EVALUATION OF TREATMENT OF ADVANCED PRIMARY AND SECONDARY GINGIVAL CARCINOMA

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Oral cancer is the most common of all forms of malignancy at the Cancer Institute, Madras, having a frequency of 34%. It therefore reflects the general pattern of cancer incidence in India. Carcinomas of the lower gingiva, whether as primary or as secondary extensions from the cheek, floor of the mouth, or tongue, form more than a quarter of all the oral cancers. The reason for this high incidence lies in the habit of tobacco, betel, and nut chewing so common in South India. The management of these cancers forms one of our most serious problems.

Materials

Our personal series of 188 cases of lower gingival carcinomas consists of 120 primary and 68 secondary gingival carcinomas. By all criteria—that is, of anatomical extent, bone involvement, and percentage of metastases—the lesions were advanced. Only 24 (13%) were confined to the gingiva, the remaining 164 (87%) involved the gingiva, cheek, and/or floor of the mouth. No lesion was less than 3 cm. in diameter. In 77 (41%) cases there was spread to the skin with or without external fungation, and 5 (2.6%) presented with supra-hyoid muscle infiltration.

Bone Involvement.—Radiologically the mandible was involved in 130 (69%) cases and free in 48 (25.5%). Radiological information was not available in 10 (5.3%) cases, and these were rejected for treatment.

Metastases.—Of the 166 (88%) cases presenting with clinical cervical-lymph-node metastases, 128 (77%) had mobile lymph nodes (stage II) and 38 (23%) were fixed (stage III). Distant metastases were present in only 3 (1.59%) cases.

Histology.—All were squamous-cell carcinomas (grade I–II, 78.2%; grade III–IV, 13.1%; and ungraded, 8.7%).

It will be obvious that our material consisted essentially of cases in an advanced stage of the disease.

Treatment

At the outset we were a little unnerved at the enormous lesions we were asked to treat; but we quickly decided that we should treat radically all advanced cancers unless the disease was so extensive as to have destroyed one-half of the face, or the neck was literally frozen by secondary malignant infiltration, or there were widespread metastases.

All cases accepted for treatment received initially either ^{60}Co beam therapy in the supervoltage range or high-voltage x-ray therapy, using a 250-KV. unit and a beam with a half-value layer of 2 mm. of copper. Our cases were too extensive for either radium mould or implantation. A tumour dose of 6,500–7,500 rads in about six weeks, using the gamma beam, or 5,000–5,500 rads in about five weeks, using the x-ray beam, was delivered. The cases were reviewed eight weeks after the end of treatment.

At this review the cases were classified into three groups: (1) lesions which had regressed but little under irradiation; (2) lesions which had apparently clinically regressed totally; and (3) lesions which had regressed partially, leaving a residue. The regression in the last group consisted of a “centripetal” contraction of the disease zone—that is, the peripheral extensions of the disease were destroyed by irradiation and the residue was *always* “central.” The biological reasons for this are obvious. This biological fact greatly facilitated surgical resection.

The lesions in our cases were so extensive that not much could be done for the first group of cases. However, all those who had a sporting chance were included in our surgical group.

All those in the second group in whom radiological invasion of the mandible had originally been demonstrated and the entire third group of cases were advised surgical resection (Table I). It has been our experience that in the presence of a mandibular focus, even though soft-tissue healing may appear complete for the time

TABLE I.—Total Cases Treated, 155

Composite resection unnecessary	..	..	23 (14.8%)
Rejected for composite resection	..	..	40 (25.8%)
Advised composite resection	..	..	92* (59.4%)

* 55 declined and 37 accepted composite resection.

being after irradiation, the disease invariably erupts into activity between 12 and 24 weeks after irradiation unless the hemimandible spontaneously sequesters. In three of our cases where this happened the disease never recurred.

The surgical procedure adopted was a monoblock resection of the cervical lymphatics (radical neck dissection) and the oral lesion in continuity. The affected hemimandible was removed as part of the mass. Local resections of the mandible were never practised, for on subsequent microscopy we have often found subtle extensions of disease into the medial pterygoid or along the mucoperiosteum of the resected alveolus that could not possibly have been detected pre-operatively. We have learned, too, by bitter experience, never to compromise with cancer. All intraoral extensions of disease are resected with never less than a 1.5-cm. margin of apparently normal tissue, and in all our later cases a frozen-section report on the “mucosal edge” has always been obtained before closure. In the resection of the primary growth anatomical demarcations are not respected, though possible physiological mutilations are always borne in mind.

Wherever possible primary closure was carried out. Where large oral defects due to extensive resections of skin were present the gaps were closed subsequently by tubed pedicle grafts.

The time interval between the end of irradiation and surgical resection has varied between 8 and 24 weeks. This variation was due to the patient taking his own time before consenting to the procedure.

The 40 cases that were rejected for composite resection after irradiation were unacceptable for the following

reasons. (1) Failure of irradiation to reduce or eliminate cutaneous lymphoedema of the face or extensive infra-temporal fossa infiltration or diminish the area of disease, which originally extended to involve more than half the oral cavity—that is, involving cheek, floor of mouth, tongue, and hard palate. (2) Fixed lymph-node metastases measuring 5–6.5 cm. in diameter which irradiation failed to regress. (3) Old and feeble patients in whom we thought the morbidity of a large oral defect and staged plastic procedures were not worth while.

Morbidity

Irradiation morbidity has been nil since the advent of ^{60}Co beam therapy, apart from the temporary discomfort of a mucosal reaction and the more persistent one of dryness of the mouth. Irradiation has prejudiced neither the operating technique nor the subsequent healing.

In the earlier years, when high-voltage x-rays were used, one patient developed sloughing of the neck-dissection wound and on the 11th post-operative day died of a secondary haemorrhage from the common carotid artery. But it would be unjust to blame irradiation alone: our folly in attempting to repair the oral defect temporarily with fine-mesh stainless-steel gauze no doubt contributed towards the result.

The main surgical morbidity has been the anatomical mutilation. With proper pre-operative psychological preparation and post-operative re-education the functional disability has at no time been devastating. Difficulties of articulation, mastication, and deglutition have in every case been temporary, and the psychological adjustment to them has been most satisfactory. But disfigurement is one of the main reasons why the less-understanding patient declines this life-saving procedure. The essence of the disfigurement is the loss of the hemimandible. Our attempts at mandibular reconstruction, both immediate and delayed, have left the patient in a worse plight than before. Until this problem is solved the surgery of oral cancer will continue to be incomplete, and some patients who could have been saved otherwise will be lost.

Oral fistulas have in all cases been temporary and never very annoying, and a new technique of closure that we have evolved has now totally eliminated them.

Results

Table II presents in line A the crude survival in all patients, whether completing the prescribed treatment or not. It includes those who declined the prescribed treatment. Line B presents the survival in patients receiving the full schedule of treatment, corrected for intercurrent disease and primary mortality. Line C presents survival in those who underwent radical irradiation but declined composite resection; line D the survival in patients receiving irradiation followed by composite resection; line E the survival where irradiation alone was considered enough.

Discussion of Results

The survivals are worked out only against the cases treated. It would obviously be unfair to evaluate our methods of treatment against patients whom we rejected for any form of therapy because they had lost half their

face to the disease or died within 72 hours of admission. It would be equally unjust to include those who declined treatment and preferred quacks and faith-healers to us.

We have not been able to trace 17 cases in the series undergoing irradiation only, and these have been excluded in the calculation of survivals. In the composite-resection series, three died of intercurrent disease, and there were three cases of primary mortality; we have therefore given both the uncorrected and the corrected (for primary mortality and intercurrent disease) survival figures. The intercurrent diseases were malaria and dysentery towards the end of the third year and primary bronchogenic carcinoma occurring towards the end of the first year. The primary mortalities were due to secondary common-carotid haemorrhage occurring on the 11th post-operative day, to a cardiac arrest on the table during hypotensive anaesthesia, and to an uncontrolled bronchopneumonia on the sixth day developing in a chronic asthmatic who passed into status asthmaticus on the third post-operative day. Deaths occurring within one month of operation have been regarded as primary mortalities. There have been no post-operative deaths in the last three years.

The five-year surgical survivor has so far lived for six years. We should have had a better series if more patients had consented to the operation, but the Cancer Institute was just beginning life at that time and we had great difficulty in carrying conviction to illiterate and ignorant village folk who panicked at the very word "operation."

It is particularly illuminating to compare the survival figures of lines C and D and E in Table II. The 55 patients who declined composite resection after irradiation and those who accepted composite resection were

TABLE II.—Length of Survival

Type of Treatment	No. of Cases	Survival in Years				
		1	2	3	4	5
A. Survival in all patients whether completing prescribed treatment or not	155	51/132 (38.6%)	39/110 (35.4%)	22/86 (25.5%)	11/68 (16.1%)	4/50 (8%)
B. Survival in patients completing prescribed treatment (corrected)	60	41/52 (78.8%)	31/38 (81.6%)	17/25 (68%)	10/16 (62.5%)	3/3 (100%)
C. Survival with radiation but declining composite resection	55	11/41 (26.8%)	8/32 (25%)	5/21 (23.8%)	1/12 (8.3%)	1/7 (14.2%)
D. Survival with irradiation and composite resection: Corrected	37	27/33 (81.8%)	19/24 (79.1%)	10/14 (71.4%)	6/9 (66.6%)	1/1 (100%)
Uncorrected		27/37 (73%)	19/28 (67.8%)	10/20 (50%)	6/12 (50%)	1/1 (100%)
E. Survival with irradiation but composite resection unnecessary	23	14/19 (72.2%)	12/14 (85.7%)	7/11 (63.6%)	4/7 (57%)	2/2 (100%)

comparable material: 87.2% of the former and 83.7% of the latter had mandibular destruction. The extent of their residual disease and their histological grading were more or less similar. The three- and four-year survival rate of those who declined surgery is only 23.8% and 8.3% while that of the operated series is 71.4% and 66.6%. The difference in these figures is striking, and it is far more striking when one remembers that the purely radiation survivals include those patients whose hemimandible sequestered six months after

irradiation and in whom no recurrence of the disease followed this natural composite resection. If these cases are excluded their three-year survival falls to 14.2% and the four-year survival to 0.

Line E of Table II gives the survival rate in those patients in whom composite resection was not considered necessary after irradiation. The mandible was not involved in these cases and the soft-tissue healing was total.

The three- and four-year survival figures of those in whom composite resection was deemed unnecessary after irradiation was 63.6% and 57% respectively, and these figures would justify our policy of universal initial primary irradiation. The composite-resection results are slightly better even though the disease was far more advanced in these cases than in the series included in line E, the reason being that every death in the latter occurred among those who had declined cervical lymphadenectomy and who died from uncontrolled cervical-lymph-node metastases without any recurrence of the primary. Every one of the patients who had lymphadenectomy is alive and well.

The survival figures of those patients in whom composite resection was considered unnecessary following irradiation also justify our use of universal initial primary irradiation. We may as well state here that our experience has been that scientifically planned and executed irradiation, utilizing modern therapeutic techniques, entails very little or no morbidity, in contrast to the anatomical and functional mutilation of a composite resection, however excellent the subsequent plastic procedure. It is also worth while noting that there was no primary mortality due to irradiation in the line E group of cases. It is obvious, too, that even with patients refusing cervical lymphadenectomy the survival figures in this group are superior to those of any series in which composite resection was indiscriminately followed in total disregard of the biology of the lesion. We are therefore convinced that composite resection is indicated when irradiation fails and where the bone is involved, and even then only after initial primary irradiation. This very definitely reduces the volume of tissue removed and the chances of post-operative recurrence. And scientific radiotherapy, using supervoltage, does not prejudice tissue repair after surgery.

All the figures seem to suggest that in the treatment of advanced oral cancers planned irradiation with subsequent composite resection is more likely to improve the survival rate than either irradiation or surgery alone. Our applicability rate for the combined procedure was 69.6%.

If one considers that the test of a method is not merely the survival rate but also the extent of its application, the combined irradiation and surgical attack is likely to emerge favourably. The lymphadenectomy part seems as important as the resection of the primary, because the proportion of occult metastases in our series of 104 consecutive radical neck dissections was 32%.

In assessing our results against those of the European centres one should always bear in mind the advanced disease that we had to tackle, the ignorance and superstition that we had to contend with, and the handicap of malnutrition that we had to face. We have little doubt that in the better material of Europe and the United States the combined method would achieve far superior results.

Summary

Oral cancers form 34% of all cases of malignancy in the South Indian population. More than a quarter of these are either primary or secondary carcinomas of the lower gingiva. Most of the cancers we see are very advanced and many involve the entire cheek and floor of the mouth in addition to the gingiva. Of the 188 cases presented in the series the mandible was destroyed in 130 (69%) and there were cervical-lymph-node metastases in 166 (88.3%) cases. Of these, one-quarter were in stage III. In 164 (87%) cases the gingiva, cheek, and/or floor of the mouth were involved and external fungation had occurred in 41%. Not one case conformed to the general definition of "early." All were squamous-cell carcinomas.

Our treatment policy was irradiation followed by composite resection eight weeks later, wherever the mandible was radiologically involved or where a residue was present.

Of the 155 cases thus treated by irradiation, 92 were considered suitable for composite resection later: 55 declined the procedure and 37 accepted it. In 23 cases composite resection was deemed unnecessary after irradiation. The first two groups offered comparable material to assess the value of composite resection in the management of these advanced cancers. The three- and four-year survivals in the resected cases were 71.4% and 66.6% against a survival of 28.3% and 8.3% in the non-resected group. In the group where resection was thought unnecessary the corresponding survival rates were 63.6% and 57.1%. Considering all the circumstances we feel justified in concluding that in advanced cancers of the oral cavity planned and scientific irradiation followed by discriminate surgery is likely to yield a higher survival rate than either of them alone. Irradiation by itself seems quite effective in the treatment of the primary lesion in reasonably circumscribed cases without bone involvement. But cervical lymphadenectomy is essential even in these cases.

In our series irradiation did not prejudice either the operative procedure or the subsequent healing and did not contribute to any morbidity. This was especially so when supervoltage therapy was employed.

In an account of the conference on family planning held in Singapore the International Planned Parenthood Federation's April issue of *News of Population and Birth Control* records that a paper by Dr. Minoru Muramatsu, of the Institute of Public Health, Tokyo, discussed recent trends in family planning activities in Japan, where in 1961 the birth rate per 1,000 fell to 16.8, the lowest recorded since 1900. "The death rate for 1961 was 7.4, so that the population of Japan is now growing at a rate of less than 1% per year. It has taken less than 15 years for Japan to accomplish a complete transition from high fertility and high mortality to low fertility and low mortality. Even in rural Japan small families are now almost universally preferred. If present trends continue Japan's population will begin to decrease by about 1985. This transition brings with it problems which Japan has hitherto never had to face. The shrinkage of working age groups and the ageing of the population will greatly affect the course of social welfare and, indeed, the nation's whole economic future. The Ministry of Health and Welfare have recently issued a white paper urging the need for plans to meet 'the population revolution.'"