reports support the concept of radical therapy, while others still propose more conservative approaches to control ameloblastoma[4]. Sehdev et al. characterize the controversy with their state-

ment, "Vitriolic arguments for and against conservative and radical excision abound with no clearcut criteria for preference of either"[4,5]. Although the issue of treatment modalities has not been settled, substantial evidence in the literature attests to the aggressiveness of these tumors. Tsaknis and Nelson demonstrated a 50% recurrence rate for the 19 patients in their study who were treated by local excision or curettage [18]. Small and Waldron had similar results with recurrence in 46% of their cases that underwent local removal or currettage[3].

Scaccia et al suggest that although limited, their experience indicates that for complete extirpation of maxillary ameloblastoma, radical surgery, including skull base resection is indicated in operable cases and offers the best possibility of cure[4]. The possible exception to this is that of tumor confined within the walls of a well-defined dentigerous cyst. Recurrence of tumor was almost universally cited as a poor prognostic factor[4]. In their 13 patients who developed recurrences, Sehdev et al found that only 36% could be salvaged by partial or total maxillectomy. They also observed that all of the patients in their study with ameloblastoma who received external irradiation or curettage as initial treatment developed recurrences[4,5].

Radiation therapy has rarely been used for primary treatment of ameloblastoma and many of these have been done with orthovoltage. Many physicians consider ameloblastomas to be radioresistant[7,8] and in fact, as previously noted, over half of the radiation oncologists surveyed recently would not treat this tumor. Other studies published in the megavoltage era confirm the radiosensitivity of this tumor[7,19].

Atkinson et al in 1984, reported 10 cases treated with megavoltage irradiation, seven with irradiation alone, and three in combination with surgery[19]. No recurrences were reported in the preoperative(one patient) and postoperative (two patients) patients, although the follow-up period was short(27 months, 30 months and 5 years, respectively). In those patients who received RT alone, all had an initial response. Of seven patients not receiving surgery, four had complete responses and one had locally controlled disease for 10 years,but died of a cerebral infarct, and two had persistent disease with later progression. They felt megavoltage irradiation would be useful in the management of these tumors particularly in those cases where full surgical excision would be technicallly difficult because of bulk and local invasion or where other medical factors, including age, would make radical surgery inappropriate. They felt a total dose of 45 Gy in 4 weeks would seem appropriate.

Gardner published a report of five cases, that were treated with radiotherapy[20]. Three patients were treated with megavoltage irradiation and two with orthovoltage. He concluded that "although radiotherapy can reduce the size of an ameloblastoma, primarily that part of the tumor which has expanded the jaw or broken into the soft tissues, it does not appear to be an appropriate treatment for an operable ameloblastoma. Its main use is in inoperable cases, primarily in the posterior maxilla".

Miyamoto et al. suggest that ameloblastomas are radiosensitive and therefore RT should be used in addition to or, in certain cases, in place of surgery[7]. The instances where it would be most indicated are postoperatively in incompletely resected tumors, preoperatively to increase the rate of resectability, in areas where surgical resection would be markedly disfiguring , and when the patient either refuses or will not tolerate surgery. This applies to primary, recurrent, and metastatic disease. Careful planning, adequate doses, and patient fixation devices must be utilized. Doses of at least 45-50Gy in 4 to 5 weeks using 1.8Gy fractions are probably necessary to control the tumor[7].

We report these two cases because ameloblastoma is rare and has been known to be radioresistant. We suggest that megavoltage irradiation would be used in combination with surgery or alone for selective cases of ameloblastomas to improve local control and decrease

local recurrence.

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국문초록=

하악부 에나멜모세포종의 수술후 방사선치료

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에나멜모세포종(ameloblastoma)은 하악부에 드물게 생기는 상피성 종양으로서 치원성(齒原性)의 모든 종양과 낭(囊)의 약 1%를 차지한다. 이들은 서서히 자라는 종양이지만 국소적으로 침습성을 보이고 높은 재발율을 나타낸다. 반면에 원격전이는 드물다.

에나멜모세포종은 방사선에 저항적이라고 알려져 있었기에 드문 경우들외에는 주로 수술적 요법으로 치료되어져 왔다.

그러나 최근에 에나멜모세포종이 방사선에 반응을 보이므로 수술과 병용하거나 방사선치료 단독으로 치료에 쓰일 수도 있다는 보고들이 나왔다.

저자들은 수술후 방사선치료 여부를 결정하기 위해 본 치료방사선과에 의뢰된 2예의 에나멜모세포종 중 1예에서 수술후 방사선치료를 실시하였기에 이들 2예를 문헌고찰과 함께 보고하는 바이다.