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NEW GROWTHS OF THE ORAL CAVITY*

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CANCER, used in its broadest sense, was the direct cause of more deaths in this country last year than occurred among the American troops in the recent war. The statistics are so appalling that every effort to reduce the ravages of this cruel disease should receive the heartiest support of every one interested in the public health.

The attention given this subject throughout the country during the recent cancer week served a very useful purpose in presenting to the public fundamental facts, freed from sensationalism, and also helped to arouse physicians and dentists to their full responsibility in properly attending to these cases.

Early diagnosis and treatment of malignant disease in any part of the body is of the greatest importance, for the earlier the condition is recognized, the greater the opportunity there is for successful treatment. This has been emphasized and reemphasized in our literature, and yet four cases within as many weeks have come to me where expectant treatment had been followed so long, that very little could be done for them.

These facts as they apply to malignant disease of the mouth, impose a great responsibility upon the dentist and upon the oral specialist. The dentist who is a keen observer, is in a position frequently to detect in the mouth early manifestations of malignant disease even before the patient complains of it. Hence, it becomes the duty of every dentist and everyone who treats diseases of the mouth, to be on the watch for its manifestations, and to seek aid when there is any doubt about the existing condition. This paper deals first with a survey of tumors, the oral cavity in general and second, with a discussion of one type in particular.

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Fig. 1.—(x 35 diameters.) Lesion in muscle. Surrounding the lime salts is chronic inflammatory tissue and many foreign body giant cells.*

Fig. 2.—(x 35 diameters.) Another section of same lesion. Proliferation of fibroblasts is more pronounced.

*Figs. 1 to 5 are taken from experimental lesions obtained in guinea pigs by injection of tartar from mouth.

CLASSIFICATION OF TUMORS

In classifying tumors the most scientific and yet at the same time, the simplest way is according to the type cell upon which the tumors are built, and from this type cell the tumor should be named. Mallory records some fifteen different distinct varieties of cells giving rise to tumors which may be denominated type cells. This method of classification recognizes that every simple tumor is due to the proliferation of one of these type cells and that the blood vessels and stroma furnished by the surrounding and included tissues are not of themselves an important part of the tumor. Proliferation of the fibroblast, no matter in what form, is called a fibroblastoma. The tumor clinically may be a benign fibroma, or it may be a malignant fibrosarcoma.

Fig. 3.—(x 275 diameters.) Chronic inflammatory tissue proliferation of fibroblasts and foreign body giant cells.

Of the various type cells, the ones most frequently giving rise to tumor formation are the fibroblast or connective tissue cell, and the epithelioblast or epithelial cell. Classification into benign and malignant tumors can never be gotten away from, and while it is impossible always to decide this definitely without a microscopic examination, the clinician finds this question staring him in the face in every case.

GENERAL CHARACTERISTICS OF TUMOR FORMATION

All tumors have certain common characteristics according to Mallory. Some of the important ones are:

First, Independence of Growth.—Normal cells are under control and the equilibrium between loss and replacement of tissue cells is maintained.

This is not so in tumor cells, their growth is unlimited and uncontrolled except by a passive resistance of the invaded tissues.

Second, Vitality.—Tumor cells appear to possess more vitality than normal cells. They will grow and multiply while normal cells are atrophying.

Function.—Physiologically all tumor cells fulfil no useful purpose and generally are dangerous to their host. Quite the reverse is the case with normal cells.

Cause.—The cause of tumor formation generally is not known. Irritation has received much attention as a cause, but this fails to entirely satisfy scientific requirements.

Manner of Growth.—Tumors grow entirely by multiplication of their own cells, not by transformation of normal cells into tumor cells. This multipli-

Fig. 4.—(x 275 diameters.) Acute inflammation (Poly-morphonucleated leucocytes) immediately surrounding the lime salts in addition to other cells in Fig. 4.

cation of tumor cells expresses itself in two ways either by expansion or by infiltration.

Recurrence.—When there is failure to remove all of a tumor, the remaining portion, if only a single cell, will continue to multiply until another tumor has formed. This is so generally recognized that no further comment is necessary. With these general facts regarding tumors in mind, I wish to discuss certain new growths appearing in the mouth. Tumors of epithelial origin form the largest and most important group of single tumors. This is the group we generally understand to be cancer. It is my experience that epithelioma is the most frequent true tumor to appear in the mouth. Early invasion of the glands of the neck in this condition constitutes a real menace to the patient. Even when an epithelioma is detected reasonably early and

thoroughly removed, with complete healing of the original lesion, later metastases in the glands of the neck will sometimes appear even though they were not palpable at time of operation. It is a safe rule to follow, in cases of lesions in the mouth of doubtful diagnosis that do not promptly respond to simple treatment, to employ radical measures to remove the condition. To pursue expectant treatment in such cases from one to six months as is so frequently done, usually means the death of the patient.

Tumors of epithelial origin are usually primary in the mouth, but rarely metastatic lesions may appear. Hypernephroma—the most important new growth of the kidney gives rise to multiple metastases, and a metastatic lesion occasionally may appear in the mouth. Such cases have been reported

Fig. 5.—(x 1000 diameters.) Single foreign body giant cell from experimental lesion. Compare with Fig. 6.

and one came under my observation in July. The general appearance of the lesion was somewhat different from the ordinary epithelial tumor.

The term precancerous has been used to describe certain lesions not definitely malignant, but which later may become so. In the mouth leukoplakia is such a lesion. This is a proliferation of the epithelial cells of the squamous type tending to cornification. It is seen frequently in those who use tobacco, particularly those who chew. This lesion is absolutely benign in its beginning and may stay so for a long time. It does tend to break down into a carcinoma. I have had several cases where microscopically the beginning malignant growth could be demonstrated in the midst of the cornified epithelium of the leukoplakia.

Cancer of the mouth presents more hideous aspects than it does in some

other parts of the body, and everyone who has to do at all with these cases cannot help but be impressed with the early radical surgical removal.

So far as the later cases are concerned necessitating complete resection of an upper or lower jaw, I have come to the conclusion that seldom does this operation serve any beneficent purpose, indeed if it does not cause added suffering. Statistics certainly do not encourage me to continue it as a routine procedure.

Proliferation of the fibroblast producing the connective tissue type of tumor is second to the epithelial group. The benign fibroma and the malignant fibrosarcoma arise from this cell. The proliferating osteoblast gives rise to the benign osteoma and the malignant osteosarcoma.

Fig. 6.—(x 1000 diameters.) Foreign body giant cell from lesion in mouth.

The chief point determining the question of benignancy or malignancy is the rate of growth of these tumors. Slow growing fibroblastomata we regard as benign, rapidly growing fibroblastomata we regard as malignant.

Perhaps the lesion we see most frequently in the mouth is the so-called epulis. The term is a clinical one and means no more than a growth on the gum. It is not descriptive of any pathologic condition itself. Epulis has meant to the surgeon a new growth bordering on malignancy, usually what we have known as a giant-cell sarcoma. To many dentists the term has meant any growth on the gum including not only the fibroma or the sarcoma, but the carcinoma as well. It is fair to say that the wide application of this term has resulted in a lack of definiteness always resulting in confusion. This is due to lack of careful attention to the pathology which is the basis not

only for an adequate conception of these lesions, but for an intelligent treatment as well.

It has been a part of our inherited belief that a large percentage of epulides are giant-cell sarcoma. As a result of this idea, radical operations have been performed which have permanently disfigured the patient. Many teeth and large portions of the maxillae have been removed, and many times the wounds have healed in such a way that any sort of mechanical restoration of the parts to repair the mutilation has been practically impossible. If these statements are true (and I believe they are) no one can deny the importance of an exact knowledge of these lesions, which will better enable us to determine just how radical the treatment must be. If it can be shown

Fig. 7.—(x 275 diameters.) From a lesion removed from alveolar process of upper jaw. Giant cells—acute and chronic inflammation, but not true tumor. Compare with Figs. 3 and 4.

that the extensive sacrifice of tissue in treatment is unnecessary except in rare cases, many persons may be spared the disfigurement which has resulted so frequently in the past.

The gross appearance of these lesions has been described by various authors, and two clinical forms have been rather sharply differentiated. First, that form which is of the fibrous type, usually called fibroma, which is described as a small growth, firm and smooth, and without projections; the mucous membrane of normal appearance, and comparatively nonvascular. Second, the giant-cell epulis usually called giant-cell sarcoma, which is described as having a deeper red color than the fibrous type; a softer consistency; a greater vascularity, with more tendency to bleeding; a greater size, and a more rapid growth. Both types are rather sharply defined. From a clinical standpoint, these descriptions are sufficiently accurate to indicate

in a general way the gross appearance of the lesions which we see most commonly. From a pathological standpoint however, these types cannot be so definitely and sharply differentiated. Furthermore, the study of over fifty cases upon which I have personally operated and followed up, and studied microscopically, leads me to believe that the pathology does not correspond in a large percentage of the cases, to the generally accepted idea that these lesions must be either fibromata or giant-cell sarcomata. These lesions of the alveolar process, both fibrous and giant-cell type, arise from the same kind of cell, namely, the fibroblast which is the ordinary connective tissue cell. The fibroblast appears as a flat cell with an oval nucleus. It produces "two kinds of fibrils: fibroglia and collagen fibrils, the latter forming an intracellular substance." I have already said that a tumor of slow growth arising from this cell is called a fibroma. When the growth is rapid

Fig. 8.

it is known as a fibrosarcoma, the rate of growth determining whether the tumor is benign or malignant. When we consider how great the variation in rate of growth may be, it can easily be seen how impossible it is to make a sharp distinction histologically between the two types under consideration. They are fundamentally the same, springing from the same sort of cell. Both are fibroblastomata. The fact that giant cells are present is of little or no importance, as I shall show later.

The type of lesion which was described first, and spoken of as the fibrous form, may be made of bundles of slowly proliferating fibroblasts, and when so made up can be correctly called a fibroma. Histologically, however, I have found that only a very small percentage of cases (four out of forty-three) of this type, not showing giant cells, are true fibromata. A large majority of the lesions prove to be chronic inflammatory tissue, granulation and scar tissue, superimposed upon which, frequently is found acute inflam-

Fig. 9.—Section from lesion shown in photograph. Acute and chronic inflammation with proliferation of fibroblasts.

Fig. 10.—(x 275 diameters.) Same lesion. Lymphocytes (chronic inflammation) and proliferation of fibroblasts.

mation as well. From a study of these cases, microscopically as well as clinically, I believe that most of these lesions are caused by some irritation which produces a reactive process, in the form of chronic inflammation. This reaction to an irritant, in whatever form it may be, results not only in the gathering of the lymphocytes, which is so characteristic of chronic inflammation, but also what is more important, a hyperplasia of the fibroblasts, with the resulting formation of new connective tissue. This increase and growth of the connective tissue is not in any sense a true tumor formation, however, even though clinically it may have that appearance. It can easily be seen in cases where the hyperplasia of the connective tissue is marked, how it

Fig. 11.

could be regarded as a fibroma, for just where the dividing line is between the two is sometimes impossible to say. Furthermore, we get mitotic figures in inflammatory tissue as well as in tumor formation, so that this feature cannot be used as an aid in differentiation. In forty-three cases studied, in which no giant-cells were present, two were almost pure granulation tissue, with some acute inflammation superficially. Four other cases showed granulation tissue present in considerable amount, together with acute chronic inflammation. Four cases as has been noted, could fairly be called true fibroma. In two of these four cases the connective tissue was very dense. Two other cases were osteofibromata, and showed a slight amount of bone formation. In all the rest of the cases chronic inflammation tissue pre-

Fig. 12.—(x 35 diameters.) From case illustrated. Almost pure granulation tissue. Clinical diagnosis of giant cell sarcoma had been made.

Fig. 13.—(x 275 diameters.) Chronic inflammation with some fibrous tissue. Clinical diagnosis had been fibroma.

dominated, with usually some acute inflammation at the periphery. In many of the cases, the clinical appearances corresponded very well with either one or the other of the types already described, yet pathologically they were nothing more than inflammatory lesions.

Of the type showing giant-cells and usually called giant-cell sarcoma, the type which is said to be the most common, I found out of the fifty-three cases, but ten. In discussing the pathology of this lesion, first let us not lose sight of the fact mentioned early in the paper, that it arises from the fibroblast. This connective tissue element is the important part of the growth. As I shall soon show, the giant-cells, while they present a striking microscopical picture, are nevertheless of secondary importance. It has been shown (Giant-cell Sarcoma, F. B. Mallory, M.D., "Journal of Medical Re-

Fig. 14.—True fibrosarcoma with many foreign body giant cells. Practically no inflammatory cells. Giant cells of no significance in diagnosis.

search," Vol. XXIV, No. 2) that two types of giant-cell which arises from multiple mitosis, and which is a true tumor cell. Second, the foreign body giant-cell which is formed by the fusion of endothelial leucocytes, and which is not a tumor cell at all. In all the cases studied, it was the foreign body giant-cell that was present, the tumor giant-cell not appearing in a single instance.

The foreign body giant-cell is a large irregular-shaped cell, the cytoplasm of which is well defined. It has many nuclei, which stain deeply, and which are also sharply defined. These cells are formed as has been said, by the fusion of endothelial leucocytes, and are found not only in tumors, but appear in inflammatory tissue as well. When they appear in true tumors, they are of no consequence, as has been said, so far as the tumor formation

is concerned. The endothelial leucocyte, which is a large mononuclear cell in the blood, is attracted into all sorts of lesions, by various substances, chiefly fat and lime salts, which may act as irritants. As they gather in numbers, they tend to fuse around the substance which has attracted them, provided it is difficult of solution, and form these foreign body giant-cells.

With this idea as a starting point, I performed some experiments to see whether or not the irritation from the calcareous deposits of the teeth could produce these phenomena. Ordinary tartar was finely powdered, and a heavy suspension, one and a half c.c. was injected into the shoulders of several guinea pigs. In the first experiment the tartar was not sterilized, but was injected with ordinary sterile precautions. Several pigs died, and most of them developed well-marked abscesses more or less localized. In the second series, the tartar was carefully sterilized with dry heat for an hour before making the suspension, and the injections were made with sterile precautions. The results will best be demonstrated by the plates, which show how almost identical, microscopically, these experimental lesions are, with one of those found in the mouth.

The pathology seems to be briefly, this.—First, the injury to the tissues causes an acute reaction which brings polynuclear leucocytes to the region. Then the irritation of the foreign body (in these experiments the tartar) results in attracting many endothelial leucocytes, some of which fuse and form foreign body giant-cells. In addition to this, the fibroblasts begin to proliferate and form new connective tissue. The whole picture as it appears under the microscope, looks strikingly like what has hitherto been regarded as giant-cell sarcoma.

That pathologists have been wrong in regarding these giant-cells as usually indicating tumor formation, has been shown by Mallory. It is probably true that diagnoses of giant-cell sarcoma have been made, which were nothing more than an accumulation of foreign body giant-cells and some proliferated connective tissue.

Of ten cases studied with a clinical diagnosis of giant-cell sarcoma, six were not true tumors. These cases, aside from the giant-cells, showed granulation tissue and chronic inflammation. Three cases could fairly be called fibrosarcomata. The remaining case was also probably a true fibrosarcoma, but it was extremely difficult to decide with positive assurance.

In the face of these facts, and with the knowledge that these lesions, even when they are rapidly growing fibro-sarcomata, do not form metastatic growths elsewhere, and in spite of what I have said earlier about the necessity of radical attention to new growth formation, it seems to me we are not justified in radical operative procedure, which removes large portions of the jaws adjacent to these growths, as is not infrequently done. Moreover, it is our duty to our patients to give them a chance, especially where a radical removal is going to disfigure the patient. It has been my experience that a thorough removal of the growth itself, and a thorough curetting at the base of the lesion which involves the periosteum, using a surgical burr where it is necessary, is quite sufficient. In none of the cases that I have operated on

in this way has there been any return of the lesion so far as I know. In some cases it is advisable to remove a tooth or teeth, in order to get more thoroughly at the base of the lesion, but removal of large sections of bone or the bone itself is not necessary as a rule. Of course cases should be kept under observation, and, in the event of any return, more radical treatment may be given. The recurrence of a lesion does not necessarily indicate malignancy, however.

We know that fibroma does recur when it has not been completely removed.

It goes without saying, that in addition to this treatment, the removal of anything that may be acting as an irritant is necessary. In three or four of my cases the edge of a gold crown running too far down under the gum at one point seemed to be a possible etiologic factor. Two cases presented amalgam fillings jammed down into the interproximal space.

In conclusion, the importance of early diagnosis and treatment of lesions of the oral cavity cannot be overemphasized, but conservative treatment of certain types of tumors is warranted from our knowledge of their pathology.