



Carcinoma of the Tongue

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-- NO MEETING NEXT WEEK --

I. ABSTRACT

CARCINOMA OF THE TONGUE

R. W. Koucky

1. Introduction

Carcinoma in any part of the body produces fear and distress to a patient but carcinoma of the tongue or mouth is particularly horrible because of the disfigurement, foul odor, the ugly fungoid mass and the loss of function. Surgery has offered a great deal to these patients but even with a cure there usually is loss of function and disfigurement. A great deal of hope has been placed in radium as an agent which will diminish these evil effects but its value is still in the process of being proven.

2. Incidence

It is estimated (Rosenfeld) that 10% of all carcinomata arise in the mouth. Eggers estimated that 3% of all deaths were due to malignancy in the mouth. In the Philadelphia Hospitals, in a group of 1,802 malignancies, 67 arose within the tongue (3+%). In a recent survey in Scotland, there were 330 deaths from carcinoma of the tongue in a population of 4,780,000 or approximately one death per 15,000 population.

3. Etiological Possibilities

Fitzwilliams states that we can say no more than Boerhaave did approximately 300 years ago when he said "any kind of irritation, externally, whether from motion, heat or acrimony, may cause cancer."

A. Irritants

Chewing and smoking of tobacco, jagged teeth, oral sepsis, alcohol and syphilis all appear to favor the development of carcinoma. The relative importance placed to any one of these agents is variously estimated by different authors. Some emphasize very strongly the role of oral sepsis. Syphilis (luetis glossitis) is considered by many to be an important factor. In

India and Ceylon where it is a common habit to chew irritating vegetable substances, the incidence of mouth carcinoma is considerably higher than in other areas. In 406 cases of malignancy, 76 were in the mouth, a percentage of over 18%.

B. Age

The maximum incidence of carcinoma of the tongue occurs between the ages of 55 and 65. However, when these figures are corrected for the number of people living in the various groups, there is a progressive increase in each decade so that the period, 75 to 85 or over, has the highest incidence.

C. Sex

Males predominate in all the series reported from the northern countries. The ratio is from 10:1 to 8:1. In India and Ceylon, this proportion of men to women does not hold true. The number of cases reported are limited but in these there is a greater frequency of cases in women than in men. This reversal of ratio is explained on the fact that women chew various irritative vegetable (betel leaves and nuts) more commonly than the men.

D. Location in the Mouth

Fraser worked out the following table, showing the frequency with which various locations in the mouth are involved by malignancy.

<u>Site</u>	<u>Percentage</u>
Anterior 2/3 of tongue	43.0
Dorsum	10.4
Side	29.5
Undersurface	3.3
Palato-glossal sulcus	20.0
Gingivo-glossal sulcus	11.0
Floor of mouth	10.0
Posterior 1/3 of tongue	.9
Remainder of oral cavity	16.0

Fraser has investigated the various anatomical characteristics of these different parts of the tongue in the attempt to discover a cause for the difference in frequency of involvement.

The only very obvious difference is in the histology of the posterior one-third which shows a large amount of lymphoid tissue with thin epithelium which is not keratinized and contains no prickle-cells. It seems more plausible to explain the frequency of involvement in the anterior two-thirds by the assumption that it is more exposed to irritation.

E. Leukoplakia

All authors agree that leukoplakia is a precancerous lesion. Various authors estimate from 10 to 54% of carcinoma of the tongue arising in leukoplakia. Probably all forms of leukoplakia are alike but four types have been described, based principally upon the gross appearance of the lesion. The Plaque may be moist and white, papillomatous and warty, red and meat-like, or finally the entire epithelial and subepithelial layer may be hard, infiltrated and nodular. The histological picture of these lesions varies. In the moist, white type, there is a marked thickening of the epithelium with edema and some leucocytic infiltration of the skin proper. In the red, meaty appearing plaque, the enormously thickened epithelium has been eroded away leaving only the deeper layers of the skin. It is assumed that this type is a late stage of the former. Nodular or indurated types are associated with fibrosis in the subepithelial layer and probably represent a modification of the previous picture. Apparently all four types of leukoplakia of the tongue are equally potential in giving rise to malignancy.

4. Pathology

The gross and microscopic appearance of carcinoma of the tongue needs no special description. The tumors may readily be graded into the four grades described by Broders. The result of the grading in the hands of different authors varies somewhat. Broders himself (quoted by Judd) stated that over 50% are in the Grades III and IV. Fraser in 68, graded them as follows: Grade I, 48%; II and III, 36%; IV, 16%. Berven graded his cases as follows: Grade I, 1%; II, 47%; III, 46%; IV, 5%.

The question of node involvement is one which is difficult to interpret. The statistics on this point based on clinical observations do not correlate with the pathological findings. Lymph nodes may be palpable because of swelling secondary to the infection in the primary tumor. On the other, microscopic sections may fail to show the presence of tumor since it may be present in another part of the node. Involvement of lymph nodes based upon clinical interpretation varies from 35% to as high as 70%. The lack of correlation between the clinical findings and pathological findings in the lymph nodes may be indicated by the following: In 20 nodes clinically considered to be negative, 5 with tumor were found on microscopic sectioning and 15 were hyperplastic. In 24 nodes considered to be positive clinically, 14 were positive pathologically and 10 were hyperplastic (Taylor). Lund and Holtan showed the same lack of correlation. In a similar manner, these authors showed that there was no correlation between the size of the lymph node and the involvement by tumor as shown by the microscopic section.

Not all tumors of the tongue are squamous carcinomata. As has been previously discussed in these meetings, there occasionally occurs such tumors as hemangiomata, fibromata, lipomata and amyloid deposits. Lymphoepitheliomata (previously described) occasionally do occur in the posterior third of the tongue and probably arise within the lymphoid tissue which is common in this portion of the tongue.

The cases of carcinoma of the tongue which do not recover following operative procedure have a poor outlook. Of 162 fatal cases collected by Estabrook, 123 died within the 1st year, 27 in the 2d year, 9 in the 3d year, 2 in the 4th year and 1 after 5 years.

The delay from the time of onset until consulting the physician is tabulated by Taylor as follows:

<u>Delay</u>	<u>Taylor</u> %	<u>Simmons</u> 1918-20	<u>Simmons</u> 1921-24
Less than one month	41.0	20.0	64.0
One to three months	28.0	27.0	12.0
Over three months	31.0	33.0	24.5

The average time from onset to consulting a physician, therefore, is well within THREE months. The average time between onset to the time of operation in the patients who were cured was 5 months (Taylor) and 6 months (Simmons). The average time between onset and diagnosis in patients who had no nodes was 4.5 months.

Metastases in most cases are limited to the neck. The older literature states that not more than 1% metastasize to the region below the clavicle. This statement, however, is undergoing revision as more and more cases are being studied at autopsy.

5. Treatment

A. General Trend

Several authors have stated that there has been no improvement in the surgical technique for carcinoma of the tongue within recent years except for the introduction of the newer methods of cautery. There is a notable divergence of opinion regarding the relative value of surgery and radium in the treatment of carcinoma of the tongue. Some clinics favor the treatment by surgery and use radiation only as a supportive measure. In other clinics, the emphasis is placed entirely upon radiation with surgery employed only in special cases.

It is difficult to interpret the various groups of statistics which are presented in the literature. In those series which have been treated surgically, one is left with the question as to what was the percentage of operability. Perhaps the number of cases quoted as operated represent only a small favorable selection. On the other hand, the cases treated by radium have been treated from

5 to 10 years ago and the methods and dosages used at that time were not as efficient as they are at present.

B. Mortality

The mortality of surgical procedures was given by Fraser as 8.3% when the resection is carried out in two stages, i.e. local resection followed by dissection of the neck later. When the entire procedure is carried out in one stage, the mortality rises to 52.6%. In the group reported by Fischel (190 patients), there were 36 deaths when the operation was done in one stage and only 3 deaths in the patients operated upon in two stages.

C. Methods

The operative procedure as outlined by Judd and Phillips is local resection by knife or diathermy followed sometime later by dissection of the neck. The treatment of the cervical region is a question which is debated. Some clinics do routine neck dissections regardless of whether the nodes are considered to be involved or not. In other clinics, the nodes are dissected only when they are considered to be invaded by tumor. Palliative excision of nodes in hopeless cases is not considered to be of any value.

D. Outcome

The cures obtained by surgical treatment are listed as follows: Fraser in 24 cases had a 33% survival for 2 years. Taylor (Massachusetts General Hospital), 22 cases, 5 year survival of 36%. Curry quotes Butlin's cases with a 2 year survival of 27%; and Capetti's series of 777 cases with 20% survival over 3 years. Estabrook in 67 cases cites a 6 year survival of 13%. The difference in outcome when the lymph nodes are involved by tumor is indicated in Taylor's series (34 cases). In 15 without lymph node involvement, there was a 53% five-year survival, and in 19 cases with lymph nodes the percentage of survival dropped to 21%.

E. Radiation

The method outlined by Bervan (1932) is one which is followed in most clinics with such variations as are necessitated by the quantity of radium and facilities. The procedure outlined by this author is a preliminary dose of external radium emanation in the form of a bomb (teleradium). After the reaction has subsided and the tumor has regressed to a certain degree, the local lesion is removed with the endotherm and interstitial radiation in the form of needle or seeds is given into the base and around the site of excision. Ligation of the common carotid artery is carried out when the lesion is large. The cervical region is included in the field of radiation given as a preliminary course. If the nodes do not disappear after an adequate series of treatment, dissection of the neck is carried out with implantation of seeds (or needles) into the operative site. Lymph nodes which are fixed to the surrounding tissues are not removed surgically and palliative radiation alone is given. By this method, Bervan reports 32% five-year survival in 104 cases. Quick follows almost an identical method. This author gives no statistics regarding end-results. Duffy of the Memorial Hospital reports 234 cases with a survival period of 34.6%. This author reports 6.2% of clinical cures in cases considered hopeless.

Impressions

1. Carcinoma of the tongue is a particularly horrible disease because of the disfigurement, foul odor, ugly mass and the loss of function.

2. In Philadelphia in a group of 1,802 malignancies, 3% were located in the tongue. Other authors quote a higher incidence, i.e. up to 10% of all malignancies. In certain parts of India, the incidence is as high as 18% (buccal carcinoma inclusive).

3. As in many malignancies, chronic irritation is considered to be an important etiological factor. In the case of the tongue, its position and motility

particularly exposes it to greater trauma from teeth, oral spesis, the use of tobacco and alcohol, temperature variations, etc. Luetic glossitis is considered by many to be another important factor. It is pointed out that in India where people chew betel leaves and nuts that the incidence of carcinoma of the mouth is as high as 18%.

4. Carcinoma of the tongue apparently follows the usual age distribution. The decade from 55 to 65 shows the greatest incidence but when these figures are corrected for total numbers living in these periods there is the usual increased incidence with increased age.

5. Males predominate in the ratio of about 8 or 10:1. In India where women chew betel leaves more frequently than men, this incidence is reversed and women show a greater incidence than men.

6. The most commonly involved sites on the tongue again indicate that the more exposed portion of the tongue is more liable to invasion by malignancy. Within the anterior two-thirds of the tongue, 43% of oral tumors occur and the sides of this portion of the tongue alone account for 29% of all the oral tumors. The posterior one-third of the tongue gives rise to less than 1%.

7. There is no significant anatomical difference between these various areas within the anterior two-thirds to account for this difference. In the posterior one-third of the tongue, there is a large amount of lymphoid tissue and the epithelium is thin and is not warty. Whether this has any significance is not known.

8. All authors agree that leukoplakia is a precancerous lesion. The estimate of 10 to 55% of tongue carcinoma arising from leukoplakia has been made.

9. Four types of leukoplakia are described which probably are all variations of the same picture. Some plaques are moist and white; in other cases, they are papillomatous, in still others, they are red and meaty, and finally the entire subepithelial layer of the tongue may be indurated and nodular.

10. In the moist, white type, there is a marked thickening and edema of the epithelium. In the meaty, red variety, the superficial layers of the epithelium have been eroded leaving only the deeper layers. It is assumed that this is a late stage of the former. The indurated types are associated with fibrosis in the subepithelial layers. All types apparently give rise to malignancy in equal numbers.

11. The grading of carcinoma of the tongue, according to Broders plan, can be readily carried out. Broders estimated over 50% to be in Group III and IV. Fraser placed 48% in Grade I and 36% in Grades II and III, with 16% in Grade IV. Bervan put only 1% in Grade I and 47% and 46%, respectively, in Grades II and III. Our own grading of tumors here has been approximately that given by Bervan.

12. The clinical interpretation of the cervical node enlargement varies considerably from the pathological findings. Some series are reported with from 35 to 70% involvement of the lymph node, apparently based upon physical examination. In one group of cases, 20 nodes which had been considered to be clinically normal were found on microscopic section to be infiltrated with tumor in 5 cases. In 24 other cases which were considered to be positive clinically, only 14 showed tumor infiltration. In a similar manner, there is no correlation between the size of the lymph node and the involvement by tumor.

13. Squamous carcinoma is the most common type of malignancy in the tongue although there may occur others such as hemangiomata, fibromata, lipomata, etc. One of the most interesting in this group and one which is probably only a variation of the usual squamous carcinoma is the lymphoepithelioma which has been discussed previously.

14. When recovery does not follow treatment, the outlook is poor. In 162 fatal cases, 123 died within the first year following observation.

15. The average time from onset until consulting a physician is well within

3 months (three series of cases). In two series of cases, it was found that the average time from onset to the time of successful therapeutic procedure was 5 months and 6 months respectively. The average time between the onset and diagnosis in patients who had no lymph node involvement was 4.5 months. From the analysis in these two series of cases, it would appear that the majority (about 65%) of patients come to the physician during the time period in which operative procedures can be considered highly successful.

16. Although it has been commonly stated that probably not more than 1% of carcinomas of the oral cavity metastasize below the clavicle more recent studies have indicated that this occurrence is not so uncommon.

17. Surgical treatment of carcinoma of the tongue was well developed a number of years ago. Practically the only modification in recent times is the development of the newer methods of cautery.

18. In recent years, questions of therapy have revolved about the relative value of surgery alone, radium alone or combined surgery and radium.

19. There are at least two factors which make it difficult to interpret the various end-results stated. In the surgical groups, one is left with the question as to whether or not the patients operated upon were not a small favorable selection from the total group. On the other hand, the cases reported now and followed up for 5 or 6 years have been treated several years ago and the methods and doses used at that time are not as sufficient as they are at present.

20. The mortality of surgical procedures is from 5 to 10% when the resection is carried out in two stages, i.e. local resection followed later by the dissection of the neck. When the entire procedure is carried out in one stage, the mortality increases very much, as high as 53%.

21. The surgical procedure which

seems to be generally accepted is a local resection of the lesion by knife or diathermy, followed later by dissection of the neck.

22. The question of whether to dissect the lymph nodes of the neck routinely or to do this procedure only when the nodes are involved is entirely unsettled. Many clinics carry out the procedure routinely. Ewing cautiously expressed himself in favor of more conservative treatment.

23. Some of the results obtained by surgical methods are as follows:
Fraser, 24 cases, 33% survival, 2 years;
Taylor, 22 cases, 36% survival, 5 years;
Butlin, 197 cases, 27% survival, 2 years;
Capetti, 777 cases, 20% survival, 3 years;
Estabrook, 67 cases, 13% survival, 6 years.

24. The opinion is quite generally expressed that when the lymph nodes are involved by tumor the outlook is very much worse. In one series of cases, in the group without node involvement, the 5-year survival was 53%, and in the cases with lymph node involvement the survival dropped to 21%.

25. In the institutions where emphasis is placed upon radium treatment, the procedure followed is some modification of that brought out by Bervan in 1932. This consists of radiation of the tongue and neck with radium bombs (teleradium). After the reaction has subsided, the local lesion is removed with endotherm and interstitial radium in the form of seeds or needles is given into the base. Following this, a course of treatment is given to the cervical area and if the nodes do not disappear surgical dissection of the neck is carried out. Palliative dissection of the neck for hopeless cases is not recommended.

26. The outcome by this method is given as follows: Bervan - 104 cases, 32%, 5-year survival; Duffy - 234 cases, 35%, 5-year survival. Six per cent of cases considered to be hopeless are reported as cured by this method.

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II. CASE REPORT

CARCINOMA (LYMPHOEPITHELIOMA) OF TONGUE

Case is that of a white male, 76 years old, admitted to this hospital 3-1-35 and who is still a patient here.

8-Months' History

8- -34 - Noted difficulty in swallowing and talking. Thought there was swelling on the right side of the tongue. This portion of the tongue became larger. Occasionally there was bleeding and lesion became painful. No treatment given. (Because of patient's difficulty in talking, more history was not obtained).

Large Non-ulcerated Tumor

3-1-35 - Admitted. Physical examination: negative except for head and neck. The right side of the tongue is swollen and enlarged as though a lymphoedema is present. No ulceration. The tumor in-

volves the entire right side of the tongue and extends back into the tonsillar region. There is a raised and bleeding area in the lateral margin about midway on the tumor. The cervical nodes do not appear to be enlarged. Laboratory: Urine - negative. Blood - hemoglobin 63%, erythrocytes 3,480,000, leucocytes 7,150, normal differential. Wassermann - negative. Progress: Patient is very definitely dehydrated and apparently has lost a good deal of weight. Nasal tube is inserted and high caloric feedings given through the tube. Additional fluid is given by the intravenous route.

3-6-35 - Clinical impression: lymphoepithelioma. Deep x-ray begun.

3-8-35 - Deep x-ray treatment.

3-9-35 - Deep x-ray treatment.

3-11-35 - The lesion has now subsided sufficiently to permit intraoral manipulation. Biopsy taken. Microscopic examination of biopsy shows that the surface epithelium is intact. Infiltrating the muscle and subepithelial layers, there are cords and masses of large endothelial-like cells with a small amount of cytoplasm and very clear vesicular nuclei. Microscopic diagnosis: lymphoepithelioma.

3-13-35 - Now able to swallow. Nasal feedings ceased. Oral feedings begun.

Marked Response to Radiation

3-16-35 - Lesion in mouth has subsided to a remarkable degree. The reaction following radiation is characteristic of lymphoepithelioma.

III. MOVIES

Title: City of Wax

Released by: The Fox Motion
Picture Corporation

IV. STAFF MEETING

Date: March 14, 1935

Place: Recreation Room,
Nurses' Hall

Time: 12:15 to 1:15

Attendance: 89

Program: Acromegaly

Discussion: L. G. Rigler
Alex Blumstein
K. W. Stenstrom
Richard Johnson
W. T. Peyton
Carl Waldron
I. Pass
N. J. Berkwitz
R. W. Koucky
B. A. Watson

Theme: L.G.R.: First patient shows classical X-ray findings of acromegaly. Skull is enlarged and sinuses are enlarged. Most striking feature is enlargement of sella. Floor of sella turcica is displaced markedly. Posterior clinoids elongated and much thinned out. Sella increased to 3 or 4 times its volume. Tufting of terminal phalanges striking. Same process shown in the toes. This particular patient was reexamined on several occasions. Plates taken later show same sellar change. Iodized oil injected in sphenoid sinus shows compression. 2 or 3 years difference in time here but not much change.

The other case is really not essentially different so far as appearance is concerned. First plates made after exploratory operation show again the process in the sella. Not quite so large a hypophyseal fossa. Anterior clinoid more distinct. Otherwise general findings the same, i.e., enlarged sinuses, tufting

terminal phalanges of feet and hands characteristic. Relatively short fingers with clubbing.

There is distinct difference between this appearance and a malignant tumor of hypophysis. Relatively benign lesions grow slowly. In malignant lesions there is actual erosion. Tumor not infrequently penetrates floor. We have seen a few cases with typical acromegaly and no changes in the sella. Certain acromegalics had such a small tumor, hypophysis is not increased and x-ray changes do not occur.

Different picture in suprasellar type of lesion. The striking change is erosion in contrast to enlargement which is not very great. Changes occurring within the fossa itself tend to enlarge it without eroding to any great extent. There is not much difference in size of sellas in people with big skulls and small skulls. Great deal of work done on what represents normal size of sella. Certain normal limits are well established. The pictures are well beyond normal.

Question: How far must disease develop before getting changes?

Answer: We have seen changes in patients with minimal clinical findings, i.e., very striking clinical findings with little x-ray change. Develops early, depending entirely upon type of change in hypophysis.

A.B.: Slides: (1) This slide is from Dr. Rasmussen's collection of a normal adult male hypophysis. He pointed out here the eosinophilic cells tend to be placed centrally. Basophilic cells are around the periphery. This is posterior lobe and this is anterior lobe. Dr. Cushing in some of his cases comments on central hyperplasia of eosinophilic elements. I have noticed no comment by him as to his knowledge of normal relations, and I wonder how he interprets it. (2) This is the tumor of the first case. Notice portion of posterior lobe here where capsule has been broken. Tumor itself shows practically no stroma while hypophysis shows good deal of connective

tissue stroma. The cells are all of about the same variety. They all take same degree of stain and stain same color. Color on microscopic preparation of the cells is violet and not the deep red of the normal eosinophiles. Most observers of tumors in acromegaly comment on violet appearance of cytoplasm. The nuclei of the cells in the tumor sometimes show an amitotic division. In this specimen I cannot see any amitotic figures. Another feature is very large, multinucleated cells. This is the type of tumor described in other cases of acromegaly.

K.W.S.: We have had several cases of this who have been given x-ray treatment. Some reported definite improvement after x-ray, stayed in good condition 2 years, then returned with return of symptoms. In the literature there is no definite statement. It has been stated in number of cases it relieved headache, with improvement of vision obtained and inhibition of growth. I have not seen any satisfactory figures. I do believe that it is worth while using x-ray thereapy when nothing else can be done, but I do not think we can expect very much.

R.J.: Asked Dr. Stenstrom how many courses of x-ray treatment tried.

K.W.S.: Two series of x-ray treatment usually. Probably about 6 individual treatments in each series. It has to be fairly heavy dose. Two series with 2 or 3 months between them should be attempted.

V.T.P.: Indications for operation in pituitary tumor are clear, i.e. loss of vision from optic nerve pressure. Do not get recovery when fibers are destroyed. Very obvious why second patient did not get result from x-ray therapy. This patient had cyst (degenerated adenoma). X-ray did not reduce cyst. Fluid, recovered when the cyst capsule was opened, and very little tumor tissue remaining. Capsule removed as far as possible. If you do not have visual changes, operative procedure is usually unsatisfactory and difficult. You have to get in under optic nerve to get tumor. Unless tumor presses on optic nerve you

cannot get at the tumor properly. In this patient it is stated here frontal lobe soft. I was at postmortem and it was a soft temporal lobe. Everybody is agreed proper procedure is frontal, not internasal approach. Very low mortality, now less than 5% as it is mainly extradural.

C.W.: Teeth are usually separated. I do not think much trouble with either the nerve or arterial supply to teeth. I was going to ask question of pathologist whether some of these tumors are identical with adamantinoma.

N.J.B.: Most common findings neurologically are eye findings. Quite surprising to do fields and find choked discs have little changes in the fields.

I.P.: Experimental work on hypophysis of animals does not show any difference in weight in single and rapid pregnancies, also type of cells remain the same.

A.B.: Operative mortality in acromegaly for other conditions is high.

R.W.K.: Had patient to be operated upon for thoracoplasty, died before we started operation. Nothing at autopsy except acromegaly. Since then trying to find in literature where operative procedure in acromegaly is dangerous.

A.B.: Two comments. One, shows postoperative mortality in acromegalies higher than in normal with same procedure. Cushing comments that operative mortality for acromegalics higher than in other type of pituitary tumor.

Cushing notes changes in Islands of Langerhans, but I do not remember his conclusions.

B.A.W.: If there is insulin factor there is the possibility that there should be increased number of Islands. In this case pancreas fails to respond sufficiently. Patient on ward now who looks like acromegalic, but not diabetic, has very severe case of hypoglycemia. X-ray of sella shows normal picture, clinically acromegalic.

Gertrude Gunn.