Clinical Research Paper

Endoscopic microwave coagulation therapy for locally recurrent nasopharyngeal carcinoma

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Background and Objective: Management of locally recurrent nasopharyngeal carcinoma (NPC) is difficult. External beam re-irradiation could cure some patients but might cause severe radiation injury. This study was to evaluate the clinical value of endoscopic microwave coagulation therapy as salvage treatment for locally recurrent NPC. Methods: Between August 1994 and April 2005, 55 patients with locally recurrent NPC (stage rT1) were treated with endoscopic microwave coagulation therapy. Local progression-free and overall survival were observed. Results: The median follow-up was 102.1 months (range, 22.4–153.9 months). The median time from last irradiation to recurrence was 22.1 months (range, 6.5–125.6 months). Five patients had loco-regional failure. The five-year local progression-free and overall survival rates were 90.7 and 93.6%, respectively. No patient had intraoperative complications. One patient had nasopharyngeal necrosis after operation, and was healed after one month. Conclusions: Endoscopic microwave coagulation is effective without severe complications in locally recurrent NPC patients. It is a minimally invasive therapy for recurrent NPC.

Yang et al.1 reported a distant metastasis-free local recurrence rate of 20.6% in nasopharyngeal carcinoma (NPC) patients receiving conventional radiotherapy. Though NPC patients who suffered from local recurrence after first course of radiotherapy could be treated by re-irradiation, the overall survival rate decreases, the incidence of irradiation-related complications increases, which would result in an increase of mortality and a descend of life quality. The five-year survival rate of NPC patients who received re-irradiation was 5.8–21.0%1,3, the occurrence rate of serious complications was 15–26% and the mortality was 2.0–3.7%.2,3 How to raise the therapeutic effect on recurrent NPC is a tough problem in clinic. Endoscopic microwave coagulation is a new therapy with endoscopy and microwave technique used in combination. In recent years, great advances have been made both at home and overseas in treating tumors in cavitary organs and tracts by this therapy. We had treated 55 early recurrent (stage rT1) NPC patients using endoscopic microwave coagulation as a salvage therapy. We reported our results in this paper.

Patients and Methods

Clinical data of the patients. From August 1994 to April 2005, 55 NPC patients who suffered from local recurrence after radiotherapy were treated with endoscopic microwave coagulation in Cancer Center of Sun Yat-sen University. Local failure was defined as the presence of local disease more than 24 weeks after completion of the primary radiotherapy.4 All cases were diagnosed as poorly differentiated nasopharyngeal squamous cell carcinoma by nasopharyngeal biopsy. Of the 55 patients, 36 were men and 19 were women, with a median age of 41 (range, 28–64). Among the patients, NPC recurred locally at 6.5–125.6 months (median, 22.1 months) after the completion of radiotherapy. Of the 55 patients, 11 had recurrent NPC at 6–12 months after radiotherapy, 31 at 1–3 years, and 13 over 3 years. Indirect nasopharyngoscopy and rhinoscopy revealed that 45 patients had their NPC foci on the posterior wall of nasopharyngeal cupula, six on the lateral wall, and four on the nasopharyngeal cupula and in the recessus pharyngeus. Indications of endoscopic microwave coagulation were as follow: the recurrent NPC focus was localized in the nasopharyngeal cavity with a diameter of no more than 1.5 cm; no parapharyngeal space invasion, no newly developed destruction of cranial nerves and bones in basilar region, and no cervical lymph node metastasis were detected by CT or MRI; no distant metastasis was detected by chest X-ray picture, B ultrasound examination and bone emission computed tomography (ECT) examination.

Instruments. Two integrated microwave medical instruments separately made by the Nanjing Optical Instrument Factory and the Zhuhai Jiahe Company were used. Both of them equipped with time-controlled counter, pedal-controlled switch, and coaxial needle-type irradiation antennae, with a microwave frequency of 2450 MHz and continuously adjustable output power of 1–100 W. The OLT10...
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model fibrous nasopharyngoscope made by the Olympus Co., Ltd. was used.

Procedures of endoscopic microwave coagulation. The fibrous nasopharyngoscope was inserted after full superficial anesthesia to observe tumor location and size. The needle-type microwave irradiation antennae were inserted into the nasal cavity close to the NPC focus under the illumination of endoscope to coagulate multiple (8–12) sites around the base of NPC focus and peripheral normal tissue, with an output power of 70–80 W/8–12 s for each site. (The NPC foci could also be excised by biopsy forceps before inserting the antennae). During the process, the tissue was coagulated, whitened, and necrotized instantly, adhered to the antennae, and were took out together with the antennae.5

Postoperative treatment and follow-up. Fibrous nasopharyngoscopy was performed and necrotic tissues, inflammatory exudates, pseudomembrane, and so on, were cleared away at 37 days after operation. The above procedure was repeated every 7–14 days till the wound surface was healed up. If necessary, a second microwave coagulation was performed. Of the 55 patients, 45 received only one course of microwave coagulation, and the other ten received two courses. No chemotherapy or radiotherapy was given after microwave coagulation. The patients were treated with antibiotics and traditional Chinese medicine after operation. All patients were followed up till May 2007, with a median follow-up duration of 102.1 months (22.4–153.9 months).

Statistical methods. Local progression-free survival rate and overall survival rate were calculated by Kaplan-Meier method using SPSS10.0 software for Windows.

Results

Survival status. During follow-up, five patients suffered from local recurrence of NPC again, two of whom recurred within once year after coagulation, two at 1–2 years, and one over two years. No distant metastasis occurred. Of the five patients, three had the preoperative recurrent foci on the posterior and lateral walls, one on the posterior wall and one in the lateral recessus pharyngeus. One of the five patients was treated by second course of microwave coagulation. (This patient had NPC recurred at different sites of the nasopharynx for three times in the past ten years, always treated with microwave coagulation, and now still survive with no evidence of NPC.) The remaining four patients received second course of radiotherapy and suffered from serious trismus, dysphagia, hypoacusis, and irradiation-related encephalopathy. Of the four patients, one died of local failure, one died of massive nasopharyngeal hemorrhage, and one died of pneumonia due to difficulty of coughing out sputum caused by trismus and irradiation-related injury of posterior cranial nerves. The quality of life of all patients who had been treated only by microwave coagulation was good, with no adverse event and sequelae. Among the 55 patients, the five-year local progression-free survival rate was 90.7% and the five-year overall survival rate was 93.6%.

Postoperative complications. Major postoperative complications were mild pharyngalgia and headache, which disappeared gradually within two weeks in general. No noticeable hemorrhage occurred after operation. One patient suffered from apparent headache and nasopharyngeal ulcer after operation, and the ulcer disappeared one month after being washed with Kangfuxin liquor.

Discussion

Second course of radiotherapy for recurrent NPC will aggravate sequelae such as irradiation-related encephalopathy, irradiation-related osteomyelitis, fibrosis of soft tissues and irradiation-related injury of cranial nerves, which affects seriously the life quality of patients. The high dose of second course of conventional external radiotherapy would cause irradiation-related death. The occurrence rate of serious complications is 15–26% and the mortality is 2.0–3.7% after second course of radiotherapy for recurrent NPC.2,3 The efficacy of conventional external irradiation on recurrent NPC is disappointing which may because the tumors recurred locally after optimal modern primary radiotherapy are usually very radioresistant, especially the recurrent NPC developed in irradiation field. Instead, intensity-modulated radiotherapy (IMRT) used in second course of radiotherapy shows an apparent advantage in its feasible random adjustment of irradiation intensity in the target site and the neighboring sensitive organs. In treating 49 recurrent NPC patients with IMRT, Lu et al.6 discovered that the irradiation tolerance of the normal organs close to the nasopharynx was lower than the stipulated irradiation dose; with a median follow-up duration of nine months, the local progression-free survival rate was 100%, but 28.6% of the patients experienced nasopharyngeal mucosa necrosis in different degrees. It can be assumed that IMPT is still a good therapy for large recurrent NPC.

The salvage nasopharyngectomy for recurrent NPC is difficult to perform and its efficacy is unsatisfied. Hsu et al.7 reported a five-year overall survival rate of 30% and a five-year progression-free survival rate of 40% in 60 recurrent NPC patients after nasopharyngectomy; in their trial, 36 patients died, 29 (81%) of who died of local failure; multivariate analysis revealed that T stage of recurrent NPC was an important factor affecting the effect of nasopharyngectomy, and the effect of nasopharyngectomy on recurrent NPC at early stage (rT1) was good. A common operation for recurrent NPC at early stage is to excise nasopharyngeal foci via the transpalatal approach. For the patients with irradiation-related trismus, this operation is difficult to be performed, with large damage, and the wound is difficult to be healed up in some cases.

In recent years, rhinoscope-guided operation shows a rapid progress with a consistent extension of its application fields, resulting in the feasibility of exposing the nasopharynx and guiding operation. Deng et al.8 excised small nasopharyngeal lumps appeared in 31 NPC patients within a definite time after radiotherapy with metal biopsy forceps under the guidance of fibrous nasopharyngoscopy; postoperative pathologic examination proved recurrent NPC in 20 patients, of whom four had not received radiotherapy or chemotheraphy after the operation and survived tumor-freely during follow-up, suggesting that small local recurrent NPC might be controlled by single excision to some extent. As a kind of high frequency electromagnetic wave, microwave treats tumors mainly by its thermal effect. The principle is as follow: body tissues absorb the energy of microwave during irradiation and lead to an exciting state of polar molecules in these tissues; these molecules vibrate with high frequency and rub with neighboring molecules to generate heat energy which causes coagulation and necrosis of tissues, therefore, clears up tumor foci.9 Some researchers firstly applied endoscopic
microwave coagulation to treat tumors in cavitary organs in the early 80’s of 20th century. Afterwards, the development and amelioration of this operation widen its application fields, but its application in treating recurrent NPC has seldom been reported. Hence, based on our experiences of excision of small nasopharyngeal nodules, we combined the amendatory method of the endoscope-guided biopsy with microwave coagulation technology for treating local recurrent NPC. The five-year local progression-free and overall survival rates are 90.7 and 93.6%, respectively in our study.

As all recurrent NPCs appear in the original irradiation field, they might originate from clonal cells that are not sensitive to irradiation and then lead to the failure of second course of radiotherapy. Some local recurrent NPC patients will be saved by endoscopic microwave coagulation when the operation indications are determined correctly. Because the recurrent nasopharyngeal area is usually smaller in endoscopic microwave coagulation group than in radiotherapy group, it is difficult to compare the effects of these two therapies on recurrent NPC. However, Lee et al. reported a five-year local control rate of 35% in local recurrent NPC patients who received second course of radiotherapy; Teo et al. reported a five-year overall survival rate of 26% and a five-year tumor-free survival rate of 30% in local recurrent NPC patients who received second course of external radiotherapy. Their results are apparently lower than the survival rates of endoscopic microwave coagulation group in our study. Moreover, the complications caused by microwave coagulation are less than those caused by second course of radiotherapy in general. The patients in our group did not suffer from adverse events and sequelae after microwave coagulation.

The indications of endoscopic microwave coagulation are shown as the same of those of the excision of nasopharyngeal lumps, that is, the tumor foci are localized in the nasopharyngeal cavity, with diameters of no more than 1.5 cm, with well-defined margin, without parasphenoidal space invasion; locating on the posterior wall of nasopharyngeal cupula is the best site for operation. Endoscopic microwave coagulation shows the following advantages in treating recurrent NPC at early stage:

• The operation is easy to perform, even by a single operator who can master endoscopy and microwave techniques, with a short duration for operation; hospitalization is unnecessary for the patients.

• The operating sites are well defined with no bleeding, smoke and burnt scabs generated; the operating field is clearly showed under endoscope, and the operation is safe.

• The operation only causes mild tissue reaction and mild injury to deeper tissues, and results in no pain, complication and sequelae for the patients.

• Showing by various basic studies, a temperature higher than 41.5°C might kill selectively cancer cells; microwave might raise the temperature of local tissue to over 60°C by its thermogenetic effect to coagulate that tissue and then eradicate local tumors.

In summary, microwave coagulation widens the field of treatment for recurrent NPC; however, the indications should be correctly determined. The patients should be followed up regularly; if the operation is found to be ineffective, other therapies could be performed as salvage.

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References