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RADIATION TREATMENT OF CARCINOMA OF THE OROPHARYNX

Report on 201 patients

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A series of 201 patients with carcinoma of the oropharynx, treated at this Institute, was analyzed with special reference to the method of irradiation, results, complications, and the prognostic factors influencing the final outcome, and the results are now presented.

Material and Methods

Among the 201 patients reported, 138 were males (69%) and 63 females (31%) ranging in age from 14 to 77 years, with an average of 45 years. The 30 to 59 year age group was the largest, with 132 patients (66%). They were treated from March 1958, when the Institute first opened, through 1974. All cases were confirmed by histopathology and received their first course of irradiation at this hospital, with a tissue dose of not less than 40 Gy. The observation time was more than 5 years in all the patients and only 5 were lost to follow-up. These 5 patients were counted as dead.

The primary location was the tonsillar fossa in 86 patients (43%), the soft palate in 53 patients (26%), the root of the tongue in 39 patients (19%), while in 23 patients (11%) it was in the peri-epiglottic structures (lingual surface of epiglottis, vallecula, epiglottic-pharyngeal fold, lateral and posterior wall of oropharynx).

As regards symptoms, 47 patients (23%) had a sensation of a foreign body, 102 (51%) had observed a mass in the pharynx, 129 (64%) had pains in the

pharynx, and 62 patients (31%) had observed a mass in the neck.

Squamous cell carcinoma was found in 107 patients (53%), poorly differentiated carcinoma in 46 (23%), anaplastic carcinoma in 28 (14%), cylindroma in 8 (4%), unclassified carcinoma in 8 (4%), salivary gland carcinoma in 2 (1%), adenocarcinoma in 1 (0.5%) and muco-epidermoid carcinoma in 1 patient (0.5%). If poorly differentiated and anaplastic types were grouped as low differentiated tumors, there were 74 patients (37%) in this group, while 127 patients (63%) had well differentiated tumors.

The patients were staged according to the TNM classification (UICC). The series comprised 43 patients (21%) with early lesions (T1N0, T2N0) and 158 patients (79%) with advanced lesions (T1T2T3, N1N2N3).

Treatment. Sixty-three patients were treated by a ^{60}Co beam, 18 by a high energy electron beam, 34 by conventional deep roentgen rays (220 kV), 49 by a ^{60}Co beam plus deep roentgen rays, 7 by a high energy electron beam plus deep roentgen rays, 17 by an electron beam plus ^{60}Co and 13 patients by an electron beam plus ^{60}Co plus deep roentgen rays.

When a continuous course was used, 5 fractions per week were given with 2 Gy per fraction up to a total dose of 40 to 70 Gy/20 to 35 fractions/4 to 7 weeks. When a split course was used the first part usually consisted of 30 to 40 Gy/15 to 20 fractions/3

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Table 1
Results of radiation therapy in 201 patients with carcinoma of the oropharynx

	Five years		Ten years		Fifteen years		Twenty years	
	Survival	Cure	Survival	Cure	Survival	Cure	Survival	Cure
No. of patients	101/201	88/201	52/144	50/144	13/51	13/51	2/12	2/12
Per cent	50.3	44	36	35	26	26	(17)	(17)

to 4 weeks and the second part of 20 to 30 Gy/10 to 15 fractions/2 to 3 weeks with an interval of 2 weeks. A continuous course was given in 143 patients (71 %) and a split course in 58 patients (29%). The split course was usually given in order to alleviate the radiation reaction in the pharynx.

The position and size of the portals were determined according to the extent and location of the primary lesion, clinical stage, and histopathologic type. It usually extended 1 to 2 cm beyond the peripheral margin of the main tumor mass and covered Waldeyer's ring and the bilateral neck node regions. Larger portals were used for the poorly differentiated tumors including the base of the skull at the middle cranial fossa, the oropharynx, hypopharynx and both sides of the neck. Smaller portals were used for the well differentiated types. Bilateral opposed facio-cervical portals were used in 155 patients and a unilateral facio-cervical portal in 39 patients. Seven patients with early squamous cell carcinoma (T1T2N0) in the soft palate were treated by intra-cavitary roentgen rays. Therapeutic irradiation of neck node metastases was given in 94 patients up to a dose of 30 to 40 Gy against wide fields, followed by an additional dose against reduced fields. To avoid damage of the spinal cord the last part of the treatment was given with a sagittal beam and a lead shield in the midline. In 107 patients prophylactic irradiation of the neck was given. If a residual tumor remained after a tumor dose of 50 to 60 Gy further treatment with 10 to 20 Gy was given either with a reduced field or an intra-cavitary cone up to a total dose of 70 to 80 Gy. In 34 per cent (36/106) of the patients the primary tumor disappeared within one year.

Results

All patients were followed for more than five years. Five were lost and were counted as dead. The results are shown in Table 1. The crude survival

Table 2
Results of treatment of oropharyngeal carcinoma by radiation therapy or surgery

Authors	Method	Five-year survival	
		No.	Per cent
BARRS et coll. (1979)	Surgery		42
	Radiation plus surgery		47
CHUNG et coll. (1979)	Surgery	1/7	25
	Radiation	6/24	
	Surgery plus radiation	1/6	
PEREZ et coll. (1976)	Radiation plus surgery	31/69	45
	Radiation	8/15	53
WELLER et coll. (1976)	Radiation		35
CHENG et coll. (1980)	Radiation	20/49	41
Present series	Radiation	101/201	50.3

rates after 5, 10, 15 and 20 years were 50.3 per cent (101/201), 36 per cent (52/144), 26 per cent (13/51) and 17 per cent (2/12), respectively. The corresponding cure rates (no evidence of disease) were 44 (88/201), 35 (50/144), 26 (13/51) and 17 per cent (2/12), respectively.

Discussion

Results of radiation therapy, surgery or combined treatment recently reported in the literature are listed in Table 2. Most authors prefer irradiation alone, which gives a 5 year survival rate of about 50 per cent. The results in early lesions are even better, and in the present series a 5 year survival of 72 per

Table 3

Prognostic factors in carcinoma of the oropharynx treated by irradiation

Prognostic factors	Five-year survival		Statistical significance
	No.	Per cent	
Age			
Below 59 years	84/153	55	p<0.05
Over 60 years	17/48	35	
Primary site			
Tonsillar fossa	48/86	56	p<0.01
Base of tongue	23/39	59	
Soft palate	21/53	40	
Peri-epiglottis	9/23	39	
Symptom			
Foreign body sensation	31/47	66	p<0.01
Neck gland	25/62	40	
Deafness, tinnitus, pain in ear	4/18	22	
Pathology			
Low differentiation	46/74	62	p<0.01
High differentiation	55/127	43	
Clinical stage			
Early lesion	31/43	72	p<0.01
Advanced lesion	70/158	44	
Source			
⁶⁰ Co	28/63	44	p>0.05
Electron beam	9/18	50	
220 kV roentgen rays	18/34	53	
Electron plus roentgen rays	3/7	(43)	
Electron plus ⁶⁰ Co	10/17	59	
⁶⁰ Co plus roentgen rays	25/49	51	
Electron plus ⁶⁰ Co plus roentgen rays	8/13	62	
Dose			
40 Gy	6/18	33	p>0.05
50 Gy	17/37	46	
60 Gy	33/57	58	
70 Gy	23/39	59	
80 GY	15/32	47	
90 Gy	4/13	31	
100 Gy	3/5	(60)	
Fractionation			
Continuous course	74/143	52	p>0.05
Split course	27/58	47	
Tumor at end of treatment			
Disappeared	65/95	68	p<0.01
Residual or no change	36/106	35	

cent (31/43 patients) was obtained. Some prognostic factors are discussed here (Table 3).

Patients under 50 years of age had a better 5 year survival (55 %) than those over 60 years (35 %). The difference was statistically significant.

The 5 year survival rates for lesions at various sites were: tonsillar fossa 56 per cent (48/86), root of tongue 59 per cent (23/39), soft palate 40 per cent (21/53), and peri-epiglottis 39 per cent (9/23). These survival rates were not significantly different. The corresponding 10 year survivals were: tonsillar fossa 49 (28/57), peri-epiglottis 31 (5/16), soft palate 28 (13/46), and root of tongue 24 per cent (6/25). The 10 year survival was significantly better for carcinoma of the tonsils than for the other locations.

The symptoms were also correlated with the 5 year survival: foreign body sensation in the pharynx 66 (31/47), a mass in the neck 40 (25/62), and tinnitus, otalgia and deafness 22 per cent (4/18). As could be expected symptoms of advanced disease thus indicated a poor prognosis.

The relation of TNM stage to the 5 year survivals appears in Table 4: T1 77 per cent, T2 44 per cent, T3 41 per cent. The survival in the latter two stages was statistically inferior to the survival in stage T1. The 5 year survival rates for N0, N1, N2 and N3 lesions were 69, 47, 42 and 41 per cent, with a significantly higher survival rate in N0 than in the other 3 groups. Patients in the early stages (T1T2N0) had a high survival rate (72 %; 31/43) while those with advanced lesions (T3N0, T1T2T3, N1N2N3) had a significantly lower survival rate (44 %; 70/158). As reported by other authors (PEREZ et coll. 1976, CHENG et coll. 1980) TNM staging had a definite prognostic value.

The choice of irradiation technique was made according to the preference of the doctor in charge. No significant difference was found between treatments with different radiation qualities (Table 3).

The relation between the 5 year survival and the dosage is also shown in Table 3. The findings suggest that the optimum dose should be 60 to 70 Gy, which is in agreement with previously reported results (SHUKOVSKY & FLETCHER 1973, SPANOS et coll. 1976).

The split course technique and the conventional continuous course gave comparable 5 year survival rates: 47 per cent (27/58) for the former and 52 per cent (74/143) for the latter. The split course technique causes less local reaction, but prolongs the treatment and makes it more expensive. In agree-

Table 4
Relation of 5-year survival to TNM staging

	N0		N1		N2		N3		Total	
	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent
T1	13/14	93	11/14	79	2/2	(100)	8/14	57	34/44	77
T2	18/29	62	9/27	33	4/11	(36)	10/27	37	41/94	44
T3	5/9	(56)	8/19	42	2/6	(33)	11/29	38	26/63	41
Total	36/52	69	28/60	47	8/19	42	29/70	41	101/201	50.3

ment with some other authors (CHENG et coll.), the split course technique did not seem to have definite advantages compared with the continuous course.

The result observed at the end of the treatment, regarding the primary focus, had a significant influence on the prognosis. In patients with a complete regression of the primary tumor a 5 year survival of 68 per cent (65/95) was obtained, while the corresponding rate in patients with residual tumor at the end of treatment was only 34 per cent (36/106). It is possible that energetic supplementary treatment, as surgery, interstitial irradiation or regional hyperthermia, should be used in the future in cases with residual tumors.

The poorly differentiated carcinomas were, as a rule, sensitive to radiation and had an early disappearance rate of 82 per cent (61/74) and a definite local control rate of 95 per cent (70/74). Local recurrences of this type of carcinoma were rare, and occurred only in 5 per cent (4/74). The 5 year survival rate was 62 per cent (46/74). However, patients with poorly differentiated carcinomas often developed distant metastases; this occurred in 32 per cent (24/74). Consequently, prevention and treatment of blood-borne metastases presents a critical problem, if the prognosis for this form of malignancy is to be improved. It would seem to be advisable that poorly differentiated carcinomas should be adequately treated against large portals which include the whole of Waldeyer's ring and both sides of the neck. Clinical trials should also be considered, using adjuvant chemotherapy and immunotherapy as well as Chinese traditional herb medicine as a supplement to the local radiation therapy. Trials with prophylactic irradiation of sites where occult metastases might be frequent, i.e. the upper abdominal or para-aortic lymph node regions, could also be considered.

The well differentiated lesions were less sensitive

to radiation and had a lower primary disappearance rate (55%; 70/127) and a higher local recurrence rate (51%; 65/127). The 5 year survival rate was 43 per cent (55/127). Most patients who succumbed due to this type of carcinoma had local failure; distant metastases occurred infrequently (9%; 12/127). The critical problem in the well differentiated form is thus local failure. Supplementary measures such as local hyperthermia, operation or interstitial irradiation should be considered.

Prophylactic irradiation in the neck region is probably important in the treatment of oropharyngeal carcinomas. In the present series, 34 of 52 patients without clinical neck node metastases were given prophylactic irradiation against the neck regions. Only 3 of them developed recurrences in the neck during the follow-up—an incidence of 9 per cent. In the remaining 18 patients, the neck was untreated and 3 developed neck node metastases—an incidence of 17 per cent. The 5 year survival rate was 74 per cent (25/34) in patients who received prophylactic irradiation and 61 per cent (11/18) in those who did not receive prophylactic treatment. Although the difference was not statistically significant this comparison may speak in favour of prophylactic irradiation of the neck. This question needs further analysis, however. The probability of later neck node metastases also increases with the extent of the primary lesion. Such metastases thus occurred in 68 per cent (30/44) of the T1 patients, in 69 per cent (65/94) of the T2 patients, and in 86 per cent (56/63) of the T3 patients.

SUMMARY

The prognosis for 201 patients with carcinoma of the oropharynx, treated mainly by irradiation, was analyzed. The crude 5, 10, 15 and 20 year survival rates were 50.3

per cent, 36 per cent, 26 per cent, and 17 per cent respectively, and the corresponding cure rates 44, 35, 26 and 17 per cent respectively. Patients under 50 years of age had a better 5 year survival than those over 60 years. The poorly differentiated and the anaplastic carcinomas had a better prognosis than the well differentiated lesions. Early stages had a much better prognosis than advanced lesions. Split course and continuous course irradiation gave similar results. The optimum dose range was 60 to 70 Gy. Early disappearance of the primary tumor during radiation therapy was prognostically favourable.

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