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INTRA-ORAL EPITHELIAL MALIGNANCIES

Moderator

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SEMINAR ON INTRA-ORAL EPITHELIAL MALIGNANCIES

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CASE 1

Diagnosis: Nevus - Palate

History: Man, age 45, had a sessile, elevated nodule 1.0 x 1.0 cm. on the hard palate. The lesion was asymptomatic and an excision biopsy was performed. (W.U.D.S. 3841)

The over-lying epithelium is intact. Beneath it there are nests of cells which sometimes approach very close to the basement membrane of this epithelium. These cells in some zones form solid sheets and in others are arranged in small nests. Individual cells have uniform nuclei that are at times vacuolated and there are no mitotic figures seen. These tumor cells infiltrate deeply into the surrounding tissues. They are separated by a variable amount of collagen and an extremely small amount of granular, brown pigment is observed.

COMMENT: This lesion is a nevus containing mole cells. It shows no functional activity and no evidence microscopically of malignant changes. The absence of melanin pigment and the infiltrative nature of the lesion could cause confusion with a malignant tumor. Such nevi within the oral cavity are rare, in our experience. The only treatment necessary is excision and we would anticipate no further trouble.

CASE 2

Diagnosis: Melanocarcinoma - Palate

History: Man, age 71, noted a black spot on the left maxillary alveolar ridge. He consulted his physician and dentist who both advised "watching" the lesion. Four months later the patient was seen at the Washington University Clinics. A purplish-brown ulcerative lesion was present which extended along the alveolar ridge from the left cuspid to the second molar region. The mass measured 3 cm. in diameter. (W.U.D.S.3810)

This is a pigmented malignant tumor involving the palate. There is an abrupt area of ulceration and in this section origin cannot be traced from over-lying epithelium. We would be particularly interested in junctional changes. The pigment is brown, granular and non-refractile and therefore I assume that it is melanin pigment. A negative stain for hemosiderin would be helpful. The tumor itself has an extremely variable pattern and in some areas suggests sarcoma. It is infiltrating deep between muscle bundles. I cannot determine whether it has been adequately excised.

COMMENT: The treatment was certainly correct for malignant melanoma. I believe also that radical neck dissection should have been considered. Irradiation is not of value. The prognosis for this type of lesion within the oral cavity is extremely poor. We have seen malignant melanoma arise within the oral cavity from the tongue and upper and lower alveolus. The upper alveolus is the most common location. Malignant melanoma can also arise within the nares, the esophagus, the eye and the meninges. With the exception of the eye, these are rare locations. The skin is by far the most common location. In this particular case we would have to see junctional activity with transition to malignant melanoma in order to be absolutely certain that it is arising within the oral cavity and not metastasizing to it from some distant skin primary.

Reference:

Ackerman, L.V.: Malignant Melanoma of the Skin. *Am. J. Path.*, 18:602-604, 1948.

CASE 3

Diagnosis: Pseudoepitheliomatous hyperplasia - Tongue

History: Woman, age 78, had an ulcer of the lateral border of the tongue of three months duration. Slide #3 is the biopsy and Slide #4 is the surgical excision of this lesion. (W.U.M.S. 3954, 4110)

There is focal hyperplasia of the over-lying epithelium. This epithelium has become quite complicated. The basement membrane is not well preserved and individual cells close to the basement membrane show considerable mitotic activity. Because of the edema produced by the inflammatory infiltrate, intercellular bridges are extremely prominent. The inflammatory process that accompanies this lesion extends rather deeply into the underlying muscle. This inflammatory process is probably related to the previous biopsy. In the biopsy itself nests of rather well differentiated squamous cells are separated from the main mass.

COMMENT: It would be very tempting to call this lesion cancer because of the complicated pattern, the nests apparently isolated of squamous cells, the lack of good definition of the basement membrane and the increased mitotic activity.

Such lesions may arise without apparent cause, or be associated with ill-fitting dentures, trauma, from sharp teeth, etc. The inflammatory infiltrate causes lack of definition of the basement membrane. The hyperplastic nature of the lesion and its complicated pattern may result in nests of squamous cells being apparently isolated. This is almost always caused by tangential cutting.

CASE 4

Diagnosis: Squamous cell carcinoma - Maxillary sinus

History: Man, age 51, had a swelling of the right side of the hard palate, accompanied by pain and trismus. X-rays showed opacity of the right maxillary sinus. A biopsy was taken from the junction of the hard and soft palate. (AFIP 758715)

There are large nests of mucous glands present but there are also masses of relatively undifferentiated tumor cells. They have a plexiform pattern with little tendency towards keratinization. In some instances the tumor shows central necrosis and keratin formation seems to be most prominent centrally. This is apparently a squamous cell carcinoma of the antrum.

COMMENT: This diagnosis has to be made on the basis of the clinical history and radiographic findings. The microscopic pattern in this instance is not too helpful. In carcinoma of the maxillary sinus which arises close to the upper jaw, there is infiltration of the jaw with loosening of the teeth. In this instance the clinical signs were clear for apparently there are radiographic findings as well as a non-ulcerated mass in the oral cavity.

Reference:

Ringertz, N.: Pathology of Malignant Tumors Arising in the Nasal and Paranasal Cavities and Maxilla. Acta Otolaryng., supp. 27, pp. 1-405, 1938.

CASE 5

Diagnosis: Squamous carcinoma, verrucous type - Gingiva

History: Man, age 72, had a large papillary lesion involving the edentulous mandibular alveolar ridge. (AFIP 507068)

There is a verrucous growth present which has a very distinctive pattern. The tongues of tumor growing deep in the tissue have a ballooned out character and are pushing rather than infiltrating the tissue. There are a few nests of apparently isolated tumor cells. There is a very prominent infiltrate. Interestingly enough, there are two nests of sebaceous glands observed. This lesion is a rather unique one which we have designated as a squamous carcinoma of the verrucous type. At one time we called these tumors verrucous carcinoma but probably the above designation is better.

COMMENT: This lesion is difficult to recognize microscopically because of the uniformity of the cells and the intact basement membrane. It occurs usually in males who have been chewing tobacco for over twenty years. It is most prominent in the gingiva of the buccal cavity. This tumor may attain considerable dimensions and in their local growth may invade the bone of the mandible, the maxillary sinus and the soft tissues of the cheek. This lesion only under the rarest instances metastasizes. It is somewhat radiosensitive. However, in the larger lesions particularly where bone has been involved, adequate excision without neck dissection is a very satisfactory method of treatment.

Reference:

Ackerman, L.V.: Verrucous Carcinoma of the Oral Cavity. Surgery, 23: 670-678, 1948.

CASE 6

Diagnosis: ~~Epidermoid Carcinoma~~ - Lower lip

History: Man, age 32, had a sore of the lower lip of three weeks reported duration. The growth was excised. (AFIP 745454)

This lesion of the lower lip shows rather abrupt transformation from a benign to a malignant zone. In this area the tumor is superficially infiltrating the muscle. It is rather well differentiated and shows keratinization. This is a classic carcinoma of the lower lip for it is well differentiated and easily cured by surgery.

COMMENT: The smaller lesions are best treated by surgical excision, whereas the larger lesions are best treated by irradiation therapy. We recommend irradiation therapy because there is less danger of deformity. There is no reason to do a so-called prophylactic neck dissection in carcinoma of the lower lip. Of all patients followed who do not have lymphadenopathy on admission, only 6% will develop regional involved lymph nodes in the future. These figures indicate, therefore, that if neck dissection were done on 100 patients with carcinoma of the lower lip without palpable enlargement of the nodes, the operation would have no value in 94 instances. The first lymph nodes to be involved in carcinoma of the lip are always the submaxillary or submandibular nodes.

Reference:

Ackerman, L.V., and Regato, J.A. ed: CANCER, 2nd ed., 1954, pp. 228-254, The C. V. Mosby Company, St. Louis.

CASE 7

Diagnosis: Metastatic adenocarcinoma - Mandible and cheek

History: Woman, age 64, had a large, fleshy, moderately hard mass which projected from the left mandibular gingiva and appeared to involve the left cheek. X-rays showed a destructive process of the left mandible. (WSS 736)

This biopsy shows an adenocarcinoma which is rather well differentiated and which is producing epithelial mucin. The pattern of this tumor is such that we do not expect it to be primary within the oral cavity or within the bone. The radiographic appearance may be helpful in suggesting metastasis. Microscopically it could come from numerous locations but we would certainly place the large bowel as one of the most logical sites of origin. It could also come from the small intestine, stomach, pancreas or gall bladder but the large bowel is the most probable site of origin. With the information we have, we know it is a metastatic lesion from the large bowel.

COMMENT: Metastatic lesions involving the mandible are rare and usually occur in a widely disseminated process. In rare instances, however, the involvement of the mandible may be the first apparent clinical manifestation of carcinoma. We have seen this occur in metastatic carcinoma from the breast, large bowel and kidney.

Reference:

Byars, L. T., and Sarnat, B. G.: Mandibular Tumors. Surg., Gyn. & Obstet., 83: 355-363, 1946.

CASE 8

Diagnosis: Reticulum cell sarcoma - Mandible

History: Woman, age 56, had a toothache in the mandibular area. A lower second molar was extracted six weeks later and the dentist told the patient a "tumor" was present in the area. Her physician later aspirated the mass and gave her six penicillin injections. The mass receded slightly but the pain continued. Examination revealed a 2 cm. mass on the lower alveolar ridge which extended lingually and buccally. X-rays showed bone destruction which was considered secondary to osteomyelitis.
(W.U.M.S. 56-6735)

This tumor is obviously a malignant neoplasm. It is made up of cells which have large nuclei and abundant acidophilic cytoplasm as well as relatively prominent nucleoli. Reticulin stain shows it to be abundant. We do not believe that this is an epithelial tumor because if this were a squamous carcinoma without keratinization there would be extreme variation in size and shape of cells. Furthermore, the over-lying epithelium is uninvolved.

COMMENT: We are not surprised seeing a reticulum cell sarcoma within the oral cavity and have seen it usually in the region of Waldeyer's ring. This includes the area of the tonsils and the lymphatic tissue of this region. However, we have also seen lymphosarcoma arising from the base of the tongue, the upper alveolus, lower alveolus, floor of the mouth, and within the bone of the mandible and maxilla. This lymphoma may be a part of a disseminated process but it is not rare to have it as a localized lesion. If it is a localized lesion, irradiation treatment is the therapy of choice. The cure rate is probably as high as 40%.

CASE 9

Diagnosis: Lichen planus - Buccal mucosa

History: Woman, age 46, had asymptomatic white patches on the buccal mucosa, palate and tongue. These did not appear to be related to irritation.
(W.U.M.S. 56-2003)

This is a relatively common lesion of the oral cavity often mistaken for leukoplakia but in reality it is lichen planus. This diagnosis can be made on the basis of the band-like infiltrate with lymphocytic infiltration. There is considerable fragmentation of the basement membrane. There is hyperkeratosis without parakeratosis. The granular layer is thickened and there is acanthosis. The tips of the rete pegs are pointed and have a "saw tooth" appearance. In my section there is increased pigmentation. These lesions do not become malignant. This lesion is primarily a chronic or subacute disease of the skin, is usually multiple and the lesions are often pruritic.

CASE 10

Diagnosis: Hyperkeratinization, hyperplasia, chronic inflammation - Lower lip
(Pachyderma oris)

History: Man, age 28, had a chronic, slowly growing white lesion of the lower lip which had been present for several months. The lesion was excised. (AFIP 702804)

This lesion of the lower lip has been designated by some as "pachyderma oris" which is an expensive name for a thick lip. It represents a localized area with tremendous hyperkeratosis and parakeratosis with some localized keratosis of the epithelium. The basement membrane is thickened and there is considerable lymphocytic infiltration with some dilatation of the small blood vessels. Mucous glands are also seen. There is no evidence of carcinoma and local excision of this lesion is curative.

CASE 11

Diagnosis: Fibrous dysplasia - Maxilla

History: Boy, age 11, had a large tumor of the hard palate of three weeks duration. This was a firm, purplish-pink mass which occupied the entire right side of the bony palate and extended into the antrum. (W.U.M.S. 49996)

This section demonstrates spicules of relatively young bone which has somewhat scalloped margins. In some zones bone spicules show cement lines and there is considerable difference in the age of the bone. There is no calcification. Between the bone spicules there is very cellular, rather highly vascularized connective tissue.

COMMENT: We believe that this is a perfectly benign lesion and should be classified as fibrous dysplasia. This is not a giant cell tumor but there are a few giant cells associated with growing bone or bone that is being absorbed. This is not a malignant tumor such as osteosarcoma for the stroma between the giant cells is perfectly benign in appearance.

We see this type of lesion in children and young adults. It is rather common in the maxilla and when it appears there it may cause considerable distortion. It is a self-limiting process but somewhat deforming. It is best treated by surgery and all of the lesion does not need to be removed. This is the type of lesion which used to be designated as fibro-osteoma but is now believed by nearly everyone to be a variant of fibrous dysplasia. It may or may not be associated with lesions in other bones.

Reference:

Schlumberger, H.S.: Fibrous Dysplasia of Single Bones. Mil. Surgeon, 99: 504-527, 1946.

CASE 12

Diagnosis: Carcinoma-in-situ - Floor of mouth

History: Man, age 53, developed a sore spot on the mucosa of the sublingual area. He consulted a dentist who made several silver nitrate applications. The lesion did not improve and several weeks later he consulted an oral surgeon who excised the lesion. (W.U.D.S. 3190)

This demonstrates a very superficial lesion which in many areas is limited to the over-lying epithelium and could be called carcinoma-in-situ. We make this diagnosis on the basis of changes throughout the entire thickness of the epithelium. There is great variety in size and shape of cells, numerous mitotic figures and these changes extend throughout the entire thickness of the epithelium. There is possible early invasion in my section in one small area. Associated with this lesion are very prominent inflammatory changes and very prominent salivary glands are present.

COMMENT: This process of carcinoma-in-situ may occur simultaneously in different parts of the oral cavity at the same time or at different times. This is particularly true of aged individuals. Furthermore, changes of carcinoma-in-situ are very common on the peripheral margins of an invasive carcinoma. This accounts for recrudescence of the tumor which may have been incorrectly treated by the surgeon or the radiologist. In other words, the surgeon did not take enough margin of epithelium and the radiologist's fields did not embrace the field of altered epithelium.

CASE 13

Diagnosis: Muco-epidermoid carcinoma - Parotid

History: Woman, age 35, developed a small lump in the parotid area. This was excised but the mass soon recurred. A second local excision was performed. One year later extensive recurrent disease required en block excision of the ear, entire parotid area, and ascending ramus. These sections came from the area medial to the ascending ramus of the mandible. (W.U.D.S. 2448; W.U.M.S. 50-5787)

This tumor has a distinctive pattern made up of two types of cells, squamous epithelial and vacuolated cells. These vacuolated cells demonstrate with a mucin stain that the vacuolation is due to epithelial mucin. There are also small cystic dilatations and this tumor is growing between muscle bundles and is also within a nerve sheath. I believe it should be classified as muco-epidermoid carcinoma of salivary origin.

COMMENT: This tumor occurs in any area where salivary gland tissue exists. It varies from very well differentiated to very poorly differentiated. It is now my opinion that all these tumors are malignant although good correlation is found between the degree of differentiation and prognosis. This lesion, if inadequately excised, may recur as a somewhat more undifferentiated tumor. It is also unfortunate that, because of excessive mucin formation, spread may be facilitated. We do not know anything about the radiosensitivity of this tumor.

Reference:

Foote, F.W., Jr., and Frazell, E.L.: Tumors of the Major Salivary Glands. Atlas of Tumor Pathology, Section IV-Fascicle 11, Publ. by the A.F.I.P., Washington, D.C., 1954.

CASE 14

Diagnosis: Eosinophilic granuloma - Mandible

History: Boy, age 3, had difficulty in eating because of sore teeth and gingiva of six months duration. Two lesions on the palate had been diagnosed as Vincent's infection. Examination revealed two 2 x 2 cm. ulcerated lesions on the hard palate. These were elevated and dark red with yellowish centers. A similar lesion was present on the alveolar process adjacent to the lower first molar. The teeth were loose.
(W.U.M.S. 55-9396)

There are two sections on this case to show better the essential pathology of this lesion. There is extremely prominent reticuloendothelial proliferation with large masses of eosinophils together with a few giant cells. There are no organisms observed.

COMMENT: The features that have been described are typical of eosinophilic granuloma. In children eosinophilic granuloma may occur particularly around the bones of the orbit and are also seen as a single lesion in long bones such as the femur or rib. However, involvement of the mandible is not unknown and has been previously reported. Although this lesion may be apparently the only one, other may develop later and the patient may develop the syndrome of Hand-Schuller-Christian disease. There may be only a single lesion when the child is first seen but this is no guarantee that other lesions will not develop in other locations. We know this lesion will respond to small amounts of radiation therapy.

CASE 15

Diagnosis: Pseudoepitheliomatous hyperplasia - Gingiva

History: Man, age 19, had a 2 x 1.5 cm. tumor on the mandibular gingival mucosa between the second bicuspid and first molar teeth. The lesion and adjacent teeth were removed. (AFIP 100651)

This lesion of the gingiva shows extremely hyperplastic epithelium with an occasional nest of well differentiated epithelium lying distinct from the over-lying epithelium. These isolated cell nests can be shown by serial sectioning to be connected to the over-lying epithelium. Therefore, this apparent invasion is false. There is considerable chronic inflammation with dilated blood vessels and an edematous stroma. These changes are related to the inflammation.

COMMENT: Because of the separation of the epithelium from the over-lying hyperplastic epithelium we have frequently seen lesions of this nature diagnosed as carcinoma but for the reasons mentioned it is perfectly benign.

CASE 16

Diagnosis: Leukoplakia - Lower lip

History: Man, age 61, had a white area on the lower lip which had been present for several years. The lesion appeared to have been enlarging in the four months prior to surgery. (AFIP 756250)

There are diffuse changes in the lip with hyperkeratosis, a prominent granulomatous layer, intact basement membrane and chronic inflammation. The under-lying connective tissue is perhaps slightly increased in vascularity.

COMMENT: If a lesion of leukoplakia is localized, it can be easily excised.

Treatment of this lesion by irradiation therapy is unsatisfactory. If the lesion is extensive and there are no areas of irregularity or ulceration, then the entire area may be superficially excised. It is relatively uncommon in our experience for epidermoid carcinoma of the lip to arise from pre-existing leukoplakia.

CASE 17

Diagnosis: Granular cell myoblastoma - Tongue

History: Man, age 45, had an asymptomatic nodule on the left lateral anterior one-third of the tongue for four months prior to removal. The nodule measured 7 x 4 mm. (AFIP 718203)

The surface epithelium shows extreme alteration with hyperplastic changes and separation of the epithelium in the deeper areas into small nests. These nests of squamous epithelium are well differentiated and it is very easy to see how a diagnosis of epidermoid carcinoma could be made. However, these changes are secondary to the under-lying process which is a granular cell myoblastoma of the tongue. It can be seen that these cells are uniform with uniform nuclei and extremely granular cytoplasm. These cells in one instance have a very intimate association with a nerve.

COMMENT: The exact histogenesis of granular cell myoblastoma is unknown although the majority opinion favors the neurogenic and tissue culture favors myogenic origin. The tongue is a common site. However, it is seen in many other places including the skin, vulva, larynx, stomach, rectum, anus, uterus, etc. The cause of the change in the over-lying epithelium is unknown, but we have seen similar alterations in lesions of the larynx, skin, vulva and anus. In several instances an erroneous diagnosis of epidermoid carcinoma was made because of the epithelial alterations over-lying the tumor.

References:

Bangle, R., Jr.: A Morphological and Histochemical Study of the Granular-Cell Myoblastoma. *Cancer*, 5: 950-965, 1952.

Crawford, E.S., and DeBakey, M.D.: Granular-cell myoblastoma. *Cancer*, 6: 786-789, 1953.

CASE 18

Diagnosis: Squamous cell carcinoma - Gingiva

History: Man age 65, developed a lesion in the buccal sulcus of the lower molar area which was attributed to an ill-fitting lower denture. He continued to wear the denture for one week and then consulted his dentist who treated the area with silver nitrate and advised the patient to leave the denture out. One week later the patient consulted an experienced oral surgeon. At this time the lesion appeared typical of an epulis fissuratum and a biopsy was taken. (AFIP 759209)

This biopsy represents a fairly well differentiated squamous cell carcinoma arising from the gingiva. In my section there is ulceration and the tumor is growing beneath the uninvolved epithelium. This tumor extends the entire depth of the biopsy.

COMMENT: The microscopic pattern of this lesion is compatible with squamous carcinoma of the gingiva. These lesions are often very well differentiated. The treatment is often debatable. If the lesion does not involve bone, irradiation therapy in the hands of men like Lampe is very successful. If the lesion involves the under-lying mandible and extends into its substance then the radio-therapeutic problem becomes much more difficult. With sterilization of the tumor there also is bone necrosis resulting in sequestration which may necessitate later operation. We would advise, therefore, if the tumor extends into the bone, to consider local excision of the tumor in continuity with the mandible. Extent of removal of the mandible depends on the extent of the tumor. We would not recommend prophylactic neck dissection. The cure rate for lesions in this region is favorable.

References:

Modlin, J., and Johnson, R.C.: The Surgical Treatment of Cancer of the Buccal Mucosa and lower Gingiva. Am. J. Roentgen. & Rad. Ther. and Nuclear Med., 73: 620-628, 1955.

Lampe, I.: Radiation therapy of cancer of the buccal mucosa and lower gingiva. Am. J. Roentgen., Rad. Ther. and Nuclear Med., 73:628-635, 1955.

CASE 19

Diagnosis: Xanthogranuloma - Tongue

History: Girl, age 3 months, had a warty, non-compressable mass on the posterior half of the left side of the tongue. The parents had noticed the mass two weeks previously and it appeared to be increasing in size.
(AFIP 759690)

There is ulceration present with large masses of cells which are quite uniform and undoubtedly represent reticuloendothelial cells. Eosinophils are numerous. Mitotic figures are relatively rare. This lesion is well vascularized. It is infiltrating between the muscle bundles.

This is a rare lesion which we believe is perfectly benign and has been designated xanthoma, eosinophilic granuloma or xanthogranuloma. Undoubtedly it is the only lesion the patient has. Local excision would be curative and probably a small amount of irradiation therapy would result in prompt regression.

CASE 20

Diagnosis: Epidermoid carcinoma-in-situ - Tongue

History: Man, age 62, had a tongue lesion of two years duration. A biopsy revealed squamous cell carcinoma. A right hemiglossectomy, bilateral suprahyoid dissection and right radical neck dissection were performed. Four months later the patient complained of pain in the floor of the mouth and a suspicious area adjacent to the healing glossectomy wound was excised. This section is from this procedure. (AFIP 743431)

The surface epithelium of the lesion shows extreme alteration with hyperplastic disorganization but an intact mucous membrane and basement membrane. There is mitotic activity and disorganization of the pattern extending through all layers of the epithelium. A chronic inflammatory infiltration accompanies this process. Mucous glands are very prominent.

COMMENT: This represents an area of carcinoma-in-situ. We see no evidence of invasion. If this is the entire lesion there can be no metastasis. At times such sections are taken from zones near an invasive carcinoma and the changes as described are merely at the peripheral margin of the tumor. Furthermore, such changes may be discontinuous and there may be multiple foci of origin. Such changes account for the high incidence of second carcinomas of the oral cavity. It is probably that many recurrences are new tumors rather than recurrences.

References:

Slaughter, D.P.: Multicentric Origin of Intraoral Carcinoma. Surgery, 20: 133-146, 1946.

Byars, L.T., and Anderson, R.: Multiple Cancer of the Oral Cavity. Am. Surgeon, 18: 386-391, 1952.

Ackerman, L.V., and Johnson, R.: Present Day Concepts of Intraoral Histopathology; presented at the Second National Cancer Conference, March 3-5, 1952 Cincinnati, Ohio.

Ackerman, L.V., and Regato, J.A. del: CANCER, 2nd Ed., 1954, The C. V. Mosby Company, pp. 254-276.

CASE 21

Diagnosis: Adenoid cystic carcinoma - Palate

History: Woman, age 29, had a swelling of the left maxillary tuberosity and hard palate. The teeth in the area were loose and the x-rays showed bone destruction. (AFIP 730219)

This is a well differentiated tumor with an intact over-lying epithelium. There are numerous glands present, often lined by a double layer of cells. In some zones they have a somewhat cylindromatous appearance. It is growing between bone spicules so it is obviously malignant. It is a relatively common malignant tumor of salivary gland origin often diagnosed as benign.

COMMENT: I have seen lesions of this type with wide spread pulmonary metastasis. It is of interest that this lesion has considerable radiosensitivity and may be held in abeyance for long periods of time, even years, with appropriately given irradiation therapy. We have even seen pulmonary metastasis completely disappear for long periods of time.

Reference:

Foot, F. W., Jr., and Frazell, E.L.: Tumors of the Major Salivary Glands. Atlas of Tumor Pathology, Section IV-Fascicle 11, publ. by the A.F.I.P., Washington, D.C., 1954.