Combined therapy for maxillary sinus carcinoma with special reference to cryosurgery

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SUMMARY

Three hundred cases of maxillary sinus carcinoma were divided into four groups according to the initial treatment: the first group was treated by irradiation of 5,000 rad (25 fractions) for 5 weeks; the second by intra-arterial infusion of 5-FU combined with irradiation; the third by sinus curetting in accordance with Denker's operation combined with the second method; and the fourth by cryosurgery once a week during the second irradiation method followed by sinus curetting at the end of initial treatment. Histologically confirmed recurrence was removed by maxillectomy, if possible. The three year cumulative survival rates in the four groups were 27.1% (first group), 55.1% (second group), 53.5% (third group) and 53.1% (fourth group). The three year local non-recurrence rates after initial treatment without maxillectomy were 26.4%, 31.1%, 55.8% and 45.4%, respectively. The frequency of distant metastasis without local recurrence was as high as 12.3% in the third group and conversely 5.6% in the fourth. These results demonstrated the usefulness of cryosurgery.

Treatment of maxillary sinus carcinoma has been associated with notorious difficulty (Ahmad et al., 1981; Jackson and Fritz-Hugh, 1977; Sisson, 1963; Wustrow, 1965). Despite the gradual advance in radiation therapy, chemotherapy and immunotherapy, clinical long-term results still remain far from satisfactory. To establish the best possible treatment, repeated careful planning of controlled studies and statistical comparisons of existing long-term results are necessary. The present paper outlines our recent 9-year experience in the treatment of maxillary sinus carcinoma and describes what we believe to be the best regimen at present. The long-term results of our treatment programs will be discussed from the standpoint of restoration of appearance and day-to-day functioning as well as improvement of the three year survival rates.

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SUBJECTS AND METHOD

The subjects analysed in this study are 300 patients with maxillary sinus carcinoma who were treated in our clinic from 1971 to 1979. These patients are divided into four groups according to the major procedures which followed irradiation, a constant regimen.

The first group of patients (41 cases) was treated by radiotherapy, Co-60 5,000 rad (25 fractions) for 5 weeks.

The second group (108 cases) was treated by radiotherapy with continuous intraarterial infusion of 5-FU (total dosage: 2.000 mg). The third group (97 cases) was treated by a combined method of radiotherapy, continuous intra-arterial infusion of 5-FU, and sinus curetting, which is repeated several times from the first week of the treatment.

The fourth group (54 cases) was treated by a combination of radiotherapy, intraarterial infusion of 5-FU, cryosurgery once a week, and sinus curetting in accordance with Denker's operation at the end of the treatment.

Another regimen used in this group was the adjuvant immunotherapy with the cell wall skeleton of Nocardia rubra (N-CWS) which were selected during controlled trials by an "envelop method".

Monthly doses of 200 mg Nocardia-CWS have been administered directly into the tumour or 500 mg intracutaneously for the past several years.

In all the groups, histologically confirmed recurrences of the tumour were treated by maxillectomy, except small lesions which were controlled by less vigorous procedures such as intracavitary irradiation and/or cryosurgery. Cervical metastases, if movable, were treated by radical neck dissection.

RESULTS

The distribution of sex, age and the extent of the tumour in terms of TNM classification proposed by the Japanese Joint Committee in 1977 were not significantly



Figure 1. Cumulative local non-recurrence rates.



different among the four groups. Cumulative survival rates calculated by actuarial method and cumulative local non-recurrence rates for the four groups are shown in Figures 1 and 2.

The frequency of maxillectomy, a secondary regimen, was reduced from 38% in the second group to 22% in the fourth group. However, regrettably, the mortality rate reached 12.3% in the third group caused by distant metastasis without local recurrence (Table 1).

The number of patients treated by immunotherapy with N-CWS has not yet been large enough to permit statistical assessment of the therapeutic effectiveness. The data so far obtained on local recurrence and metastasis is summarized in Table 2.

group	no. of cases	local recurrence	metastasis
Nocardia-CWS	16	8 (50%)	0 (0%)
control	20	14 (70%)	1 (5%)

 Table 2.
 Preliminary results of Nocardia-CWS immunotherapy as an initial treatment of maxillary sinus carcinoma.

DISCUSSION

For the treatment of maxillary sinus carcinoma, Gensoul (1827) originated maxillectomy, Holmgren (1928) applied radiotherapy for the first time, and Larsson and Mårtensson (1954) reported the usefulness of preoperative irradiation.

In Japan, Asai (1958) established the method of "en bloc" resection of the maxilla; Yamashita (1968) combined radiotherapy with sinus curetting; and Sato (1970) combined minor surgery, radiotherapy and local chemotherapy. These

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therapeutic group	no. of cases	cumulative survival rate	cumulative local non- recurrence rate	frequency of maxillectomy	frequency of successful	frequency of neck metastasis without local	frequency of distant metastasis without local
K1 alone	41	27.1%	26.4%	3	0	recurrence 2	recurrence
combined with AI	100		States in	(1.3%)	(%0)	(4.9%)	1 40/ 1
	100	%1.cc	31.1%	42	31	2	(0/
combined with CU	97	53 50%	EE ON	(0/.0.00)	(28.7%)	(1.9%)	(3.7%)
		N/	%8.00	22	6	6	12
combined with CR	54	53.1%	45.4%	(0/0/27)	(6.2%)	(6.2%)	(12.3%)
A DAY AND A				(70 201)	4	3	3
RT: irradiation				(0/ 7.77)	(1.4%)	(5.6%)	(5.6%)
AI: intra-arterial infu	Ision					N THE ST	

CU: curettage CR: cryosurgery

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intensive efforts have led to the present multi-disciplinary regimen which now constitutes the core of maxillary cancer treatment and utilizes both immunotherapy and psychosomatic medicine.

Since 1957 our treatment programs have been improved (Sakai, 1976; Shigematsu, 1971. The constant regimens throughout have been radiotherapy as the initial treatment, and maxillectomy as the last resort.

The resultant findings include:

- 1. The adequate therapeutic dose of irradiation is 5.000 rad. and given in 25 fractions over a 5 week period.
- 2. The drug of choice for intra-arterial infusion is 5-FU in a total dose of 2.000 mg over a 4 week period during the radiotherapy.
- 3. Cryosurgery at weekly intervals is useful in reducing tumour mass.
- 4. Surgical reduction of tumour mass by sinus curetting which is conducted in accordance with Denker's operation under general anesthesia, is indispensable.
- 5. Immunotherapy with the cell wall skeleton of Nocardia rubra as adjuvant appears to be effective.

The recent decline in the need for maxillectomy is due to the general tendency to restore eating and communicating functions as well as appearance, and owes much to the advent of less vigorous but more efficacious regimens which have successfully reduced local recurrence.

Here, we would like to refer to cryosurgery, one of our major concerns. Its advantages include:

- 1. The absence of bleeding and severine pain. Safe use in ambulatory patients.
- 2. The surgeon can determine the extension of sites to be frozen, during repeated procedures.
- 3. Less involvement of surrounding normal tissues and the resultant assurance of the restoration mechanisms.
- 4. Little mechanical irritation which minimizes distant metastases.

5. Suggested suppression of recurrence by the so-called cryo-immunity.

Introduction of sinus curetting into the first step of the treatment for maxillary sinus carcinoma has greatly reduced local recurrence rates. Nevertheless, this progress had not necessarily been associated with increased survival rates before the advent of cryosurgery, which has improved survival rates greatly in spite of little changes in local recurrence rates. This is due to the reduction in distant metastases and mortalities from other illnesses.

Indeed, cryosurgery has significantly contributed to the welfare of patients with maxillary sinus carcinoma, who now enjoy greater 5-year survival rate without facial disfigurement.

The treatment of cancer should not be inflexible but should be tailored to the

individual patient. The initial manipulation, however, must be based upon a consistent policy for achievement of an ultimately satisfactory result.

RÉSUMÉ

Trois cents cas de carcinome du sinus maxillaire furent divisés en quatre groupes d'après le traitement initial: le premier groupe fut traité par irradiations de 5.000 Rad (25 fractions) durant 5 semaines; le deuxième groupe par infusion intra-artérielle de 5-FU, en association avec l'irradiation; le troisième groupe par curettage du sinus suivant l'opération de Denker, en association avec la deuxième méthode; et le quatrième groupe par cryochirurgie, effectuée une fois par semaine lors de la deuxième méthode d'irradiation, et suivie par un curettage du sinus à la fin du traitement initial.

Une recurrence histologiquement confirmée fut enlevée par maxillectomie, si possible.

Les taux cumulatifs de survie à 3 ans dans les quatre groupes furent de 27,1% (premier groupe), de 55,1% (deuxième groupe), de 53,5% (troisième groupe) et de 53,1% (quatrième groupe). Les taux de non-recurrence locale à 3 ans après le traitement initial sans maxillectomie furent respectivement de 26,4%, de 31,1%, de 55,8% et de 45,4%. La fréquence de métastase à distance sans recurrence locale fut de 12,3% dans le troisième groupe et par contre, de 5,6% dans le quatrième groupe. Ces résultats ont démontré l'utilité de la cryochirurgie.

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