Proton Radiation Therapy for Clivus Chordoma

—Case Report—

Yoshihiko YOSHII, Takashi TSUNODA, Akio HYODO, Tadao NOSE,
Hirohiko TSUJII*, Hiroshi TSUJI*, Tetsuo INADA*, Akira MARUHASHI*
and Yoshinori HAYAKAWA*

Department of Neurological Surgery, Institute of Clinical Medicine, and

**The Particle Radiation Medical Science Center, University of Tsukuba,
Tsukuba, Ibaraki*

Abstract

A 57-year-old male with clival chordoma developed severe hoarseness, dysphagia, and dysphonia 1 month after a second removal of the tumor. Magnetic resonance imaging demonstrated a mass 10 cm in diameter in the region of the middle clivus enhanced inhomogeneously by gadolinium-diethylenetriaminepenta-acetic acid, and a defect in the skull base. There was evidence of compression of the anterior surface of the pons. He received proton irradiation employing a pair of parallel opposed lateral proton beams. The dose aimed at the tumor mass was 75.5 Gy, to the pharyngeal wall less than 38 Gy, and to the anterior portion of the pons less than 30 Gy. Time dose and fractionation factor was calculated at 148. Thirty-one months following treatment, he was free of clinical neurological sequelae. Proton therapy should be considered in treatment planning following initial surgical removal or for inoperable clivus chordoma.

Key words: chordoma, clivus, proton, radiation therapy

Introduction

Chordoma is an uncommon lesion occurring along the craniospinal axis, and is probably of notochordal origin.⁸⁾ The management of chordomas at the base of the skull is a complex problem due to the characteristics of the anatomical location. Many tumors are not removed completely by surgery,⁶⁾ and postoperative radiation therapy is used to control the bulky residual tumor.

However, anatomical structures such as the brainstem, spinal cord, and optic nerve limit the safe dosage of adjuvant conventional radiation therapy, preventing local control of the tumor. Therefore, conventional radiation modalities cannot always prevent local recurrence of the tumor.²⁾ Fortunately, protons have physical characteristics which allow the delivery of high doses of radiation to tumors in such critical locations.^{1,13)}

We report a patient with clival chordoma treated by proton radiation therapy after operation and the

clinical and neuroradiological course for 31 months after treatment.

Case Report

A 57-year-old male developed a feeling of fullness in the throat in January, 1988. He admitted to a private general hospital where the otologist noticed a clival mass on computed tomographic (CT) scans and magnetic resonance (MR) images. Partial removal of the tumor in the nasal cavity was achieved through the transnasal approach, and a chordoma was diagnosed in March, 1988. He noticed hoarseness and some difficulty in swallowing in July, 1988. A second operation partially removed the intracranial extension of the chordoma through the facial split approach in December, 1988. One month later, he complained of severe hoarseness, dysphagia, and dysphonia. CT scans and MR images of the skull base revealed a destroyed, lytic clival bone, and a homogeneous high-intensity residual mass was seen in that area on the T₁-weighted images. There was radiographic evidence of tumor extension to the

anterior surface of the pons. He was referred to the University of Tsukuba, Department of Neurological Surgery and Particle Radiation Medical Science Center (PARMS) for possible proton irradiation in January, 1989.

On admission, examination showed abnormalities confined to the skull base region. He had paralysis of the right pharyngeal muscle and right vocal cord, and evidence of involvement of the right XIIth and XIth cranial nerves. MR images demonstrated a mass 10 cm in diameter in the region of the middle clivus and a defect in the skull base. The tumor was inhomogeneously enhanced by gadolinium-diethylenetriaminepenta-acetic acid on T₁-weighted images (TR 500 msec, TE 20 msec). The anterior surface of the pons was compressed by the mass. CT gave similar findings to MR imaging.

The primary proton energy (500 MeV) at PARMS is too high for medical applications, so is reduced to 250 MeV by passing the beams through a graphite absorber. The maximum penetration for protons of this energy is 37.6 cm in water, which is suitable for treatment of deep-seated tumors. To obtain the spread out Bragg peak, the beam is modulated using an aluminum ridge filter or range-modulator made of an acryl plate 5 mm thick.¹⁴⁾ Field placement is checked by fluoroscopic x-ray imaging every treatment day. This technique was developed in PARMS and combines fluoroscopy with a real-time digital image processing unit. The current field is displayed on one TV monitor, and is compared with any picture previously stored on the other TV monitor. This system has shortened the set-up time from 15–20 minutes to only 5–10 minutes. Furthermore, the field position is routinely checked by x-rays each treatment day. At PARMS there are two treatment rooms, one with vertical beams and the other with horizontal beams.

He was managed by both the neurosurgeon and proton radiation oncologist groups. The basic plan was to employ a pair of parallel opposed lateral proton beams. The dose aimed at the tumor mass was 75.5 Gy, to the pharyngeal wall less than 38 Gy, and to the anterior portion of the pons less than 30 Gy. The treatment plan was based upon serial CT scans using the VAX 11/750 computer system. The programs for dose calculations and bolus design were developed at PARMS. The target volume was defined with the smallest possible margins around the tumor periphery. The lateral fields were 120 mm high and 60–80 mm wide. The composite dose distribution of the proton beam is presented in Fig. 1. The dose at the anterior surface of the pons is estimated at between 7.6 and 22.7 Gy. The lateral field was delivered

Fig. 1 Representative proton radiation dose distributions in our patient with clivus chordoma. *upper*: Diagram, showing the proton target volume (outlined area) on the lateral view of the scout CT scan. *lower*: Diagram, showing the dose distribution of the proton beam used in the treatment of this patient. Note the tumor area (white outlined area) exposed to 100% dose and the medulla or spinal cord area (outlined area) with exposure varying from 50% dose at the inner side to 10% dose at the outer side on a CT scan at the craniobasal level.

with the patient supine, head fixed in a face mask, and further immobilized by a fixing device. The fraction size ranged from 2.5 to 3.0 Gy. There were 5 fractions of 2.5 Gy and 21 of 3.0 Gy. Total treatment time was 47 days, and time dose and fractionation factor was calculated at 148. This unusual treatment schedule was selected based upon the operation schedule of the accelerator.

He complained of head dullness after about 30 Gy of proton radiation therapy, but he improved with 1 mg/day Decadron administration for 1 week. There was no symptomatic pharyngeal reaction or neurotoxicity. Twenty-nine months later, there was radiographic evidence of decreased tumor volume in the clivus and MR images showed no signs of radiation injury (Fig. 2). Thirty-one months following treatment, he was free of clinical neurological sequelae.

Fig. 2 Sagittal T₁-weighted MR images (TR/TE: 500/20 msec) of this patient. *left*: Note the large chordoma occupying the middle and inferior clivus and displacing the lower pons, medulla, and spinal cord before proton radiation therapy. *right*: Note the definite decrease in tumor volume and the normal position of the lower pons, medulla, and spinal cord 29 months after 75.5 Gy proton radiation therapy.

Discussion

The results of surgery and radiation therapy for chordoma have been discussed.^{2,5,10,12)} However, the management of this tumor is still controversial because of the small number of patients. Nath Sen *et al.*⁹⁾ stressed that this tumor should be treated by aggressive surgical removal when initially diagnosed, and this can be accomplished with low morbidity. All patients have been evaluated preoperatively and postoperatively with CT or MR imaging since 1980, but before this surgical removal must often have been incomplete due to unsuitable approaches because strict radiological criteria were not used to evaluate the treatment modalities.

However, the transbasal and infratemporal approaches still present difficulties in reconstruction of the craniectomized skull base, dural repair, a restricted exposure, and the risk of infection and operative morbidity.^{4,5,12)} Therefore, all patients with clivus chordoma also receive postoperative radiation therapy to control tumor regrowth, usually with a total dose of more than 65 Gy.^{1-3,10,11)}

Recent reports have emphasized the effectiveness of proton beam irradiation for treatment of this tumor.^{1,13)} Protons have favorable physical characteristics which allow the delivery of high doses of radiation to critical locations. Additionally, improved modern neuroimaging techniques and rigid immobilization systems allow confirmation of the target position relative to the proton beam at each treatment, treatment planning based on beam trajec-

tory, dose at each anatomical point, bolus based on accurate assessment of density along each pixel, *etc.* Therefore, modern therapeutic strategy of the clivus chordoma should include proton therapy following initial surgical removal or for inoperable tumor.

Proton therapy in our institute showed that the patient could tolerate radiation doses 15–20% higher than those of conventional radiation therapy used. The follow-up period was short in our case, but the absence of major neurological sequelae is significant. Proton therapy may become a feasible therapeutic strategy for tumors in the skull base region. The efficacy of focused high-energy radiation should be compared with surgical removal in a randomized study.

Acknowledgment

We thank Dr. Kazufumi Itoh of the Department of Neurosurgery, Hitachi General Hospital for preparation of the manuscript.

This work was supported in part by a Grant-in-Aid for Scientific Research from the Ministry of Education of Japan.

References

- 1) Austin-Seymour M, Munzenrider J, Goitein M, Verhey L, Urie M, Gentry R, Birnbaum S, Ruotolo D, McManus P, Skates S, Ojemann RG, Rosenberg A, Schiller A, Koehler A, Suit HD: Fractionated proton radiation therapy of chordoma and low-grade chondrosarcoma of the base of the skull. *J Neurosurg* 70: 13–17, 1989
- 2) Cummings BJ, Hodson DI, Bush RS: Chordoma: The results of megavoltage radiation therapy. *Int J Radiat Oncol Biol Phys* 9: 633–642, 1983
- 3) Dahlin DC, MacCarty CS: Chordoma. A study of fifty-nine cases. *Cancer* 5: 1170–1178, 1952
- 4) Derome PJ, Visot A, Monteil JP, Maestro JL: Management of cranial chordomas, in Sekhar LN, Schramm VL (eds): *Tumors of the Cranial Base. Diagnosis and Treatment*. New York, Futura, 1987, pp 607–622
- 5) Fisch U, Pillsbur HC: Infratemporal fossa approach to lesions in the bone and base of the skull. *Arch Otolaryngol* 105: 99–107, 1979
- 6) Higinbotham NL, Phillips RF, Farr HW, Hustu HO: Chordoma: Thirty-five year study at Memorial Hospital. *Cancer* 29: 1841–1850, 1979
- 7) Kamrin RP, Potanos JN, Pool JL: An evaluation of the diagnosis and treatment of chordoma. *J Neurol Neurosurg Psychiatr* 27: 157–165, 1964
- 8) Murad T, Murphy M: Ultrastructure of a chordoma. *Cancer* 25: 1204–1215, 1970
- 9) Nath Sen C, Sekhar LN, Schramm VL, Janecka IP:

- 1989 chordoma and chondrosarcoma of the cranial base: An 8-year experience. *Neurosurgery* 25: 931-941, 1989
- 10) Pearlman AW, Friedman M: Radical radiation therapy of chordoma. *AJR* 108: 333-341, 1970
- 11) Rich TA, Schiller A, Suit HD, Mankin HJ: Clinical and pathologic review of 48 cases of chordoma. *Cancer* 56: 182-187, 1985
- 12) Sekhar LN, Janecka IP, Jones NF: Subtemporal-infratemporal and basal subfrontal approach to extensive cranial base tumors. *Acta Neurochir (Wien)* 92: 83-92, 1988
- 13) Suit HD, Goitein M, Munzenrider J, Verhey S, Davis KR, Koehler A, Linggood R, Ojemann RG: Definitive radiation therapy for chordoma and chondrosarcoma of base of skull and cervical spine. *J Neurosurg* 56: 377-385, 1982
- 14) Yoshii Y, Maki Y, Narushima A, Takano S, Hashikawa M, Nose T, Nakagawa K, Kitagawa T, Inada T, Oohara K, Maruhashi A, Ishikawa N, Takakura K, Kitamura K: Use of radiotherapy by high-energy protons in the postoperative treatment of brain tumor. *Neurol Med Chir (Tokyo)* 26: 219-226, 1986

Address reprint requests to: Y. Yoshii, M.D., Department of Neurological Surgery, Institute of Clinical Medicine, University of Tsukuba, 1-1-1 Ten-nodai, Tsukuba, Ibaraki 305, Japan.