Photodynamic Therapy in Management of Head and Neck Cancers and Precancerous Lesions

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Abstract

Photodynamic therapy (PDT) is a new form of cancer treatment with low morbidity. In this study, PDT was evaluated for its effectiveness in management of recurrent or widespread precancerous lesions, primary cancers in inoperable sites, recurrent or residual cancers which were refractory to radiotherapy and chemotherapy, and advanced tumors in the head and neck. Fifty-one patients were treated over a period of 5 years. A 91.67 per cent complete response rate was observed for T_1 tumors (primary and recurrence) with a recurrent rate of 27.27 per cent. Nasopharyngeal carcinoma was highly responsive to PDT since all T_1 and T_2 tumors responded completely. This was in contrast to cancers in the soft palate which failed in most cases possibly due to inadequate light dose distribution. PDT was remarkably effective in curing premalignant diseases (100% complete response rate). Postoperative PDT was equally effective in treating the microscopic residual malignancy. For advanced tumors, PDT in adjunct to conventional modalities could induce complete response in 5 out of the 10 patients and resolve symptoms in 4 cases. The mean follow-up time for this series was 28.3 months (range 3-66 months). In conclusion, PDT is a useful modality for the treatment of head and neck tumors and precancerous lesions presenting in forms or under conditions that posed considerable difficulties in management by conventional approaches.

Key word : Photodynamic Therapy, Head and Neck Cancers, Primary and Recurrent Cancers, Precancerous Lesions

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Radiotherapy and/or surgery are the mainstay of treatment for nonmalignant changes and cancerous growth in the head and neck[1,2]. The choice of treatment modality is usually based on a number of factors such as pathology and staging of the diseases, accessibility of the lesion, anticipated morbidity and mortality[1]. Despite the dramatic improvements in modern surgical and radiothera-

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peutic procedures,[2] certain clinical circumstances continue to be problematic. For instance, field cancerization leading to multicentric lesions involving the entire upper aerodigestive tract[3]. Surgical resection of the synchronous or metachronous primaries along with the premalignant lesions is likely to result considerable multilation. For radiotherapy, long-term effect of radiation on the regional mucosa remains unclear. But there are concerns about the possibility of ionizing radiation in converting the premalignant disease into anaplastic and frankly invasive cacinoma[4]. In patients with premalignant changes, the presence of erythroplakia in addition to leukoplakia generates a significant risk to neoplastic transformation[5]. Surgery is the treatment of choice. Nevertheless, surgical resection is effective for localized disease but can induce high morbidity for lesions with widespread involvement. Persistent or recurrent tumor after radical treatment is another example presenting therapeutic dilemma when a decision must be made of how to properly manage this group of patients.

Obviously, an alternative form of treatment with low morbidity is highly desirable for the management of cancers in the head and neck. Photodynamic therapy (PDT) is a relatively new modality of treatment utilizing a photosensitive drug which is selectively localized and retained in the tumor organ[6,7]. The drug by itself is noncytotoxic but can be activated by light of specific wavelength matching its absorption peak to destroy malignant cells by photooxidative process[6,7]. Since drug uptake occurs in both tumor tissue and stroma, tumor necrosis is induced *via* several mechanisms including direct tumor cell killed by oxygen radical production and vascular shutdown caused by PDT-induced tumor inflammation[6]. In contrast to conventional treatments, PDT can elicite tumor-specific immune reaction which is crucial in attaining long-term tumor control[6]. Because there is less sensitizer accumulating in the adjacent normal tissue, selective destruction of the tumor occurs while the affected normal tissue heals completely following PDT[6,7]. This feature makes PDT rather attractive for head and neck cancers where excessive tissue loss can result in significant functional debilities[8]. All these factual facets support the notion that PDT neither causes systemic toxicities like chemotherapy nor induces the same types of late sequelae as encountered in radiotherapy.

Since PDT is an entirely different process, prior use of surgery, radiotherapy or chemotherapy does not preclude the use of PDT in treating recurrent or residual diseases which are refractory to conventional treatments, or as an intraoperative adjuvant therapy for relatively massive tumors[7]. Owing to the limiting depth of light penetration, i.e. 0.5-1.0 cm necrotic depth as achieved by the first generation sensitizers[9], PDT has been continuingly demonstrated to be effective for treating early-stage cancers or early recurrent tumors with an average complete response rate of 92 per cent [4,10-20]. Treatment of nonmalignant conditions such as recurrent laryngeal papillomatosis with PDT is also reported in the literature[21]. This report highlights the clinical findings compiled over a period of 5 years in using PDT as (1) a curative treatment for precancerous lesions, squamous papilloma, early primary and recurrent or residual tumors, (2) a postoperative adjunct to laser excision, and (3) combined treatment with surgery or radiotherapy or/and chemotherapy for patients with advanced head and neck cancers.

MATERIAL AND METHOD

Patients

Patients who were selected for PDT were those with diseases presenting in forms or underconditions that appeared to be unsuitable for standard treatments. This included those patients with (a) recurrent or widespread precancerous lesions including squamous papillomatosis, (b) primary cancers originating in locations where surgery would lead to structural deformity, functional debility or significant morbidity, (c) recurrent or persistent tumors after receiving full treatment with standard modality, (d) tumors resected by surgery that failed to generate tumor free margin. Patients who refused conventional treatments were also admitted for this clinical trial. Additionally, the patients who were eligible should have Kanofsky scores of 70 per cent or greater, normal kidney and liver function, no evidence of pregnancy and porphyria. All patients signed informed consent before treatment.

PDT treatment

The patients were treated by an institutionally approved protocol on human rights related to research involving human subjects based on the declaration of Helsinki. Before PDT treatment, patients underwent physical examination, endosco-

pic investigation and biopsy, CT scan and chest X-rays including routine laboratory check-up.

Hematoporphyrin derivatives, HpD (5mg/ml, the Queen Elizabeth Hospital, Woodville, Australia) was injected intravenously into the patient as an outpatient procedure. The dosage of 3mg/kg was administered as small bolus dose over a period of 5-10 minutes. After 48 hours the lesion was exposed to a laser beam (630 nm) from KTP 532 pumped dye laser system (Laserscope, California, USA). The illuminated field covered the tumor plus at least 0.5 cm beyond the tumor margin. A light dose of 100 J/cm^2 was delivered by a flat cut optical fiber (with a core diameter of 400 μm, Laserscope, California, USA) at a fluence rate of 100 mW/cm^2. The light dose given in 1000 seconds was divided into 4 fractions with a few minutes break. Multiple field of exposures were prescribed for those lesions with widespread extension.

The treatments were conducted mostly under local anesthesia except for those patients with diseases in the nasopharynx and tracheobronchial tree. These patients were treated endoscopically under general anesthesia. Postoperative adjuvant PDT was performed 1-2 weeks after tumor resection and the tissue specimen confirmed the presence of residual microscopic disease. Combined treatment with conventional modalities was given 2-3 months after PDT debulking of the massive tumor.

Post-treatment management and evaluation

Postoperative management included prescription of analgesic and antibiotics to combat-infection. For 3-6 weeks, patients were advised to gargle with mouth wash for cases whose diseases were located in the oral cavity and nasal douching for patients with nasopharyngeal carcinomas (NPC). Toilet endoscopy was scheduled weekly over a period of 4-6 weeks for patients who received treatment of the nasopharynx.

During the first three months, patients were observed monthly for magnitude of tumor response and extent of normal tissue healing. Long-term follow-up checks were scheduled at 6 months, 1, 2, 3, 4, 5 years post-treatment. The treatment effects were categorized as follows : (a) complete response (CR) = absence of detectable lesion and biopsy proven negative, (b) partial response (PR) = reduction by at least 50 per cent in the largest diameter of the treated area, (c) no response (NR) = reduction by less than 50 per cent of the largest diameter of the treated area or continued tumor growth.

Safety measure

Patients were advised to refrain from outdoor activities for at least 30 days and also avoid exposure to bright room light. Exposed parts of the body should be covered by wearing trousers and long-sleeved shirts. The patients should also put on sunglasses and carry an umbrella or wear a hat whenever they wanted to do some outdoor activities.

RESULTS

Fifty-one patients who were eligible for analysis were treated from March 1994 to February 1999 with a mean follow-up time of 28.3 months (range 3-66 months). The patient characteristics describing distributions of age and sex, sites of disease and pathology are presented in Table 1. In this series, PDT was given with curative intent for squamous papillomatosis and precancerous lesions, early primary and recurrent or residual cancers and the tumor bed after surgical resection. For diseases in the advanced stages, PDT was used as an adjunct to conventional treatments to provide disease control or symptom relief.

PDT in the treatment of squamous papillomatosis and precancerous lesions

Eleven patients with squamous papillomatosis or leukoplakia with erythroplakia were treated by PDT for various reasons, namely recurrent or residual from surgery; surgery would cause considerable multilation because of widespread extention of the disease; and some patients even refused surgery (Table 2). Complete response could be observed in all cases. In 2 patients, one with squamous papilloma and the other with leukoplakia and erythroplakia, their diseases recurred 24 and 15 months after PDT. However, further surgical resection or a second course of PDT successfully kept the diseases under control for a follow-up period of 22 and 33 months respectively (Tables 2 and 7).

PDT in the management of T_1-T_2 primary cancers.

Patients whose diseases were located in sites where surgical resection would lead to structural deformity or functional debility, or who refused conventional modalities were recruited for

PDT. Fourteen patients with a total of 15 sites were treated. A 60 per cent complete response rate was achieved for this group of patients (Tables 3 and 7). Over a mean follow-up time of 23.5 months, (range 3-65 months), one patient recurred 10 months after the treatment. However, the patient was retreated with PDT. The disease resolved completely and no evidence of disease could be

Table 1. Patient characteristics.

Description	Characteristics	Number
Patient : Sex/Age	Male/57.6[a] (35-90)[b]	27
	Female/62.6 (14-83)	24
Site of disease	Oral cavity	
	• Buccal mucosa	13
	• Soft and hard palate	11
	• Floor of mouth, lip, gum and retromolar trigone	9
	• Tongue	4
	Oropharynx	
	• Tonsil	2
	• Post pharyngeal wall	1
	Nasopharynx	12
	Nose and nasal cavity, maxillary sinus	7
	Ear	2
	Main bronchus	1
Pathology	Squamous papilloma	2
	Leukoplakia, erythroplakia, dysplasia	9
	Verrucous carcinoma	3
	Basal cell carcinoma	6
	Squamous cell carcinoma	33
	Mucoepidermoid carcinoma	1
	Adenoid cystic carcinoma	2

a = Mean; b = Range

Table 2. Photodynamic therapy in the treatment of benign condition and precancerous lesion in the head and neck.

Patient	Age/Sex	Site	Histology	PDT response	Follow-up (month)	Remark
1	72/F	Hard palate	Squamous papilloma	CR	33	Recur from surgery
2	57/F	Hard palate	Leukoplakia, erythroplakia	CR	48	Surgery was multilating
3	71/M	Floor of mouth	Dysplasia	CR	15	Refuse surgery
4	61/M	Lt.lateral tongue	Leukoplakia	CR	39	Refuse surgery
5	44/M	Both buccal mucosa	Leukoplakia, erythroplakia	CR	34	Surgery was multilating
6	64/M	Both buccal mucosa	Leukoplakia, erythroplakia	CR	39	Recur from surgery
7	67/F	Rt. buccal mucosa	Squamous papilloma	CR	24[c]	Surgery was multilating
8	67/M	Lt.buccal mucosa	Leukoplakia, erythroplakia	CR	37	Residual from surgery
9	81/F	Both buccal mucosa	Leukoplakia, erythroplakia	CR	60	Surgery was multilating
10	90/M	Both buccal mucosa	Leukoplakia, erythroplakia	CR	13	Surgery was multilating
11	52/F	Both buccal mucosa	Leukoplakia, erythroplakia	CR	15[d]	Surgery was multilating
	53/F	Lt.buccal mucosa	Leukoplakia, erythroplakia	CR	33	Recur from PDT

CR = complete response; PDT = photodynamic therapy.
c = The disease recurred after 2 years as a few scattered foci which were easily removed by laser excision.
d = The disease recurred after 15 months and could be successfully controlled by second course PDT.

observed over 21 months. It was noteworthy that patient number 3 (Table 3) whose disease was first described as unknown primary cancer had the hidden primary unveiled in the nasopharynx by photodiagnostic imaging[22]. Since the patient had undergone neck dissection and received large field irradiation covering nasopharynx, tonsils, base of the tongue and pyriform sinuses, the discovered primary was therefore treated with PDT. Complete remission was observed over a follow-up period of 31 months.

PDT in the treatment of T_1- T_2 recurrent or residual cancers.

There were 12 patients with early recurrent or residual cancers (i.e. T_1 – T_2 tumors) enrolled in the PDT treatment program. It was quite interestingly that all patients with diseases in the nasopharynx responded completely (Table 4). The response of cancers in the oral cavity, on the otherhand, was rather disappointing. The overall complete response rate was 83.33 per cent (Table 7). The mean follow-up time for this group of patients was 23.6 months (range 4-66 months).

PDT as a post-operative adjunct to laser excision

Six patients with diseases in the nose and tongue underwent surgical resection and failed to generate tumor free margin. PDT was subsequently delivered to the tumor bed. All patients remain disease-free after a mean follow-up time of 29.3 months (range 8-52 months) (Tables 5 and 7).

PDT in combination with conventional treatments in treating advanced cancers.

There were 10 patients who were eligible for analysis. Only patients who responded partially to PDT were recruited for study. After receiving further treatments with either radiation or/and chemotherapy or/and surgery, the diseases resolved completely in patients with T_1 – T_2 tumors including massive verrucous carcinoma. (Table 6) For patients with advanced diseases, the combined treatments yielded only palliative outcomes in most cases. The complete response rate was 50 per cent with a mean follow-up time of 33 months (range 7-60 months)

DISCUSSION

Photodynamic therapy (PDT) has been evaluated and reported to be effective for the management of head and neck cancers for more than 15 years[8,13,19]. Over 700 patients have been treated worldwide[4,8,10-20]. It has now been established that PDT is highly effective in treating early cancers of the head and neck[8,13]. A 91.63 per cent

Table 3. Photodynamic therapy in the treatment of T_1-T_2 primary cancers in the head and neck.

Patient	Age/Sex	Site	Histology	Staging	PDT treatment	
					Response	Duration (month)
1	39/M	Rt.ear	Basal cell Ca	T_1 NoMo	PR	3
2	51/F	Dorsum nose	Basal cell Ca	T_1 NoMo	CR	29
3	38/M	Nasopharynx	SCC, poorly diff	T_1 NoMo	CR	31
4	71/M	Floor of mouth	SCC, mod. diff	T_1 NoMo	CR	19
5	69/M	Lt. gum c̄ floor of mouth	SCC, well diff	T_2 NoMo	CR	9
6	80/F	Hard palate	SCC, mod. diff	T_2 NoMo	CR	65
	82/F	Rt.retromolar trigone	SCC, poorly diff	T_1 NoMo	CR	10[e]
7	71/M	Hard palate	Verrucous Ca	Noninvasive	CR	15[f]
8	56/F	Lt.lateral tongue	SCC, well diff	T_2 NoMo	NR	-
9	54/M	Lt.soft palate c̄ tonsil	SCC, well diff	T_2 NoMo	PR	3
10	52/M	Soft and hard palate	SCC, mod. diff	T_2 NoMo	NR	-
11	81/F	Rt. buccal mucosa	SCC, well diff	T_1 NoMo	NR	-
12	43/M	Lt.post pharyngeal wall	SCC, undiff	T_2 NoMo	NR	-
13	76/F	Lower lip	SCC, well diff	T_1 NoMo	CR	21
14	14/F	Lt. main bronchus	Mucoepidermoid Ca	T_1 NoMo	CR	53

SCC = squamous cell carcinoma ; Ca = carcinoma ; CR = complete response ; PR = partial response ;
NR = no response ; PDT = photodynamic therapy.
e = The disease recurred ofter 10 months and was successfvlly controlled by second course PDT.
f = The patient died from car accident after a follow-up time of 15 months.

Table 4. Photodynamic therapy in the treatment of T_1 - T_2 recurrent or residual cancers in the head and neck.

Patient	Age/Sex	Site	Histology	Disease/Staging	Previous treatment (Initial staging)	PDT treatment	
						Response	Duration (month)
1	55/F	Lt. buccal mucosa	Verrucous Ca	Residual/Noninvasive	S 1996 (Noninvasive)	CR	28
2	67/M	Lt. retromolar trigone	SCC, poorly diff	Residual/T_1	R 1997 (T_1NoMo)	CR[g]	4
3	83/F	Rt. retromolar trigone	SCC, mod. diff	Recur/T_1	PDT 1996 (T_1NoMo)	CR	21
4	80/F	Lt. lower gum	SCC, poorly diff	Residual/T_2	S+R1994 (T_3NoMo)	NR	-
5	46/M	Soft palate	SCC, mod. diff	Residual/T_2	R1997 (T_3NoMo)	NR	-
6	69/M	Rt. nose	Basal cell Ca	Residual/T_1	S 1995 (T_1NoMo)	CR[h]	24
7	45/M	Nasopharynx	SCC, poorly diff	Residual/T_1	R + C 1992 (T_4NoMo)	CR[i]	66
8	35/M	Nasopharynx	SCC, poorly diff	Recur/T_1	R + C 1994 (T_3NoMo)	CR	12
9	43/M	Nasopharynx	SCC, poorly diff	Recur/T_2	R + C 1988 (T_3N_3Mo)	CR	34
10	72/M	Nasopharynx	SCC, poorly diff	Residual/T_2	R + C 1994,1997 (T_3N_{2c}Mo)	CR	21
11	57/F	Nasopharynx	SCC, poorly diff	Recur/T_2	R + C+S 1991 (T_3N_{2a}Mo)	CR	16
12	37/F	Nasopharynx	SCC, poorly diff	Recur/T_2	R + C 1996 (T_3N_{2b}Mo)	CR	10

SCC = squamous cell carcinoma ; Ca = carcinoma ; CR = complete response ; PR = partial response ; NR = no response.
PDT = photodynamic therapy ; R = radiotherapy ; C = chemotherapy ; S = surgery.
g = The disease recurred 4 months after PDT. The patient refused conventional treatments and received 3 additional courses of PDT to continuingly induce partial response over a period of 11 months. However, the disease progressed on the fourth PDT attempt.
h = The disease recurred after 2 years.
i = The patient died of unrelated cause one year after PDT.

Table 6. Photodynamic therapy as adjunct to conventional treatments in management of advanced cancers in the head and neck.

Patient	Age/Sex	Site	Histology	Disease (Staging)	Number of treatment				Response	Follow-up (month)	Remark
					PDT	S	R	C			
1	70/F	Rt. buccal mucosa	Verrucous Ca	Residual (Nonivasive but massive)	1	1	0	0	CR	39	Disease free
2	54/M	Lt. soft palate & tonsil	SCC, well diff	Primary (T_2 NoMo)	1	0	35[j]	6[j]	CR	60	Disease free
3	71/F	Tongue	SCC, poorly diff	Residual (T_3NoMo)	2	0	0	2[k]	NR	-	Expire
4	80/F	Rt. buccal mucosa	SCC, mod diff	Recurrent (T_1 N_1Mo)	2	1	35	0	CR	21	Disease free
5	43/M	Nasopharynx	SCC, poorly diff	Residual (T_3NoMo)	2	0	0	6	PR	30	Expire
6	53/F	Nasopharynx	SCC, poorly diff	Residual T_3 $N_1$$M_1$	3	0	0	6	CR	36	Disease free
7	62/M	Nasopharynx	SCC, poorly diff	Residual (T_4 NoMo)	2	0	0	6	PR	36	Symptom free
8	59/M	Nasopharynx	Adenoid cystic Ca	Residual (T_3NoMo)	2	1	0	0	PR	22	Symptom free
9	62/M	Nasopharynx	SCC, poorly diff	Residual (T_4 NoMo)	3	0	12[k]	0	PR	7	Symptom free
10	39/M	Rt. ear	Basal cell Ca	Primary (T_2 NoMo)	1	1	0	0	CR	46	Disease free

SCC = squamous cell carcinoma ; Ca = carcinoma ; CR = complete response ; PR = partial response; NR = no response.
PDT = photodynamic therapy; S = surgery; R = radiotherapy; C = chemotherapy .
j = Curative dose, k = Palliative dose was given when the tumor did not respond to the treatment appreciably.

Table 5. Photodynamic therapy as a post-operative adjunct to laser excision.

Patient	Age/Sex	Site	Histology	Staging	Disease	PDT treatment	
						Response	Duration (month)
1	82/F	Lt. lateral tongue	SCC, well diff	T_1 NoMo	Primary	CR	33
2	59/F	Rt. alarnasi (nose)	Basal cell Ca	T_1 NoMo	Primary	CR	34
3	65/M	Rt. nostril	SCC, well diff	T_1 NoMo	Primary	CR	52
4	32/F	Rt. nostril	SCC, well diff	T_1 NoMo	Primary	CR	38
5	57/F	Lt. nostril	Basal cell Ca	T_1 NoMo	Primary	CR	8
6	65/F	Rt. maxillary sinus	Adenoid cystic Ca	T_3 NoMo	Residual	CR	11

SCC = squamous cell carcinoma; Ca = carcinoma; CR = complete response; PDT = photodynamic therapy.

Table 7. Rate of complete response to photodynamic therapy in management of nonmalignant and malignant diseases in the head and neck.

Indication	Number of treated sites	Response			CR rate (%)	Follow-up time (month)
		CR	PR	NR		
Squamous papilloma, precancerous lesions	12	12	0	0	100.00	32.5[l] (13 - 60)[m]
T_1 - T_2 primary cancers	15	9	2	4	60.00	23.5 (3 -65)
T_1 - T_2 recurrent or residual cancers	12	10	0	2	83.33	23.6 (4 - 66)
Tumor bed after laser excision	6	6	0	0	100.00	29.3 (8 - 52)
Combined treatments for advanced cancers	10	5	4	1	50.00	33.0 (7 - 60)

CR = complete response ; PR = partial response ; NR = no response; l = Mean ; m = Range

complete response rate is estimated from data published in the literature of 243 patients mostly with T_1 tumors presenting as primaries, recurrent or residual diseases. Rate of recurrence varies within 20 per cent[4,10-20]. In the present series, complete response rate for 12 T_1 tumors was 91.67 per cent and the diseases recurred at a rate of 27.27 per cent. For the disease at T_2 stage (i.e. 13 cases), PDT could induce complete response only in 46.15 per cent of the patients.

Effectiveness of PDT appeared to vary among anatomical sites. Treatment of the larynx,[19] lip[12] and nasopharynx[20] yielded 100 per cent complete response. In our study, the most interesting finding was the responsiveness of nasopharyngeal carcinoma (NPC) to PDT. In contrast to cancers in other locations, complete response could be induced in all T_1 and T_2 tumors. For staging beyond T_2, NPC still responded appreciably although not completely. The effectiveness of PDT for early NPC observed in our series could be partly attributed to the adequate light dose delivered to the lesions mostly located in the posterior wall. PDT induced antitumor inflammatory reaction and tumor specific immune response[6] could be another contributing factor. In the submucosal layer of the nasopharynx, marked aggregation of lymphoid tissue is observed to be a unique feature for this organ[23]. Acute and chronic inflammation are quite common reactions in responding to damages of the nasophasyngeal mucosa[23]. In animal tumor models, PDT has been shown to arouse a selective increase of neutrophils which in turn inflict damage to endothelial cells while remaining in the tumor blood vessel and engage in destruction of tumor parenchyma upon extravasation[6]. At the same time, monocytes/macrophages are activated by PDT to destroy the tumor target by releasing TNF-α

or by mediating tumor-specific immune response through activation of cytotoxic T cells[6]. These PDT-induced inflammatory and immune responses have been demonstrated experimentally to be related to tumor control[6]. In humans, the effect of immunopotentiation by PDT has been reported by Lai et al who observed the significant increase in serum IL-2 and NK cell activity in 24 patients with persistent or recurrent NPC after the treatment of PDT[24].

In the oral cavity, PDT was effective for T_1 lesions in the hard palate, floor of the mouth and lip. PDT failed to induce dramatic response in one patient with a T_1 lesion in the buccal mucosa where uniform light dose could be easily achieved. However, the disease was successfully controlled by ionizing radiation. This rare example suggested different mechanisms and targets in tumor destruction between PDT and radiation. Anatomical complexity and relative inaccessibility of some structures such as retromolar trigone, gum and soft palate could further reduce treatment efficacy. For example, PDT could produce complete response in all T_1 lesions in retromolar trigone but the disease recurred in 2 out of 3 patients treated. PDT performed poorly for cancers in the soft palate which contains uvular and membranous part next to the hard palate. For this setting, it was likely that the disease might invade through the choanal site and extend deeper than that might be recognized by clinicians. Wenig et al demonstrated with the aid of magnetic resonance imaging that lesions in the soft palate tended to invade as deep as 1 cm regardless of a lesion as large as 2.2 cm or as small as 1 cm in diameter[15]. Complete response was achieved only by front surface irradiation in combination with interstital implantation[15].

Although the role of PDT as a primary treatment modality for early cancer has not yet been determined, it did generate significant clinical impact in cases where surgery or radiotherapy would be associated with high morbidity and mortality. This was exemplified by the case of a young patient who had a T_1 tumor in her left main bronchus in close proximity to the carina where effective treatment seemed impossible. The patient is still disease-free after a follow-up time of 53 months. A 38 year old male patient who had a primary cancer uncovered in the nasopharynx only after the completion of radiotherapy for the unknown primary. For this patient, further treatment of the nasopharynx with radiation would lead to unacceptable late complications. Again, no evidence of disease was observed over 31 months of follow-up. A number of patients had widespread premalignant changes in the buccal mucosa where surgery could lead to considerable multilation. All these patients still remain disease-free with the longest follow-up time of 60 months. In the management of early recurrent or persistent cancers, there seems to be a common consensus on the effectiveness of PDT for this clinical setting. In our series, 83.33 per cent of the patients responded completely. Two cases that failed were patients with diseases in the lower gum and soft palate, the sites where PDT performed poorly.

In a certain group of patients whose diseases seemed not to be effectively controlled by single treatment or patients who had advanced diseases, PDT was useful in debulking the tumor without adding any morbidity and permitted further radical treatments to be conducted in a less morbid manner since the size of the tumor or the field of treatment had become smaller. Although tumors in some patients failed to respond completely, the combined treatments could effectively resolve symptoms. PDT was also found to be effective when used after surgical resection that left behind residual microscopic disease which might lead to local recurrence or even metastatic disease without further treatment. Six cases were treated. All patients remain disease-free with the longest follow-up time of 52 months.

Because PDT is a noninvasive treatment and does not cause much tissue loss like surgery, it was also used to treat widespread premalignant lesions as well as those recurring after surgical resection. Although diseases in 2 out of the eleven patients recurred, the lesions could be effectively controlled by laser excision or a second dose of PDT because the sizes of the recurrences were much smaller than the original.

Our findings as well as those appearing in the literature,[4,8,10-21] strongly support the role of PDT either used alone or in adjunct to conventional treatments in the management of complicated nonmalignant conditions and neoplastic diseases in the head and neck.

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การรักษามะเร็งบริเวณศีรษะและลำคอและรอยโรคก่อนกลายเป็นมะเร็งด้วยวิธีโฟโตไดนามิค

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การรักษาด้วยวิธีโฟโตไดนามิค (PDT) เป็นวิธีการรักษามะเร็งแบบใหม่ที่มีผลข้างเคียงต่ำ งานวิจัยนี้ได้ศึกษาประสิทธิภาพของ PDT ในการรักษามะเร็งบริเวณศีรษะและลำคอตลอดจนรอยโรคก่อนกลายเป็นมะเร็ง ซึ่งก่อความยากลำบากต่อการรักษาโดยวิธีมาตรฐาน ซึ่งได้แก่ รอยโรคก่อนกลายเป็นมะเร็งที่แผ่ขยายเป็นวงกว้างหรือรอยโรคที่กลับเป็นซ้ำภายหลังการผ่าตัด มะเร็งปฐมภูมิในตำแหน่งที่ยากต่อการผ่าตัด มะเร็งย้อนกลับหรือไม่ตอบสนองต่อรังสีรักษาและเคมีบำบัด ตลอดจนมะเร็งในระยะลุกลาม มีผู้ป่วยเข้ารับการรักษาตลอดระยะเวลา 5 ปี จำนวน 51 ราย พบว่ามะเร็งขนาด T_1 (ทั้งมะเร็งปฐมภูมิและมะเร็งย้อนกลับ) ตอบสนองต่อ PDT ด้วยอัตราการตอบสนองแบบหมดจด (complete response) คิดเป็นร้อยละ 91.67 และมีอัตราการย้อนกลับของโรคร้อยละ 27.27 มะเร็งในบริเวณโพรงหลังจมูกตอบสนองต่อ PDT ได้ดีเยี่ยม เนื่องจากการตอบสนองแบบหมดจดเกิดในมะเร็งระยะ T_1 และ T_2 แตกต่างจากมะเร็งที่เพดานอ่อน ซึ่งส่วนใหญ่จะตอบสนองต่อการรักษาไม่ดีนัก ทั้งนี้อาจเป็นเพราะการกระจายของแสงภายในเนื้อร้ายเกิดขึ้นได้ไม่สม่ำเสมอ PDT สามารถควบคุมรอยโรคก่อนกลายเป็นมะเร็ง หรือมะเร็งที่หลงเหลือจากการผ่าตัดด้วยประสิทธิภาพที่สูงยิ่ง (complete response rate = 100%) สำหรับโรคในระยะลุกลาม การใช้ PDT ร่วมกับวิธีการรักษาอื่น ๆ สามารถทำลายเนื้อร้ายได้อย่างหมดจดในผู้ป่วย 5 ราย จากจำนวนทั้งหมด 10 ราย และ 4 ราย การรักษาให้ผลเพียงบรรเทาอาการ ระยะเวลาของการติดตามผลโดยเฉลี่ยสำหรับผู้ป่วยทั้งหมดนาน 28.3 เดือน (ระหว่าง 3-66 เดือน) กล่าวโดยสรุปคือ PDT เป็นประโยชน์ต่อการรักษามะเร็งในบริเวณศีรษะและลำคอรวมทั้งรอยโรคก่อนเป็นมะเร็งที่มีขอบเขตของรอยโรคและการตอบสนองซึ่งก่อให้เกิดความยากลำบากแก่การรักษาโดยวิธีมาตรฐาน

คำสำคัญ : การรักษาวิธีโฟโต้ไดนามิค, มะเร็งบริเวณศีรษะและลำคอ, มะเร็งปฐมภูมิและมะเร็งกลับเป็นซ้ำ, รอยโรคก่อนกลายเป็นมะเร็ง

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