Case Report

A Case of Locally Advanced Hypopharyngeal Cancer Treated With Curative Resection after Thermoradiotherapy

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Abstract: Fifty four-year-old patient with unresectable hypopharyngeal cancer of T4N2cM0 was treated with accelerated hyperfractionated radiotherapy (1.5Gy twice a day) and hyperthermia. Good tumor response was achieved by combined four sessions of hyperthermia with radiotherapy of 75Gy. Laryngo-pharyngectomy, cervical esophagectomy, and bilateral neck dissection were performed for regrowth of the primary site 2.5 months after thermoradiotherapy. There were no viable cells in all metastatic nodes although scattered cancer nests were seen in the primary site.

He has a local disease-free eleven months after resection.

Key Words: hypopharyngeal cancer, metastatic cervical lymph nodes, hyperthermia, radiotherapy

Introduction

The combination therapy of surgery and radiotherapy has been considered as the most successful approach for advanced head and neck squamous cell carcinoma, hypopharyngeal cancers are often unresectable because of their local extension and nodal states. Multidisciplinary treatments including radiotherapy, hyperthermia, and/or chemotherapy have been applied for large tumors unable to be controlled by radiotherapy alone [1-3]. Recently, several reports have shown that full-dose irradiation with altered fractionations is more effective than standard fractionation for local control of advanced head and neck cancer [4-6]. In this article, we present a case with advanced hypopharyngeal cancer who could undergo thermoradiotherapy combined with accelerated hyperfractionation, and salvage operation for local residual disease without severe morbidity.

Case report

A 54-year-old male patient presented with a 10-month history of swallowing difficulty and pain, and mild dyspnea with supine position. On fiberscopic examination a huge tumor extended up from the

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pyriform sinus, aryepiglottic fold, and onto the right wall of the mesopharynx. The right cervical lymph node, measuring 45×45mm, was found as the metastatic tumor by physical examination. An X-ray CT scan also showed swelling of the right upper deep cervical nodes with extracapsular invasion (Fig. 1a, 1b). In the left upper deep cervical region, two swelled nodes also were detected as diameters of 18mm and 9mm. A histological examination of a hypo-mesopharyngeal tumor showed a squamous cell carcinoma. The patient was staged as T4N2cM0 according to the UICC criteria in 1997. As the patient refused laryngectomy and chemotherapy, a combined radiotherapy with hyperthermia was selected.

Hyperthermia was applied with an 8MHz RF-capacitive heating apparatus (Thermotron RF-8 : Yamamoto Vinita Co.). Hyperthermia was administered at four sessions of 45 minutes each on days 9, 23, 32, and 37 (in absorbed doses of 21Gy, 42Gy, 60Gy, and 69Gy, respectively) from the starting point of radiotherapy. The first session of hyperthermia was performed over 20Gy in absorbed doses, when the patient lay in the supine position without dyspnea. We selected an electrode, 10cm in diameter, to place on the right side along the swelled metastatic nodes, and one of 14cm in diameter for the left contralateral site. These electrodes also covered most part of the primary tumor. Bolus covers of these electrodes were chilled with deionized water circulating at 30°C on the right side, and at 10°C on the left side. A thermocouple thermometer was guided by ultrasound and placed into the right metastatic node at 2.5cm depth from the skin surface (Fig. 2). During the administration of the first and second sessions of

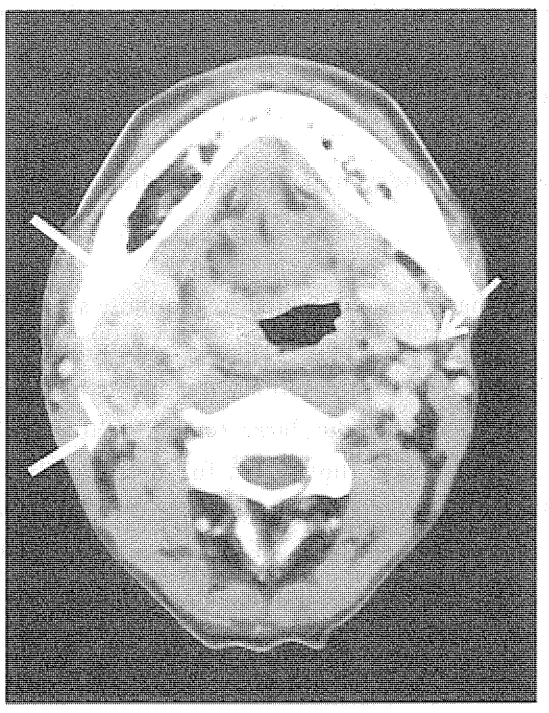

Fig. 1a : X-ray CT scan shows a right upper deep cervical metastatic node with an extracapsular extension (→). The primary hypopharyngeal tumor extends up to the right mesopharyngeal wall (＊). On the left upper deep cervical region, small but irregularly enhanced nodes (→) were also detected.

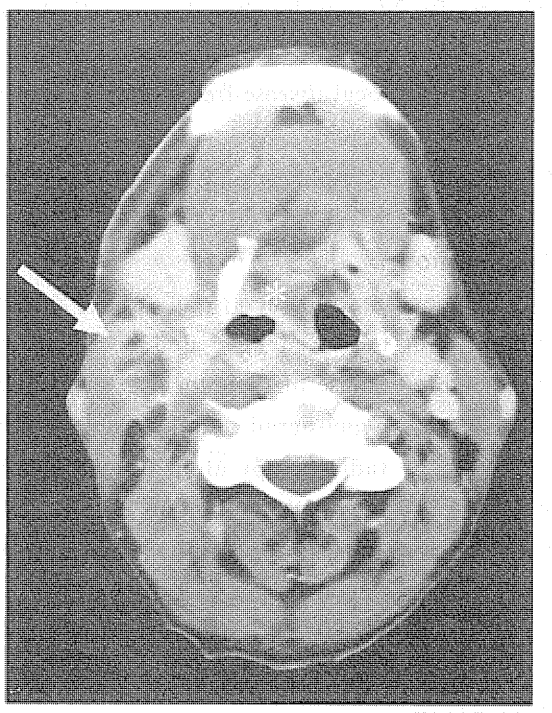

Fig. 1b : The primary hypopharyngeal tumor extended from the right pyriform sinus up to the aryepiglottic fold, and the right wall of the mesopharynx.

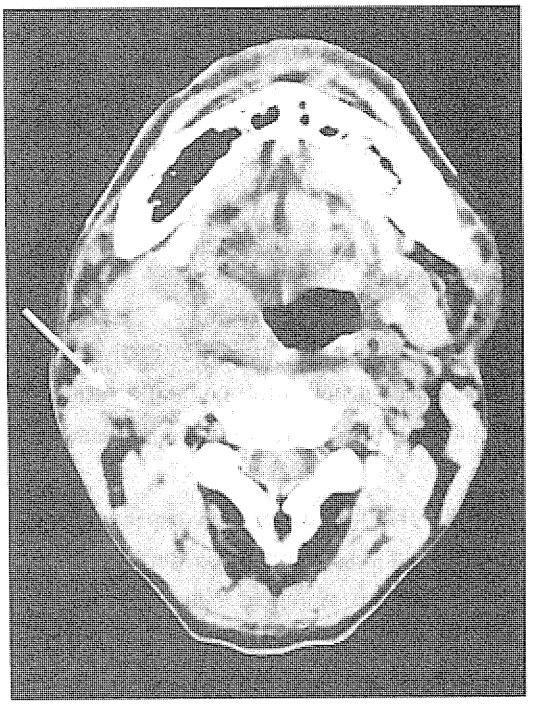

Fig. 2: On the first session of thermotherapy, a thermocouple thermometer was placed in the metastatic node at 2.5cm depth from the skin surface.

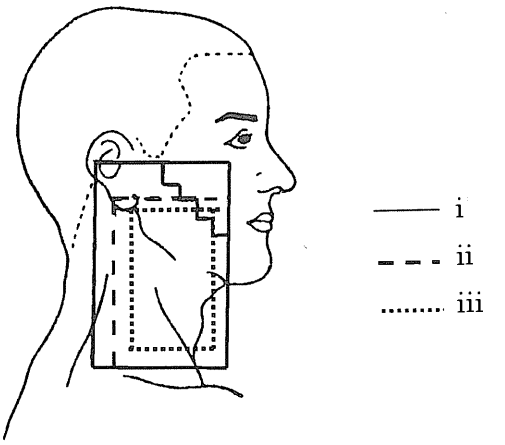

Fig. 3: Irradiation field and dose for external radiotherapy. Two laterally opposed field was adopted, and field was shrunk gradually. Field i: 0-45.0Gy, Field ii: 45.0-64.5Gy, Field iii: 64.5-75.0Gy

thermotherapy, the tumor temperature was monitored by this thermometer. Gauze filled with echo-jelly covered the auricula to avoid making hot spots.

Starting time of hyperthermia was set 30-60 minutes after first fraction of radiotherapy in the morning, and the second fraction was performed in radiotherapy alone on the concurrent treatment day of thermoradiotherapy.

The patient was treated with a linear accelerator of 4 MV photon using the plastic shell for immobilization (Efficast: EuroMediTech, Co.). Radiation was given 1.5Gy b.i.d. hyperfractionation to 75Gy by two laterally opposed fields. The interfraction interval was 6 hours. The boost therapy of 10.5Gy was added to the tumor after 64.5Gy. Irradiation field and dose for radiotherapy is showed in (Fig. 3). Spinal cord was shielded after 45Gy. Overall treatment time was 39 days including a 5-day split due to acute laryngitis after 39Gy.

Table I shows the intratumor temperature and the power output during RF-hyperthermia. At the first session of hyperthermia, power output was elevated to 800-910 watt. Intratumor temperature was kept over 40°C for 29 minutes. Hyperthermia was performed at the second session with the thermometer slipped to the tumor edge of metastatic cervical node, and without monitoring the intratumor temperature at the third and fourth sessions. Power output was monitored during the each session of hyperthermia. For more than 20 minutes the maximal power output was kept over 790 watt at each session.

Patient had a partial response for both primary lesion and metastatic cervical lymph nodes. As the treatment related morbidity, grade 3 of mucositis and grade 2 of dermatitis (National Cancer Institute-

Table I Treatment results: Intra-tumor Temperature and Power Output during RF-Hyperthermia

No. of treatment	Tmax (°C)	Tmin (°C)	Tave (°C)	Pmax* (watt)	total time (minutes)
1.	40.6	40.1	40.4	910	45
2.	38.7	38.2	38.5	805	45
3.	—	—	—	794	45
4.	—	—	—	810	45

* Pmax is defined as maximum power output continued over 20 minutes.

Common Toxicity Criteria) appeared. He complained severe mucosal pain after the forth session of hyperthermia (over 69Gy) and required narcotics. He had a rice-gruel and elemental diet. The parenteral alimentation was added intravenously for nutritional support. These adverse effects healed several weeks after thermoradiotherapy.

The patient complained of dyspnea again, and regrowth of the primary lesion was suspected (Fig. 4). Laryngo-pharyngectomy, cervical esophagectomy, and bilateral neck dissection were performed at 2.5 months after thermoradiotherapy. A classical radical neck dissection on right side, and functional dissection on left side were performed. A surgical specimen of all metastatic cervical nodes, showed necrotic tissues with keratinized material. These findings suggested treatment-related change from squamous cell carcinoma (Fig. 5). Scattered small cancer nests were found around the ulcer on the right wall of pyriform sinus (Fig. 6a, 6b). He had a disease-free eleven months after the salvage operation.

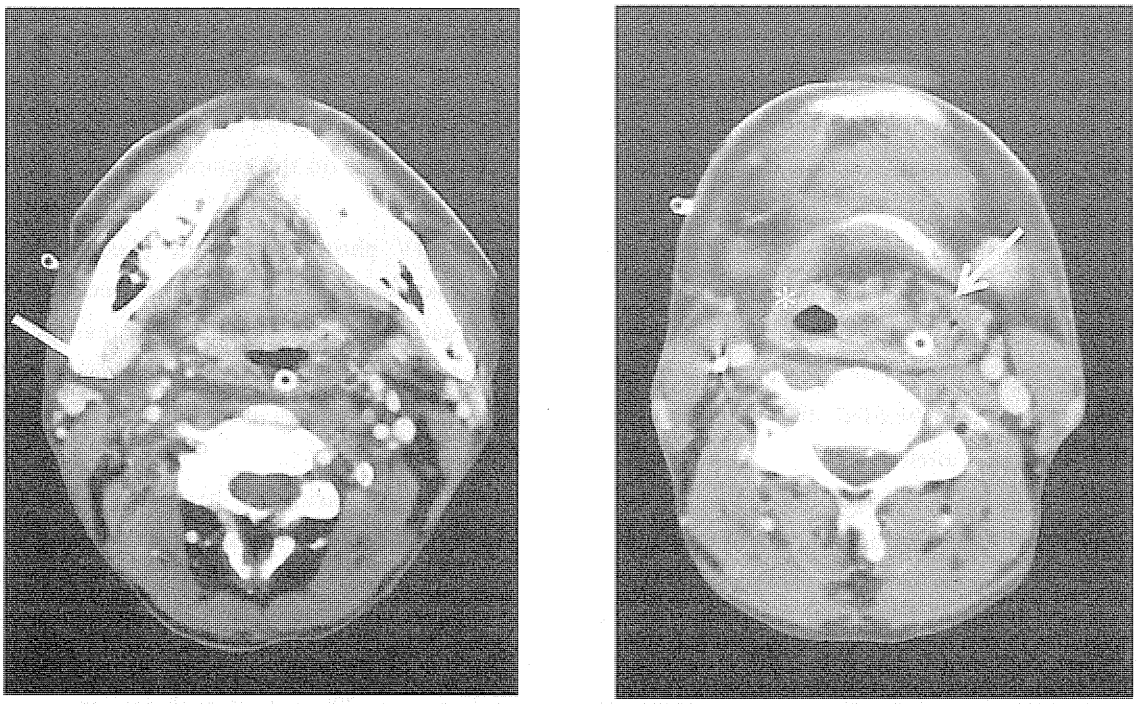

Fig. 4: X-ray CT scan two months after the end of thermoradiotherapy. Cervical metastatic nodes were shrunk and markedly decreased enhanement effect (4a →). However laryngeal edema was occurred and regrowth of the local tumor was suspected (4b).

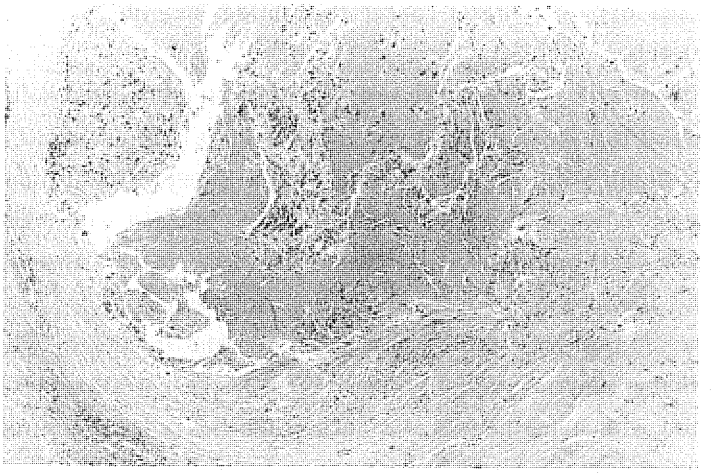

Fig. 5: Pathological findings of the necrotic cervical node. The morphological change of necrotic tissue with keratinized material showed treatment-related disappearance of squamous cell cancer. H&E×100

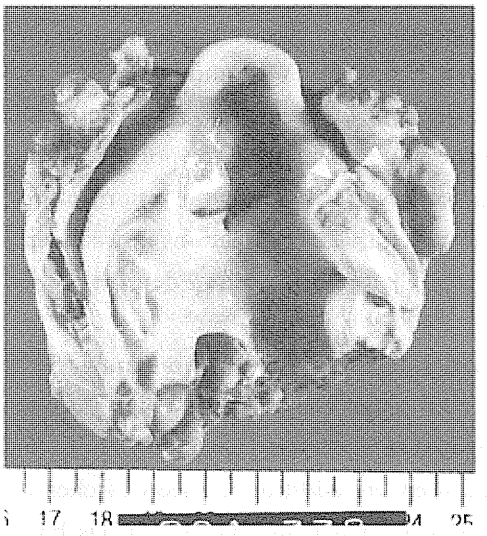

Fig. 6a: Macroscopic findings of a surgical specimen of hypopharynx. A ulcer formation has been showed on the right wall of the pyriform sinus.

Fig. 6b: Microscopic findings of the right pyriform sinus. Only scattered cancer nests were found marginally around the ulcer lesion. H&E×100

Discussion

In this patient with advanced hypopharyngeal cancer, we employed the combined accelerated hyperfractionated (AHF) radiotherapy with hyperthermia to obtain the better local control. It has been reported that higher doses of at least 75Gy at conventional fraction (2.0Gy/fraction, for 5 days in week) is necessary to control metastatic lymph nodes measuring 3.5 to 6.0cm [8]. It has been reported that patients undergoing conventional radiotherapy, who are treated with surgery followed by radiotherapy have a better prognosis than those treated with radiotherapy alone [11–14]. The presented case was

unresectable for advanced hypopharyngeal cancer infiltrating mesopharynx, and nodal extracapsular extension around the vessels.

Recently, several reports [4) 5) 9) 10)] have shown that hyperfractionated radiation therapy is more effective than conventional fractionated therapy (1.8-2.0Gy daily) for advanced head and neck cancer. For patients with larger tumor volume, especially over 100cm^3, locoregional tumor control and survival were associated with lower efficacy, although they have been maneged with AHF radiotherapy [6)]. We have also tried to apply AHF radiotherapy for hypopharyngeal cancer after 1997, the rates of local control at two years was 100%, vs 16%, for T1-2, vs T3-4, respectively [15)].

It has reported that radiotherapy plus hyperthermia in the treatment of metastatic lymphnodes achieve nodal control that is superior to that obtained by radiotherapy alone [1) 2)]. So hyperfractionated radiation in combination with hyperthermia was anticipated better local control not only for cervical nodes, but also for primary lesion. Hyperfractionated radiotherapy (total dose 69.6-76.8Gy, 1.2Gy b.i. d. five times a week) combined with external hyperthermia was studied in a phase I-II study [16)]. In this study neck nodal overall response rate was 92%, and feasibility of this combined treatment was demonstrated with acceptable toxicity. Our presented case with AHF radiotherapy plus hyperthermia revealed all necrotic changes in metastatic cervical lymphnodes and only spotty residusal cancer nests of primary lesion in microscopic findings. Wang et al. showed [7)] that after preoperative irradiation of squamous cell carcinoma of the head and neck, only 18.5% of surgical specimens of a stage IVb tumor contained no viable tumor cells. This case encourages us for favorable tumor control by bimodality, such as combined hyperfractionated radiotherapy with hyperthermia. And treatment related morbidity for normal tissues was acceptable for salvage operation 2.5 month after thermoradiotherapy. It has been reported that preoperative hyperthermia did not increase the possibilities for postoperative complications in treatment for breast cancer [17)], and rectal cancer [18)]. On the presented case, treatment related grade 2 dermatitis was revealed using mask system during radiotherapy.

A combination of chemotherapy and concurrent radiotherapy, known as chemoradiotherapy [14) 19)], has been claimed to be more effective than radiotherapy alone. Although chemoradiotherapy showed no statistically significant superiority to accelerated hyperfractionated radiotherapy alone in treating for hypopharyngeal cancer patient [20)]. There must be prudently regarded the additional effects of chemotherapy for local and distant tumor control, and also as the treatment related morbidity. It has been reported that hyperthermia, radiation, and low-dose weekly cisplatinum for locally advanced head and neck tumors introduce greater cutaneous toxicity [1)].

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切除不能進行下咽頭癌として温熱・放射線治療を施行し，根治切除術が可能となった1例

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要　旨：下咽頭癌は頭頸部癌のなかでも予後不良であるが，多くは原発巣，転移リンパ節とも進行した状態で診断されることが多いためである．今回我々は54歳男性，切除不能下咽頭癌T4N2cM0の1例に温熱放射線療法を施行した．放射線治療は加速多分割照射を適応しshrinking field法で75Gyを投与した．温熱療法は放射線治療の施行日に4回行った．治療終了後2.5ヶ月で手術療法を施行し，リンパ節転移部は全て壊死となったことを確認した．原発巣には微細な癌巣が残存していた．救済手術後11ヶ月局所再発なく社会的生活を送っている．