Proton Beam Therapy for Ameloblastic Carcinoma of the Maxilla: Report of a Rare Case

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Ameloblastic carcinoma (AC) is a rare malignant odontogenic tumor that combines the histologic features of ameloblastoma with those of cytologic atypia. The standard treatment for this lesion is wide local excision. Proton beam therapy (PBT) can deliver high irradiation doses to the target and avoid irradiation to surrounding normal tissues, but no reports of PBT for AC have been published thus far. This report describes the case of a 70-year-old woman with a pathologic diagnosis of maxillary AC who refused surgical resection and received hypofractionated PBT at a total dose of 69 Gy in 23 fractions. She has been alive for more than 5 years after PBT without any evidence of recurrence and side effects. This is the first reported case of successful treatment after curative radiation therapy for maxillary AC.

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Ameloblastic carcinoma (AC) is a rare malignant odontogenic tumor, with fewer than 200 reported cases.[1] AC combines the histologic features of ameloblastoma with those of cytologic atypia regardless of whether it has metastasized. The standard treatment for the disease is wide local excision with cervical lymph node dissection, but the efficacy of radiotherapy (RT) or chemotherapy seems limited.[2] There are some case reports describing RT treatment using gamma ray, x-ray, and carbon ions[3-6] but no reports on the use of proton beam therapy (PBT) for AC. The main role for RT is adjuvant or salvage treatment after surgery. Patients treated with conventional external-beam radiation have been reported to have long-term control for more than 10 years after treatment with relatively few side effects. The present report describes the first case of successful treatment by PBT for AC of the maxilla.

Report of Case

A 70-year-old woman was referred to the authors' department in 2012. She had a 2-month complaint of a tumor in her left maxillary gingiva. Her medical history disclosed uterine fibroids and goiter. Examination of the oral cavity showed a soft elastic mass measuring approximately 20 × 15 mm adjacent to the left molar region of the maxilla (Fig 1), but she did not complain of trismus. T2- weighted magnetic resonance (MR) images showed a 43- × 22- × 21-mm high-intensity tumor located at the posterior of the maxillary sinus that extended to the pterygomaxillary fossa. There was no cervical lymph node metastasis (Fig 2). A biopsy specimen from the maxillary gingiva was obtained under local anesthesia and histopathologically showed basal cell-like tumor cell growth, irregular nests, and peripheral tumor cell nests with penetrating palisades.

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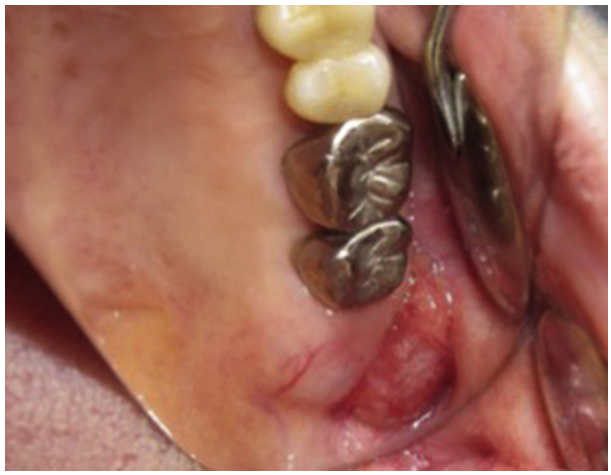

FIGURE 1. Examination of the oral cavity. Intraoral examination showed a soft elastic mass measuring approximately 20 × 15 mm in the posterior left molar region of the maxilla.

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Inside the nest, tumor cell density was low and tumor cells exhibited pleomorphism and a stellate reticulum-like structure. Mitotic figures differed in size and showed moderate to severe nuclear atypia. Nuclear mitosis was frequently observed (>10 per 10 high-power fields). Based on these histopathologic findings, her tumor was confirmed as AC (Fig 3).

The cancer board recommended curative surgical resection of her tumor, but she refused and wanted to receive definitive RT as an alternative treatment. Radiation oncologists explained the characteristics of photon RT and PBT, and she selected PBT for her treatment. Hypofractionated PBT at a total dose of 69 Gy in 23 fractions with a fractional dose of 3 Gy over 5 weeks, equivalent to 74.5 Gy with a conventional fraction dose of 2 Gy when using the linear-quadratic model (α/β = 10), was performed. PBT was planned using a 3-dimensional planning system based on computed tomographic (CT) images with 5-mm slice thickness. The patient was immobilized in a supine position under a thermoplastic mask. The initial clinical target volume included a visible tumor with 10-mm margins in all directions and the left maxillary sinus, and PBT fields were decreased incrementally 3 times (Fig 4).

Treatment was uneventful except for grade 2 dermatitis and stomatitis that occurred at 40 Gy. Five years after PBT, the patient is still alive with neither recurrence nor side effects. MR images depicted slight hypertrophy of the sinus mucosa that has remained unchanged for 5 years since PBT (Fig 5). She continues to receive follow-up examinations.

Discussion

AC was systematically reviewed by Saluja and Hosalkar[1] (153 cases). The 2005 World Health Organization (WHO) classification divides AC into primary and secondary (intraosseous and peripheral) types. Most cases of AC appear to arise de novo, but some cases have been reported to arise from pre-existing ameloblastoma. Although the present case was consistent with primary-type AC, this subclassification might be unnecessarily complex for a rare lesion, and the 2017 WHO classification lists a single diagnostic entity

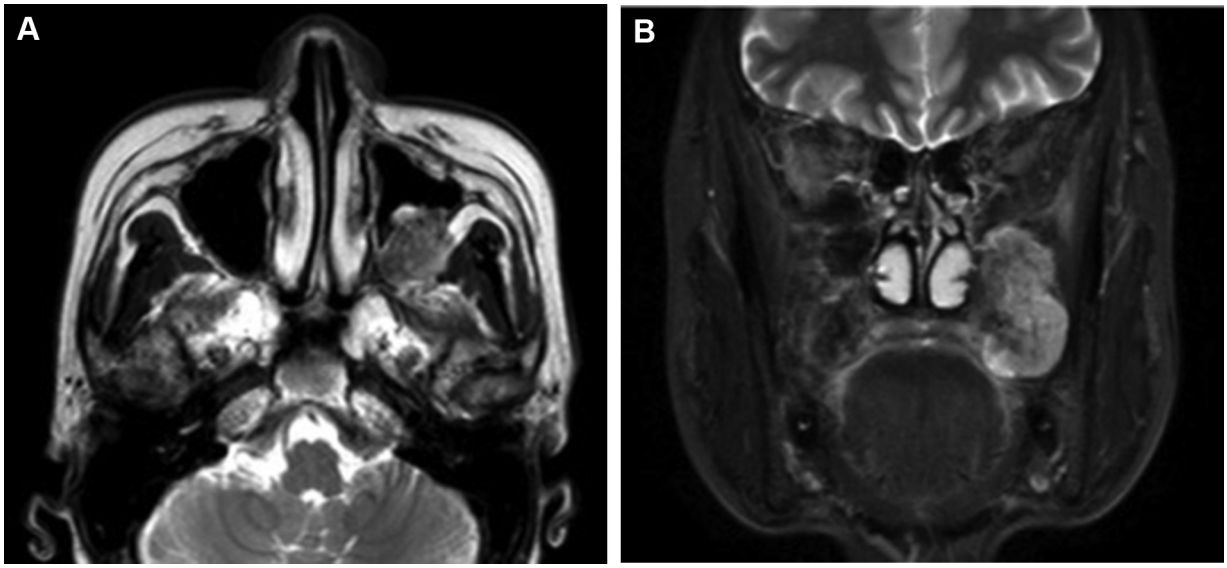

FIGURE 2. Magnetic resonance imaging findings. *A*, Axial T2-weighted and *B*, coronal short T1 inversion recovery images depicted a 43- × 22- × 21-mm mass with high signal intensity. The mass was located at the posterior of the maxillary sinus and extended to the pterygomaxillary fossa.

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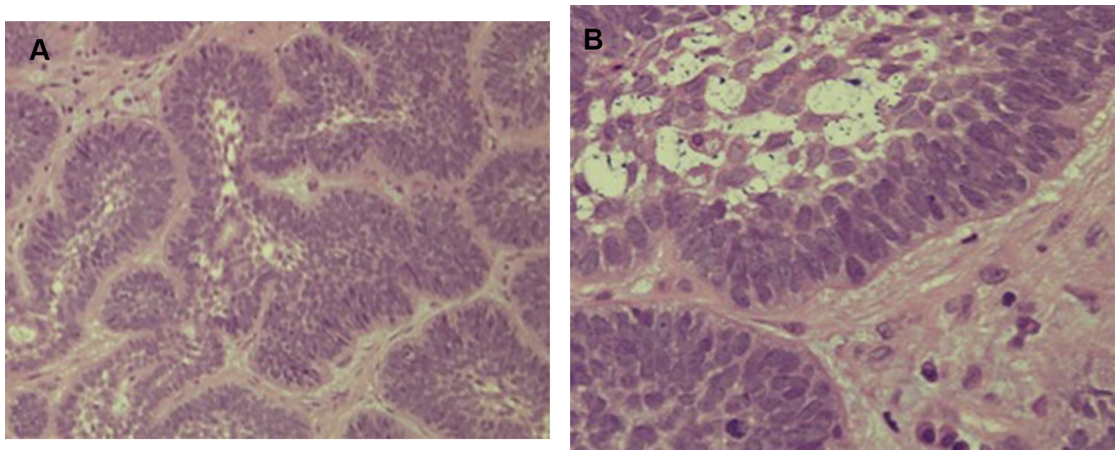

FIGURE 3. Pathologic findings at *A*, low- and *B*, high-power magnification (hematoxylin and eosin stain). The basal cell-like tumor cell growth showed irregular nests and peripheral tumor cells of penetrating palisade nests. A follicular-growth pattern was observed with stellate reticulum-like tumor cells. The mitotic figures were different in size and showed moderate to severe nuclear atypia, with frequent nuclear mitosis (>10 per 10 high-power fields).

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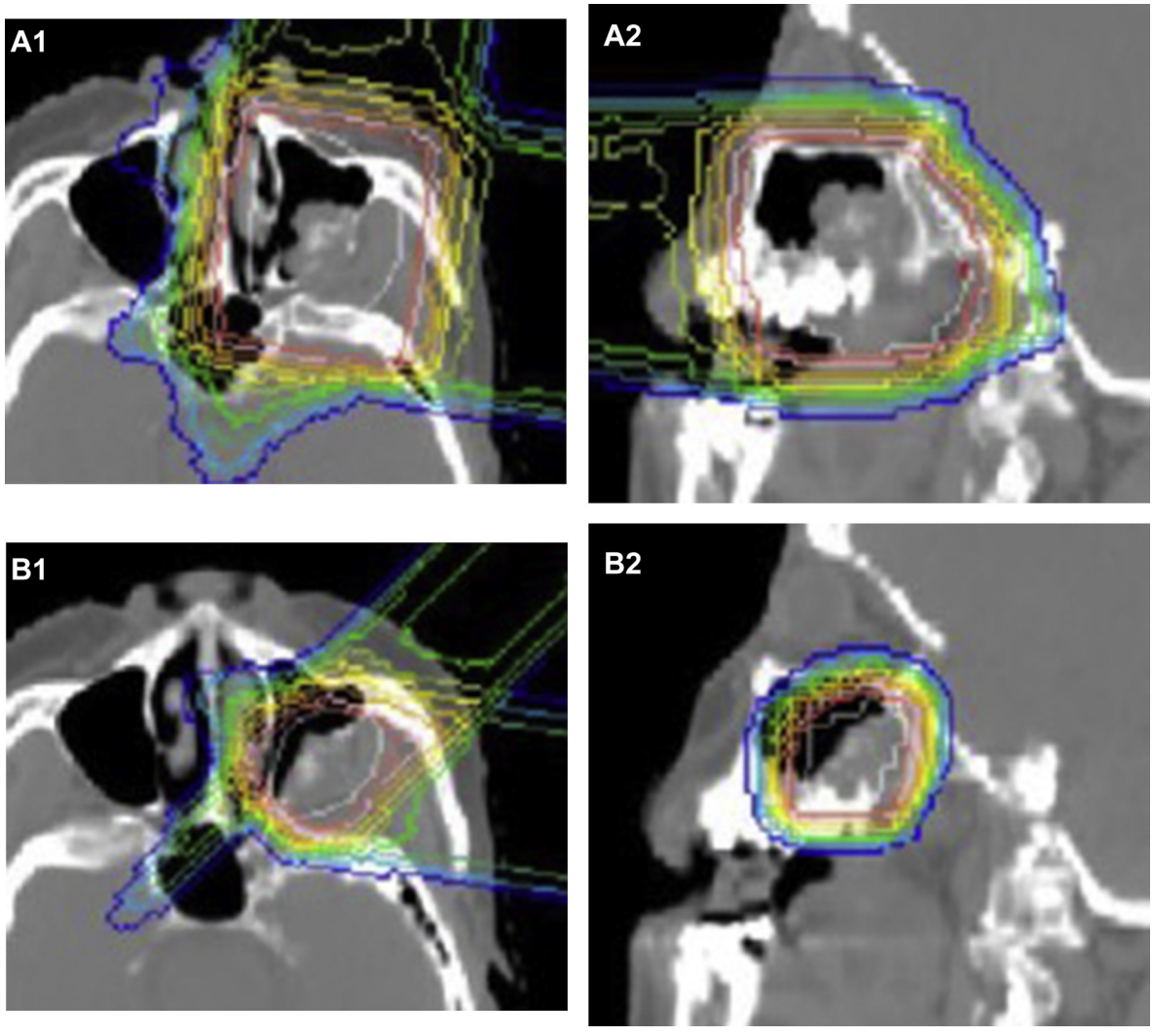

FIGURE 4. Proton beam therapy dose distribution of 69 Gy in 23 fractions (equivalent dose, 74.5 Gy). *A1*, Initial treatment plan (axial view). *A2*, Initial treatment plan (lateral view). *B1*, Final (fourth) treatment plan (axial view). *B2*, Final (fourth) treatment plan (lateral view).

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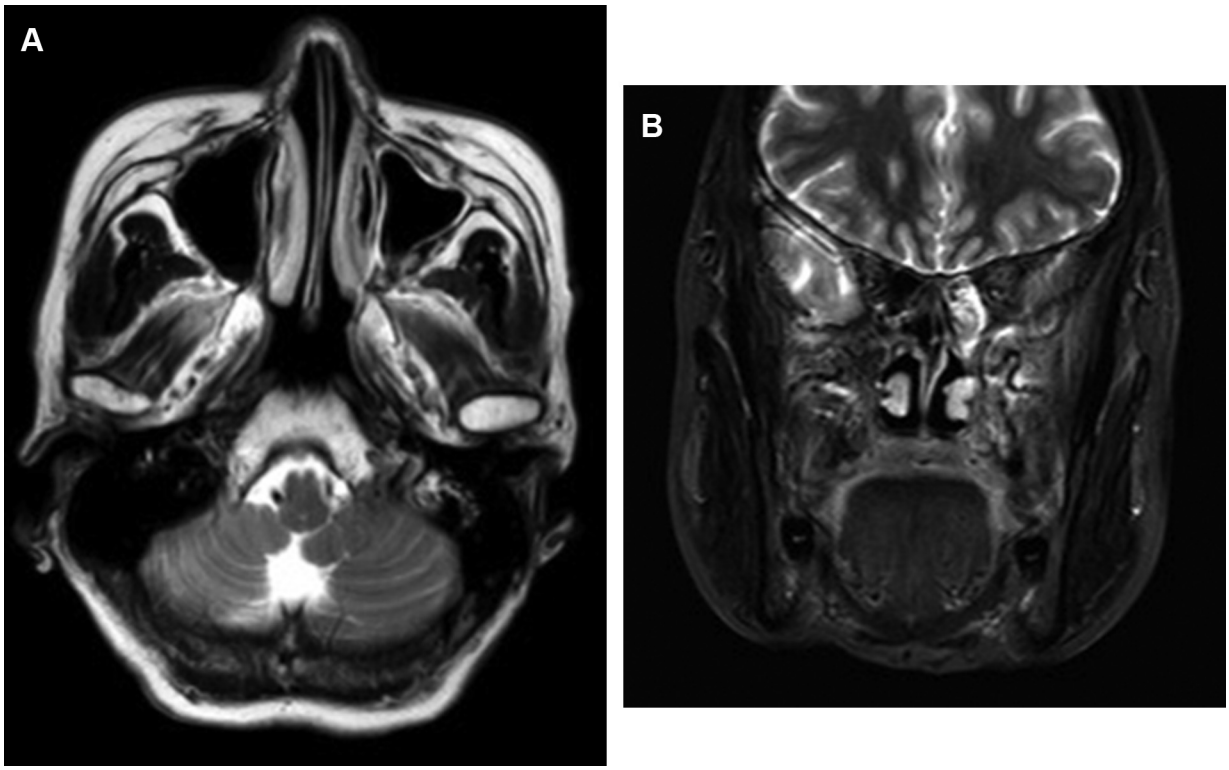

FIGURE 5. Follow-up magnetic resonance imaging 5 years after proton beam therapy. *A*, Axial T2-weighted and *B*, coronal short T1 inversion recovery images showed slight hypertrophy of the sinus mucosa, which did not change during the 5-year follow-up period.

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of AC but acknowledges different histologic features.[7] AC presents different clinical features in the maxilla and mandible and has a lower incidence in the maxilla than in the mandible.[8] Maxillary AC lesions appear to occur slightly later in life (average age, 56.7 years) than mandibular AC lesions.[9] Although AC lesions tend toward aggressive local growth and local relapse, distant metastases are uncommon.[10] In the present case, the patient was older than the average age in previously reported cases, and the AC did not exhibit aggressive growth and relapse.

When AC arises de novo, diagnosis can be difficult because it must be differentiated from primary intraosseous squamous cell carcinoma, metastatic carcinoma of the jaw, and central high-grade mucoepidermoid carcinoma. Therefore, histologic features typical of ameloblastoma, such as peripheral palisading, reverse polarity, and a stellate reticulum-like structure, provide clues to a diagnosis of AC.[11] Although the present case arose de novo, the diagnosis was not particularly difficult because of the peripheral palisading, stellate reticulum-like structure, and frequent nuclear mitosis.

The most favorable treatment for AC is believed to be early surgical management with or without RT or chemotherapy, determined by the site and extent of

Table 1. REPORTED NONCONVENTIONAL RADIOTHERAPY TREATMENTS FOR AMELOBLASTIC CARCINOMA

Patient	Study (yr)	Age (yr)/Gender	Treatment	Dose (Gy/Fr)	Prognosis	Duration
1	Jensen et al[4] (2011)	71/M	Carbon ion therapy	60/20	Alive	3 mo
2	Perera et al[3] (2013)	35/M	Gamma knife stereotactic radiosurgery	16/1	Death from cancer	2.5 yr
3	Koca et al[6] (2014)	35/M	Helical tomotherapy	60/—	Alive	1 yr
4	Takahashi et al[5] (2016)	58/M	Helical tomotherapy	25/1	Alive	19 mo
5	Present case (2018)	70/F	Proton beam therapy	69/23	Alive	5 yr

Abbreviations: F, female; Fr, fractions; M, male.

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the tumor,[1] because it produces the longest mean survival time (140 months; 95% confidence interval [CI], 106-174) compared with RT (17.5 months; 95% CI, 2.95-32.1) and chemotherapy (8 months; 95% CI, 8-8).[1] The main role for RT is adjuvant or salvage treatment after surgery,[2] and patients treated with postoperative conventional RT often have long-term local control for more than 10 years with relative few late sequelae.[12] However, outcomes of nonconventional RT for each of 2 cases with recurrences or residual tumors after surgery have been reported as case presentations (Table 1). Jensen et al[4] reported on a successful case treated with carbon ion therapy for recurrent AC, but the follow-up period was very short (3 months). Perera et al[3] reported on the use of gamma knife stereotactic radiosurgery for AC, with a survival of 2.5 years from treatment without disease at the treated site. Helical tomotherapy, a unique intensity-modulated RT delivery system, was performed for 2 cases of AC for the postoperative treatment of residual tumors.[5,6] The 4 cases were treated with miscellaneous dose fractionation schedules at different total doses ranging from 16 to 60 Gy and followed for 3 to 30 months. In the present case, a prescribed PBT dose was initially set at 60 Gy in 20 fractions, but the tumor remained visible on CT images after 51 Gy. Therefore, the authors added a boost PBT of 9 Gy in 3 fractions directed at shrunken fields covering only tumors without any margins (Fig 4). This is the first report showing a successful case treated with definitive RT as initial treatment, and this patient has been followed for the longest period (>5 years) without any recurrences. Furthermore, no severe acute or late complications were observed. This result suggests that PBT can be used to manage AC in patients who are regarded as not only medically inoperable but also suitable for curative surgery. Further experience could show the efficacy of PBT for patients with AC in the future.

References

1. Saluja TS, Hosalkar R: Reconnoitre ameloblastic carcinoma: A prognostic update. Oral Oncol 77:118, 2018
2. Benlyazid A, Lacroix-Triki M, Aziza R, et al: Ameloblastic carcinoma of the maxilla: Case report and review of the literature. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 104:e17, 2007
3. Perera E, Lindquist C, Hughes C, Thomas S: The use of gamma knife stereotactic radiosurgery in the treatment of ameloblastic carcinoma. Int J Oral Maxillofac Surg 42:934, 2013
4. Jensen AD, Ecker S, Ellerbrock M, et al: Carbon ion therapy for ameloblastic carcinoma. Radiat Oncol 6:13, 2011
5. Takahashi Y, Bandoh N, Miyamoto A, Kamada H: Single-fraction helical tomotherapy for ameloblastic carcinoma. J Oral Maxillofac Surg 74:302, 2016
6. Koca T, Basaran H, Arslan D, et al: Prominent response with helical tomotherapy in recurrent ameloblastic carcinoma of maxillary sinus: A case report. Radiat Oncol 9:157, 2014
7. Speight PM, Takata T: New tumour entities in the 4th edition of the World Health Organization Classification of Head and Neck Tumours: Odontogenic and maxillofacial bone tumours. Virchows Arch 472:331, 2018
8. Kruse AL, Zwahlen RA, Gratz KW: New classification of maxillary ameloblastic carcinoma based on an evidence-based literature review over the last 60 years. Head Neck Oncol 1:31, 2009
9. Dhir K, Sciubba J, Tufano RP: Ameloblastic carcinoma of the maxilla. Oral Oncol 39:736, 2003
10. Avon SL, McComb J, Clokie C: Ameloblastic carcinoma: Case report and literature review. J Can Dent Assoc 69:573, 2003
11. Yoon HJ, Hong SP, Lee JI, et al: Ameloblastic carcinoma: An analysis of 6 cases with review of the literature. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 108:904, 2009
12. Kennedy WR, Werning JW, Kaye FJ, Mendenhall WM: Treatment of ameloblastoma and ameloblastic carcinoma with radiotherapy. Eur Arch Otorhinolaryngol 273:3293, 2016