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CLINICAL OUTCOME OF SACRAL CHORDOMA WITH CARBON ION RADIOTHERAPY COMPARED WITH SURGERY

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Purpose: To evaluate the efficacy, post-treatment function, toxicity, and complications of carbon ion radiotherapy (RT) for sacral chordoma compared with surgery.

Methods and Materials: The records of 17 primary sacral chordoma patients treated since 1990 with surgery ($n = 10$) or carbon ion RT ($n = 7$) were retrospectively analyzed for disease-specific survival, local recurrence-free survival, complications, and functional outcome. The applied carbon ion dose ranged from 54.0 Gray equivalent (GyE) to 73.6 GyE (median 70.4).

Results: The mean age at treatment was 55 years for the surgery group and 65 years for the carbon ion RT group. The median duration of follow-up was 76 months for the surgery group and 49 months for the carbon ion RT group. The local recurrence-free survival rate at 5 years was 62.5% for the surgery and 100% for the carbon ion RT group, and the disease-specific survival rate at 5 years was 85.7% and 53.3%, respectively. Urinary-anorectal function worsened in 6 patients (60%) in the surgery group, but it was unchanged in all the patients who had undergone carbon ion RT. Postoperative wound complications requiring reoperation occurred in 3 patients (30%) after surgery and in 1 patient (14%) after carbon ion RT. The functional outcome evaluated using the Musculoskeletal Tumor Society scoring system revealed 55% in the surgery group and 75% in the carbon ion RT group. Of the six factors in this scoring system, the carbon ion RT group had significantly greater scores in emotional acceptance than did the surgery group.

Conclusion: Carbon ion RT results in a high local control rate and preservation of urinary-anorectal function compared with surgery. © 2011 Elsevier Inc.

Chordoma, sacrum, carbon ion radiotherapy, surgery.

INTRODUCTION

Chordomas are rare malignant tumors arising from embryonic notochordal remnants. They account for only 1–4% of all primary malignant bone tumors (1, 2) and 17.5% of primary malignant tumors of the axial skeleton, with a reported incidence of 0.5 to 0.8/1,000,000 persons (3, 4). Lesions can arise from the sacrococcygeal region (47%), skull base (38%), and vertebral bodies (15%) (5, 6). Many sacral chordomas are quite large at diagnosis and can involve adjacent neurovascular structures and vital organs owing to their deep location within the pelvic cavity. Surgery is the mainstay treatment of chordomas because the tumor has a poor sensitivity to conventional radiotherapy (RT) and chemotherapy (5, 7, 8). Although many investigators have reported surgical resection margins to be the most important predictor of survival and local recurrence, recurrence is not uncommon (6, 9). Moreover, neurogenic dysfunction is a frequent consequence of surgery with adequate surgical margins, and these complications strongly depend on the resection level.

Chordomas have been shown to be refractory to conventional photon RT at doses <60 Gy. The RT can be facilitated with the use of heavy charged particles such as protons or carbon ions, which provide greater physical selectivity. Also, the carbon ion beam possesses unique physical and biologic properties. It has a well-localized energy deposition

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(high-dose peak) at the end of the beam path, called the Bragg peak, leading to improved dose distributions and permitting dose escalation within the target and sparing of adjacent normal tissues. Recently, several investigators have reported on the efficacy of carbon ion RT against sacral chordoma, describing a markedly high local control rate and low toxicity (10–12). However, no studies have focused on the differential oncologic and functional outcomes between surgery and carbon ion RT from identical institutions and using consecutive series of patients. In the present study, the local recurrence-free and disease-specific survival, postoperative complications, and ambulatory, urinary-anorectal, and musculoskeletal function were retrospectively analyzed in patients with sacral chordomas treated with surgery or carbon ion RT at our institutions.

METHODS AND MATERIALS

Between 1990 and 2007, patients with tumors originating from the sacrum that had been histologically proven to be chordomas by experienced pathologists were reviewed. The therapeutic indications varied between before and after 1999. Before 1999, surgical resection was considered the treatment of choice. After 1999, however, patients in whom an adequate surgical margin would be difficult to achieve have undergone carbon ion RT. After 2004, patients were allowed to choose their preferred modality after a detailed explanation of the expected complications and functional impairments after the specific treatment. Carbon ion RT was provided by the National Institute of Radiological Sciences in Chiba, Japan. The specific technique of carbon ion RT used at the National Institute of Radiological Sciences has been previously published (10, 11, 13, 14). In brief, we used dosages from 54.0 to 73.6 Gray equivalent (GyE) on the basis of the results from previous trials of bone and soft tissue tumors. Carbon ion RT was performed once daily, 4 d/wk, for a total of 16 fixed fractions within 4 weeks. Generally, we used fraction doses of 4.4 GyE and 4.6 GyE. The bowel was removed from the treatment area for carbon ion RT. All patients signed an informed consent form.

A total of 17 patients referred to the orthopedic units of our institutions (Nagoya University Hospital, Nagoya Memorial Hospital, and Aichi Cancer Center Central Hospital) participated in the present study. Data regarding age, gender, location, tumor size, American Joint Committee on Cancer staging (15), treatment, surgical margin, local and systemic relapse, follow-up period, and oncologic and functional outcome were obtained. Lower extremity function after treatment was evaluated according to the scoring of Enneking *et al*. (16) at the postoperative point at which functional scores have been shown to plateau. The Musculoskeletal Tumor Society (MSTS) score consists of six items: pain, overall function, emotional acceptance, walking ability, walking supports, and gait handicap or limp. Each item is rated on a scale of 1–5, with 5 the most favorable score. The total score is calculated by summing the individual items. Patients treated with surgery or carbon ion RT were followed up with physical examinations, computed tomography, and magnetic resonance imaging at the outpatient unit of orthopedic surgery in our institutions. In the analysis, the patients lost to follow-up were included to the point at which their health status was last known.

We used the Kaplan-Meier product limit method to estimate the overall and local recurrence-free survival for the group and to illustrate the effect of the individual factors. The log–rank test was used to evaluate the differences between survival curves. The chi-square test or Fisher's exact test was used for the comparison of proportions. In cases of skewed distribution, nonparametric Mann-Whitney tests were used. Statistical analysis was done using Statistical Package for Social Sciences, version 15.0, for Windows (SPSS, Chicago, IL).

RESULTS

No patients had undergone previous RT with photons. No patients presented with recurrent tumor after surgery at other institutions. A total of 18 patients had sacral chordomas. One patient who refused any medical treatment was excluded, for a total of 17 patients included in the present study. No patients had distant metastasis at their initial referral for treatment. Of the 17 patients, 9 were men and 8 were women. According to the American Joint Committee on Cancer Staging System, of the 17 tumors, 4 were Stage IA, 12 were Stage IB, and 1 was Stage IIB. The most proximal tumor extension was L5 in 1 patient, S1 in 5, S2 in 7, S3 in 2, and S4 and S5 in 1 each. No patients received chemotherapy or photon RT. Of the 17 patients, 10 underwent surgery and 7 underwent carbon ion RT. The surgical margins were wide in 8 patients and intralesional in 2. All 17 patients were followed up at the orthopedic units of our institutions. The median follow-up was 56 months (range, 7–118) for all patients. Only 1 patient underwent RT (50 Gy) postoperatively. A total of 3 patients each developed local recurrence and distant metastasis. A total of 3 patients died of disease and 1 of pneumonia unrelated to the chordoma. The clinical data of all 17 patients are listed in Table 1.

The disease-specific and local recurrence-free survival rate for all 17 patients was 73.8% and 77.4% at 5 years, respectively. For the 10 patients who underwent surgery, the 5-year disease-specific and local recurrence-free survival rate was 85.7% and 62.5%, respectively. For the 7 patients who underwent carbon ion RT, the disease-specific and local recurrence-free survival rate at 5 years was 53.3% and 100%, respectively (Fig. 1). However, statistical analysis using the log–rank test revealed no significant difference between the surgery and carbon ion RT groups in either disease-specific ($p = .19$) or local recurrence-free ($p = .14$) survival. Also, no significant factors were noted that influenced the prognosis, except for gender, which showed a marginally significant result for local recurrence-free survival ($p = .043$; Table 2). No difference was found in overall survival for the patients treated before vs. after 1999, when carbon ion RT was introduced for patients with sacral chordoma (Fig. 2).

The mean patient age was 55 years in the surgery group and 65 years in the carbon ion RT group ($p = .28$). The mean major axis of the tumor was 8.2 cm in the surgery group and 10.1 cm in the carbon ion RT group ($p = .13$). The median follow-up was 76 months (range, 7–118) and 49 months (range, 35–72) in surgery and carbon ion RT groups, respectively ($p = .29$). Of the 17 patients, 9 were able to walk without an assistive device, 7 used a single cane, and 1 relied on a wheelchair. In the surgery group, the ability to walk was reduced in 6 of 7 patients with tumor extending above S2