Case Report

A Case of Recurrent Ampullar Carcinoma Undergoing Photodynamic Therapy after Surgical Resection

Yorihisa Sumida,1 Atsushi Nanashima,1 Takaumi Abo,1 Toshiya Nagasaki,1 Shigekazu Hidaka,1 Hiroaki Takeshita,1 Hidetoshi Fukukawa,1 Kenji Tanaka,1 Terumitsu Sawai,1 Toru Yasutake,1 Takeshi Nagayasu,1 Toshikazu Matsuo,2 Kazuhiro Shimizu1

1 Department of Surgical Oncology, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan
2 Department of Surgery, Omura Municipal Hospital, Omura, Nagasaki, Japan
3 Department of Dermatology, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan

We report a successful treatment of photodynamic therapy in patients with remnant ampullar carcinoma who underwent local resection of duodenal papilla. A 56-year-old male patient showed ampullar carcinoma without invading pancreas or duodenum. Pancreatic body and tail were obviously atrophic and local resection of duodenal papilla was performed at associated hospital 3 months ago. However, a resected specimen showed the remnant carcinoma at the edge, and the follow-up endoscopy showed a protruding tumor in the resected portion. Similar to the resected specimen, endoscopic biopsy showed a well differentiated adenocarcinoma in this tumor. Since additional resection was difficult because of the pancreatic function, photodynamic therapy with laser beam of 630 nm wavelength by eximer dye laser (4 mJ/pulse, 40 Hz) was applied to the ampullar carcinoma through endoscope for consecutive two days. Follow-up endoscopy performed 4 weeks after photodynamic therapy showed a remarkable reduction of the tumor, and no cancer tissue was observed by a biopsy. Ablation with argon beam laser was additionally applied to the remnant mass region. Tumor recurrence was not observed for 8 months after photodynamic therapy.

ACTA MEDICA NAGASAKIENSIA 51: 111 - 114, 2006

Keywords: Photodynamic therapy; Porflimer sodium; Eximer dye laser; Ampullar carcinoma; Endoscopy

Introduction

Adjuvant treatment for bile duct carcinoma (BDC) is often necessary after resection because of remnant tumor at the stump of bile duct.1-3 To date, there are no data supporting the survival advantage of adjuvant radiotherapy and/or chemotherapy after surgery.4-6 Photodynamic therapy (PDT), a laser treatment, has led to remarkable regression of malignant tumors, including BDC, since the 1980s.7 Several investigators reported the clinical usefulness and survival benefits of PDT for non-resectable BDC or resectable BDC.8-10 Thus, PDT is currently a useful modality for local treatment in BDC. We previously reported the clinical trial of PDT for remnant BDC at the stump of bile duct after surgical resection or for non-resectable BDC11; the results demonstrated the effective local control of tumor recurrence or tumor reduction, indicating survival benefits for BDC patients. We report here our experience of the successful treatment of PDT in a patient with recurrent ampullar carcinoma after partial resection of duodenal papilla.

Case report

Present status

A 56-year-old male was suffering from chronic pancreatitis and pancreatic abscess caused by heavy alcohol drinking (approximately 240 g of ethanol per day for 26 years) since 5 years ago and pancreatic body and tail were severely atrophic. The patient was also suffering from diabetes mellitus, which was controlled by insulin injection. In January, 2005, the patient had the hepatic dysfunction and an ampullar carcinoma was found by endoscopy. Since pancreatic head

Address correspondence: Atsushi Nanashima, M.D., Department of Surgical Oncology, Nagasaki University Graduate School of Biomedical Sciences, 1-7-1 Sakamoto, Nagasaki 852-8501 JAPAN

TEL: +81-(0)95-849-7304, FAX: +81-(0)95-849-7306, E-mail: a-nanasm@net.nagasaki-u.ac.jp

Received February 6, 2006; Accepted June 27, 2006
resection could not remain pancreatic parenchyma, local resection of
duodenal papilla and lymphadenectomy around pancreas head was
carried out at associated hospital in February, 2005. Histological
findings showed moderately differentiated tubular adenocarcinoma
of the papilla Vater with slight tumor invasion to the venous system
(\(v_1\)) and no evidence of lymph node metastasis. Horizontally and
vertically resected margins of the specimen showed cancer cell posi-
tive, and therefore the patient was referred to our institute for adjuvant

treatment.

Laboratory data at admission were all in the normal range except
for the blood sugar, which was high (142 mg/dL) before meal. Serum
carcinoembryonic antigen (3 µg/mL) and carbohydrate antigen 19-9
(27 U/mL) were in the normal range. Red blood cell protoporphyrin (44
µg/dL) and uroporphyrin (22 µg/gC) were in the normal range (<36
µg/gC). The dermatological skin test showed no photosensitization
in the patient. The thin-slice computed tomography showed enhanced
protruding mass lesion of 8 mm in diameter in the descending duode-
num without infiltration to pancreas head (Figure 1). Either pancre-
atic body or tail was not observed and common bile duct was mildly
dilated.

Endoscopic findings showed protruding tumor with sutured thread
(Figure 2). Biopsy specimens of the tumor showed moderately dif-
ferentiated tubular adenocarcinoma. For the purpose of local con-
trol, PDT with endoscope was selected in the present case.

**Photodynamic therapy**

Porfimer sodium (Photofrin®; Wyeth Pharmaceuticals, Collegeville,
PA and Wyeth K.K., Tokyo, Japan), a hematoporphyrin derivate,\(^1\)
was intravenously injected at a dose of 2 mg/kg body weight (106 mg
in this patient) 48 hours before PDT. After injection of Photofrin\(^2\), the
patient stayed in a dark room shielded by curtain (100-300 lx) for 4
weeks to prevent skin phototoxicity.\(^3\) Protoporphyrin, uroporphyrin
and conventional blood parameters were monitored every week after
administration of Photofrin\(^4\). The apparatus used was PDT EDL-1
(Hamamatsu Photonics K.K., Hamamatsu, Japan).\(^5\) Laser beam of
630 nm wavelength by eximer dye laser (4 mJ/pulse, 40 Hz) was
applied to multiple target lesions of the tumor through endoscope
for 10 minutes. The work was, on average, 100 joules per cm\(^2\) of
surface.\(^6\) In the present case, PDT was applied for consecutive 2
days because of thick mass lesion.

On day 1 (48 hours after administration), laser was radiated to
4 parts of the tumor (400 J) and additional laser radiation was ap-
plied to 3 parts (300 J) on day 2 (72 hours after administration).
Antibiotic prophylaxis was administered after cholangioscopy. Figure
3 A shows the endoscopic findings on day 7 after PDT; a half of
the tumor reduced and turned into hematoma. Discharge of bile from
orifice of bile duct was more remarkable. Surrounding normal du-
odenal epithelium showed no abnormal changes. On day 28, mass le-
sion was still reduced and only the flat lesion remained (Figure 3 B).
Histological findings by biopsy showed a papillitis with dysplastic
glands but showed no malignant cells. Since dysplastic cells were
remained, argon laser coagulation was finally radiated on the whole
surface of lesion (Figure 3 C).

Changes in red blood cell protoporphyrin and uroporphyrin are
shown in Figure 4. Protoporphyrin level transiently increased on
day 1 and day 5 but returned from day 14 to the level similar to
that before PDT. On the other hand, uroporphyrin level began to
increase from day 14, but it remained within the normal range on
day 28. Skin photo test on day 35 showed hyper-reaction. Mild
photodermatitis was observed on the right hand and neck, but this
skin reaction disappeared within a couple of days by steroid cream.
Ophthalmologic examination showed no abnormality in the cornea
or retina. The severe complications were not observed during hos-
pital stay, and the patient was discharged on day 41 and has kept
protecting photosensitivity. Tumor recurrence was not observed 8
months after PDT.

![Figure 1](image1.png)

**Figure 1.** Enhanced computed tomography showing a protruded tumor le-
son of 8 mm in diameter at the site of resection (arrow). There was no
lymphadenopathy around pancreas head.

![Figure 2](image2.png)

**Figure 2.** Endoscopic findings of ampullar tumor after resection of papilla
Vater.
Figure 3. Changes in endoscopic findings of ampullary tumor. A. Findings on day 7 after PDT. B. Findings on day 28 after PDT. C. Findings just after the argon beam coagulation therapy.

Figure 4. Changes in the levels of red blood cell protoporphyrin (mg/dl and uroporphyrin (μg/gC) before and after PDT. Normal range of uroporphyrin is under 36mg/gC.

Discussion

The effect of PDT is specific to cancer tissue compared to normal surrounding tissue because of the trapping and accumulation of the photosensitizer in cancer cells. PDT gives rise to mild damage during the laser exposure but provides good effectiveness. Microwave and other laser ablations are also effective for local cancer treatment but tumor damage is extensive due to the higher energy of these two modalities compared to PDT. Since 2001, we have applied PDT to bile duct carcinoma as an adjuvant treatment after surgical resection or tumor occlusion of main bile ducts. Our pilot study showed that efficacy of tumor reduction was remarkable and tumor was reduced without bleeding or degradation debris. Patients had no severe side effects by this treatment and, furthermore, longer survival benefit might be acquired. In the present case, less invasive local treatments were necessary because of the history of severe chronic pancreatitis. Since the tumor did not invade deeper in the present patient, partial surgical resection to remain pancreas head would be better for patient's prognosis. However, the patient underwent pancreatic surgery twice and therefore such a delicate operation was difficult. The patient first chose non-operative modality giving us informed consent. This is the reason why we applied PDT to the present case. This modality is very helpful to cover the limits of the surgical procedure, while the effect of adjuvant chemotherapy or irradiation remains controversial.

The problem in the present case concerning PDT was the thickness of tumor, approximately 1cm by computed tomography. We regret that the endoscopic sonography was not performed and therefore vertical infiltration of tumor was not evaluated in the present case. Mimura et al. reported that the eximer dye laser penetrated tissues deeper than did other laser beams. We therefore anticipate that PDT will also be effective to tumor cells located in deeper lesions. Wiedmann et al. reported a phase II pilot study of neoadjuvant PDT in patients with hilar cholangiocarcinoma, the histological findings of which revealed no viable cancer cells in the inner layer up to 4
mm but some viable nests in lymphatic spaces and nerve sheets of the outer layer (5-8 mm). Recently, Zoeppf et al. have clarified, by a randomized controlled study, the safety and usefulness of PDT as a palliative modality for bile duct carcinoma. In the present case, laser was irradiated not only to the front but also to the side of the protruding tumor. Furthermore, PDT was performed for consecutive 2 days to accomplish the sufficient cytoidal effect in the deeper lesion of the tumor. The results showed a remarkable reduction in tumor mass and disappearance of cancer cells as was expected. We consider that PDT was very effective in this case for local control of ampullary carcinoma.

We previously reported that 4 of 8 patients administered photosensitizer had problems related to skin phototoxicity. The present case also had a mild sunburn-like dermatitis on day 28 when he was released from the stay in dark room. Rumalla et al. also reported skin phototoxicity after PDT in a few patients. Although no patients including the present case developed serious skin phototoxicity in our series, such side effects must be anticipated, and patients must be instructed in skin care and should be followed up by dermatologists. The present case received dermatological examination of skin phototoxicity every week for 2 months. Theoretically, Photofrin level in normal tissues decreases 35 days after administration. Our previous study showed a higher level of uroporphyrin on day 28 and porphyrin derivatives therefore might remain in the skin for more than one month after PDT. In the present case, uroporphyrin level was also increased, though within the normal range, and we therefore carefully followed the patient. In 2004, a new photosensitizer was developed for treatment of lung cancer, which may improve the treatment in the future.

In conclusion, PDT was performed in a patient with remnant ampullary carcinoma after surgical resection. PDT was very effective for the local control of tumor growth and led to no serious adverse effects. Adjuvant PDT therapy is a safe and useful treatment option for bile duct carcinomas.

References