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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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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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 ($\alpha/\beta = 10$), 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 Hosalkar1 (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 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).


of AC but acknowledges different histologic features. AC presents different clinical features in the maxilla and mandible and has a lower incidence in the maxilla than in the mandible. Maxillary AC lesions appear to occur slightly later in life (average age, 56.7 years) than mandibular AC lesions. Although AC lesions tend toward aggressive local growth and local relapse, distant metastases are uncommon. 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. 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 (2011) | 71/M | Carbon ion therapy | 60/20 | Alive | 3 mo |
| 2 | Perera et al (2013) | 35/M | Gamma knife stereotactic radiosurgery | 16/1 | Death from cancer | 2.5 yr |
| 3 | Koca et al (2014) | 35/M | Helical tomotherapy | 60/- | Alive | 1 yr |
| 4 | Takahashi et al (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.

the tumor, 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). The main role for RT is adjuvant or salvage treatment after surgery, and patients treated with postoperative conventional RT often have long-term local control for more than 10 years with relative few late sequelae. 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 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 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. 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