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THE EFFICACY OF GOLD-198 GRAIN MOLD THERAPY FOR MUCOSAL CARCINOMAS OF THE ORAL CAVITY

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Gold-198 grain mold therapy was given to 27 patients with 29 oral cancers and the results were analysed. Single plane mold alone was chosen for treatment when the maximum thickness of the tumor was below 2 mm. For thicker tumors, external irradiation prior to mold therapy was added. The 5-year survival following these principles was 82%. Initial tumor control was obtained in all 27 lesions followed for more than 2 years but recurrence took place in 7 (26%). Of 20 patients whose primary lesion did not recur within 2 years, 6 subsequently required surgery (2 cases) or non-surgical treatment (4 cases) for bone complications. The results obtained by single plane mold therapy are encouraging, particularly with regard to gum cancers showing a minimum bone invasion, and should therefore be advocated for selected patients with oral carcinoma.

A mucosal carcinoma of the jaw appears in the thin mucosal membrane covering the surface of the bone. Carcinomas that develop in this area cannot be adequately treated by a linear radioactive source. The main therapy for such carcinomas is surgical excision (1–5). However, there are patients who do not wish to undergo surgery and patients who have concurrent medical problems which contraindicate surgery.

An alternative intraoral method to implantation therapy is the use of a specially constructed applicator in the form of an oral mold that bears radioactive material (2, 3, 6). Oral-mold therapy is the treatment of choice for tumors situated in the hard palate or the lower or upper alveoli, where the mucosa is too thin to hold an implant. Lip cancers are usually treated by external irradiation or by direct implantation of radioactive substances, but the use of a double mold should be mentioned because of the short treatment time and the excellent cosmetic results (4, 7).

Only a small number of patients have been treated by mold therapy to date and no report of the results achieved by this method have appeared in the literature. This study was undertaken to describe our way of providing gold-198 mold therapy and to report on the results obtained after treating 29 oral cancers in 27 patients.

Material and Methods

Twenty-seven patients who received Au-198 mold therapy between 1978 and 1992 for carcinomas in the mucosa of the oral cavity were included in the study (Table 1). Two patients had 2 separated lesions each, so that a total of 29 lesions were included in the analysis. Another 2 patients were treated for recurrent lesions in the lower gum following radium needle or gold-198 grain therapy for cancers in the floor of the mouth and only parts of these 2 recurrent lesions were included in the previous target areas. On evaluation of plane skull x-rays and/or orthopantomograms of 26 cases with upper or lower gum cancer, a saucer-shaped type of bone involvement, caused by an expanding tumor, was found in 12 cases. Cases manifesting the 'moth-eaten' type of bone destruction were not given mold therapy.

Tumors were classified according to the principles of UICC (1987), 4 lesions were classified as T1, 20 as T2, 3 as

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Table 1

Patients

Case No.	Age	Sex	Sites	Stage	Dose (Ext)	Dose (Mold)	Comp.	Result
1	49	M	Lip	T2	15 Gy	94 Gy	–	Alive wo D.
2	51	F	Palate	T1	—	75 Gy	–	Dead of Ne.
3	58	F	U. Gum	T2**	30 Gy	71 Gy	+	Alive wo D.
4	69	M	L. Gum	T3**	25 Gy	73 Gy	R S	Alive af S.
5	56	F	L. Gum	T2**	30 Gy	73 Gy	+	Alive wo D.
6	67	M	L. Gum	T2	—	68 Gy	–	Dead of I.
7	67	M	L. Gum	T2	35 Gy	75 Gy	–	Alive wo D.
8*	68	M	L. Gum	rT2**	—	60 Gy	+ S	Dead of I.
9	40	M	L. Gum	T3**	40 Gy	69 Gy	+ S	Alive wo D.
10	59	M	L. Gum	T2**	22.5 Gy	62 Gy	–	Dead of Ne.
11	52	F	U. Gum	T2**	30 Gy	70 Gy	+	Alive wo D.
12	78	F	U. Gum	T2	42.5 Gy	70 Gy	–	Dead of I.
			L. Gum	T2	42.5 Gy	78 Gy	R	
13	78	M	U. Gum	T2	17.5 Gy	61 Gy	R	Dead of D.
14	80	F	U. Gum	T2**	30 Gy	72 Gy	–	Alive wo D.
15	66	F	L. Gum	T2**	30 Gy	75 Gy	+	Alive wo D.
16	67	M	U. Gum	T2	16 Gy	83 Gy	+	Alive wo D.
17*	49	F	L. Gum	rT2	—	64 Gy	–	Alive wo D.
18	71	F	U. Gum	T1	—	82 Gy	R S	Alive af S.
			L. Gum	T1	—	76 Gy	R S	
19	83	F	L. Gum	T1	30 Gy	78 Gy	+	Alive wo D.
20	80	M	L. Gum	T3	—	87 Gy	+	Alive wo D.
21	65	M	F. of M.	T2	—	74 Gy	+	Alive wo D.
22	82	F	Palate	T2**	—	83 Gy	+	Alive wo D.
23	71	F	U. Gum	T2**	40 Gy	74 Gy	R	Dead of D.
24	87	M	F. of M.	T2	—	58 Gy	+	Dead of I.
25	64	F	Palate	T2	—	68 Gy	–	Alive wo D.
26	70	M	Palate	T2	—	80 Gy	–	Alive wo D.
27	72	F	Palate	T2**	—	78 Gy	S	Alive af S.

Abbreviations: Dose (Ext) = Dose given by external irradiation; Dose (Mold) = Dose given by mold therapy; Comp. = Complication; * = Cases treated by mold treatment for recurrent lesion; ** = Cases with bone involvement; U. Gum = Upper Gum; L. Gum = Lower Gum; R = Local Recurrence; S = Surgery; Alive wo D. = Alive without disease; Dead of Ne. = Dead of neck or distant metastasis; Alive af S. = Alive after surgery for local recurrence; Dead of I. = Dead of intercurrent disease; Dead of D. = Dead of primary failure

T3, and 2 as rT2 lesions. On admission to the hospital, clinical evidence of regional metastasis was found in 3 cases. No case was lost to follow up and all were followed to death or to January 1995, the end-date of this study, implying a minimum follow-up period of 2 years.

The process for making a mold follows the same principle as that for making a prosthesis and takes about 10 days. The mold is composed of a clear type acrylic resin carrier and a lead protector. First, an impression of the upper or lower gum containing the tumor is made using alginate impression material. Based on this impression, a plaster dental model is made. The paraffin wax model is replaced by a prototype mold of clear acrylic resin. This mold is then checked to ensure a perfect fit when placed over the target area and jaw. The programmed dose to be given by mold therapy is calculated according to the Paterson-Parker rules for a planar mold.

Gold-198 grains are used in the mold. Each grain is a small granule, 0.8 mm in diameter and 2.5 mm in length and covered by platinum. The half-life is 2.7 days, and the gamma ray energy is relatively low (0.412 MeV). The spots where gold-198 grains are to be placed are mapped on the surface of the mold. Where the tumor interfaces with the mold, holes of 3 mm depth are drilled into the mold to hold the gold-198 grains. A lead protector covered by acrylic resin is made to cover the sites of the gold-198 grain in order to protect the normal tissue from the irradiation. The gold-198 grains are then sealed into the mold by covering them with a quick self-curing type of acrylic resin to ensure sealing of these grains into position. This sealing can be accomplished in a few minutes. As the mold is composed of clear acrylic resin, the position of the gold-198 grains can be checked by a radiogram. The patients are able to keep the intra-oral mold in a steady position for 5 to 7 days, removing it only for meals.

For superficial lesions, the type of mold used is a single mold (Fig. 1). As we put the sources to a 3 mm depth in the mold and estimate the 5 mm depth dose as the target

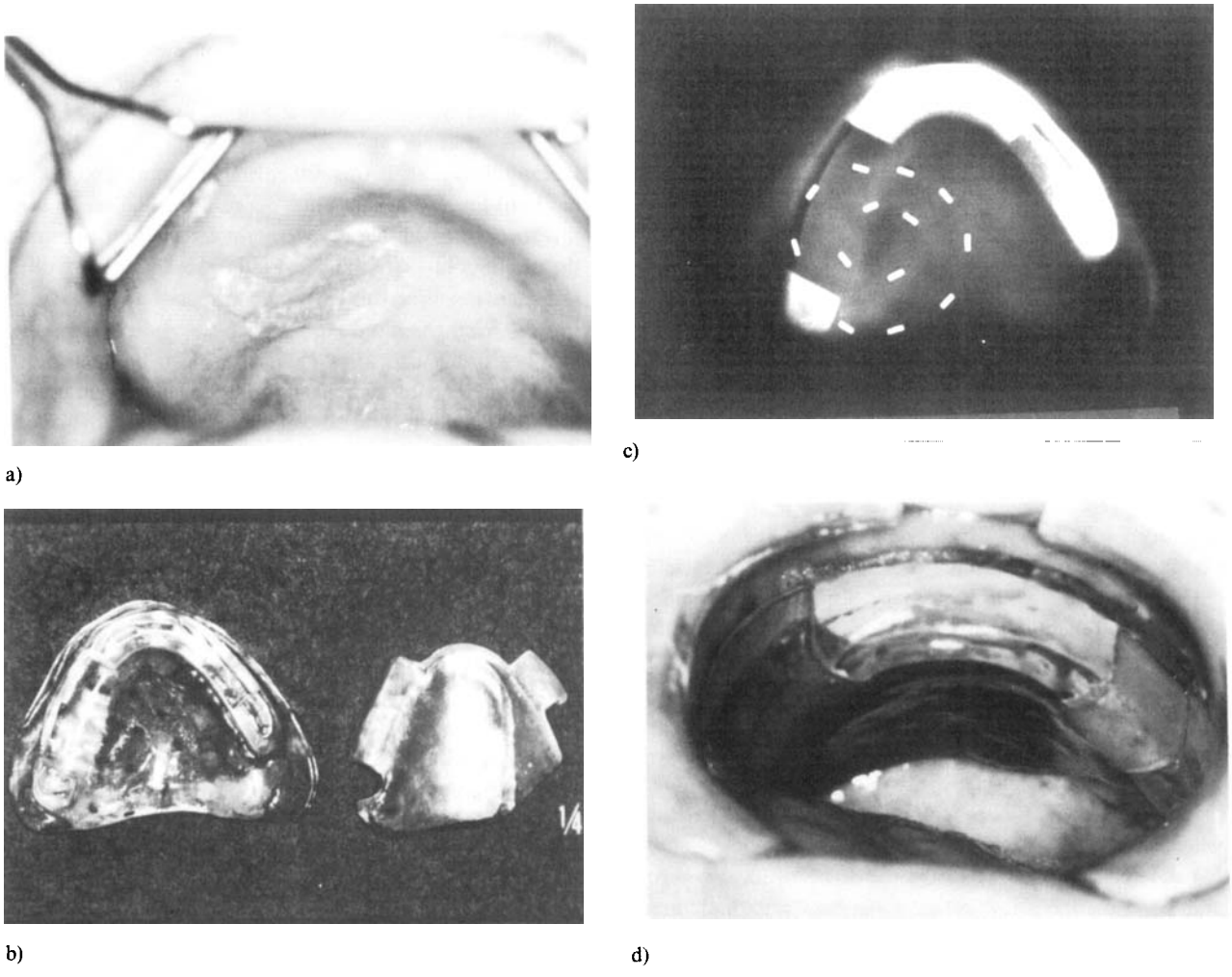

Fig. 1. Single mold therapy for a T2 carcinoma of the hard palate. a) Squamous cell carcinoma of the hard palate before treatment. b) Acrylic resin mold and detachable lead protector loaded in the acrylic resin. c) x-ray photo of a mold containing gold-198 grains. d) The mold and protector in place.

dose, 2 mm is the maximum thickness of the tumor for single mold alone therapy. For tumors having a thickness of over 3 mm, external irradiation is given to reduce the tumor thickness prior to the mold therapy. The dose of external irradiation ranged from 30 Gy in 3 weeks to 40 Gy in 4 weeks. However, the impossibility of getting an adequate depth dose from a single intra-oral mold limits the effective use of this method. It is possible to use a safer type of intra-oral applicator, a double mold. When using this type of mold, the lesion is sandwiched between two source planes, one internal and the other external. The double mold, which is used for thick lesions, is made in the same manner as a single mold, but care should be taken to ensure that the two planes or gold-198 grains are kept reasonably parallel. When cases require a double mold, the dose at the center of the gum or lip is calculated. The double mold was used for 4 gum cancers and one lip cancer in the present study.

For two cases in which the tumor extended from the gum to the floor of mouth, combined therapy was used; mold therapy for the gum tumor and direct insertion of a radioactive source for the tumor in the floor of mouth. The target volume area for mold treatment ranged from 2 cm^2 to 11 cm^2 and the mean treated area was 4.9 cm^2. The radiation dose delivered by mold treatment varies depending on the dose delivered by external irradiation and ranged from 58 Gy to 94 Gy (mean: 73 Gy).

Statistics

The survival rates were calculated from the initial date of treatment by the Kaplan Meier method and differences were evaluated using the χ^2-test.

Results

The actuarial 5-year survival rate following mold therapy amounted to 82% for the 27 patients. Five patients died of their diseases; 3 cases within 1 year and 2 cases within 2 years following the treatment. Two cases among

the 5 failures were patients who died of regional failure without local recurrence. Twenty-seven lesions in 25 patients were evaluated for primary control status and possible complications.

Of 27 primary lesions, 7 (27%) recurred. Salvaging operations were successful in 4. The recurrence incidence among the upper and lower jaw cases showing bone involvement was 3/11 (27%), which did not differ from what was observed among the cases without bone involvement (4/14 = 29%). Also, no difference was found in the incidence of a local failure between cases given external irradiation prior to mold therapy and those who were not given external irradiation.

Two of the patients with widespread intra-oral leukoplakia had separated upper and lower gum cancers and these 4 lesions were eradicated by gold-198 grain mold treatment. Recurrent or additional primary carcinomas developed subsequently in the leukoplakial region at the periphery of the treated area in both of these patients.

Of 20 patients with a primary lesion who remained disease-free for more than 2 years, 12 developed exposure of bone 5 months to 3 years following mold therapy. Six of these 12 cases had transient exposure that healed within 3 months. Two among these 12 patients subsequently underwent sequesterotomy for osteoradionecrosis. Another 4 cases were treated conservatively. No difference was noted in the incidence of bone complication between patients who received external irradiation and those who did not. No difference was noted in the incidence of local control and bone complication between patients who had bone involvement and those who did not.

Ten patients developed regional neck metastasis during or after mold treatment and 8 were successfully treated by radical neck dissection (7 cases) or radiotherapy (1 case).

Five subsequent carcinomas were found in 4 patients during the follow-up period; 2 tongue cancers, 1 stomach cancer, 1 contralateral gum cancer and 1 lung carcinoma.

Discussion

When the situation permits, oral-mold therapy is superior to direct implantation of a radioactive source (7, 8). No premedication is needed, the possibility of trauma or use of anesthesia of any type is avoided, and a more evenly distributed radiation field is obtained (4, 6). Our patients included 5 patients over the age of 80, who usually would be considered too old to undergo operation or curative radiotherapy.

The mold therapy control rate of 82% is not inferior to that obtained by surgical treatment (1). As for complications, 12 cases of bone exposure were encountered. The incidence of complications necessitating further treatment amounted to 30% (6/20). It has often been said that the use of surface mold requires special experience that can only be gained by much clinical practice (4, 7), but at our institution, this has not been the case.

Prior to the introduction of gold-198 grain molds, we had treated 30 cases using cobalt-60 molds for oral carcinomas at different sites. In providing cobalt-60 mold therapy, however, it was difficult appropriately to arrange the hard linear sources. Thus the results obtained in using this form of mold therapy were not satisfactory. However, the use of gold-198 grains facilitated the distribution of the radioactive sources and with no necessity to remove the sources from the mold (6, 8).

When using a mold, a higher dose can be delivered to the lesion than by external irradiation. Furthermore, the rapid dose fall-off is an advantage of mold therapy, since it spares the underlying structures. A single mold at a 5 mm treating distance with a moderate dose of 70 Gy is tolerated with reasonable safety. There was no difference in the incidence of bone complications between those who were treated by mold alone and those who were treated by combined external irradiation and mold therapy. The size of the lesion was not the limiting factor of Au-198 mold therapy. When using a double mold, the depth-dose falls much more slowly. Even so, when a double mold is used, 80 Gy can be prescribed for small areas and 70 Gy for larger treated areas.

There are some limitations in using molds for treating oral carcinomas. Whether there is a bone involvement or not is an important factor in determining the indication for mold therapy. Only patients with superficial carcinomas manifesting bone destruction of the saucer-type can be considered for mold therapy (3). In this regard, no difference was observed in the treatment results between cases with no bone destruction and those having saucer-type bone destruction. Cases having diffuse and penetrating lesions into the upper and lower alveoli, on the other hand, cannot be considered. Furthermore, cases with multiple oral cancers arising from widespread leukoplakia were difficult to treat by mold therapy. However, mold therapy can be indicated for patients with leukoplakia if the entire area of leukoplakia can be encompassed by the mold. Cancers extending posteriorly to the oropharynx are also difficult to treat due to the difficulties in keeping the mold in position. Hence, mold treatment constitutes a highly selective therapeutic procedure.

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