The Clinical Importance of Cystic Squamous Cell Carcinomas in the Neck

A Study of 136 Cases

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BACKGROUND. Predominantly cystic squamous cell carcinomas in the neck often present without a clinically apparent primary and therefore are frequently considered to be of branchial cleft origin. It is the authors' hypothesis that the anatomic site of the primary carcinoma that produced the neck metastasis can often be predicted on the basis of the histologic features.

METHODS. Cases of cystic squamous cell carcinoma in the neck diagnosed between 1971 and 1991 were retrieved from the Otorhinolaryngic Pathology Registry of the Armed Forces Institute of Pathology. Histologic features were reviewed and patient follow-up was obtained and analyzed.

RESULTS. In cases wherein the primary site was discovered subsequently, 64% of the primaries were in the lingual or faucial tonsil. An additional 8% of cases were in nasopharyngeal tonsillar tissue. The cases that did not originate in Waldeyer's tonsillar ring generally differed in histologic appearance from the tonsillar cases. The tonsillar primaries were discovered within an average of 12.4 months, but many were not discovered for years (up to 11 years). Most were small, indicating a slower growth of the primary than is usually expected for squamous cell carcinoma. Patients with such carcinomas had a much better prognosis than patients with metastatic squamous cell carcinomas of other upper airway mucosal sites.

CONCLUSIONS. In most cases of prominently cystic squamous cell carcinomas in the upper neck, the origin of the primary site will be in faucial or lingual tonsillar crypt epithelium. Knowledge of the probable site of origin allows for more tailored therapy in which the patients can be treated relatively conservatively with surgical excision and subsequent field-limited radiation therapy only, with 77% survival at 5 years. None of the cases reviewed in this study was a branchiogenic carcinoma. ***Cancer* 1998;82:944–56.**

KEYWORDS: tonsillar carcinoma, branchial cleft cyst carcinoma, cystic metastases in the neck.

Some squamous cell carcinomas (SCCs) discovered in the upper neck are predominantly cystic macroscopically. Most lesions have been observed by the patient over a period of 2 weeks to 84 months, with little evidence of growth. The preoperative and operative diagnostic impression of such carcinomas is often that of a branchial cleft cyst. Histologically, the lesion is composed of a thin, relatively uniform epithelial lining. When no other anatomic site subsequently demonstrates carcinoma, as is often the case, such carcinomas have

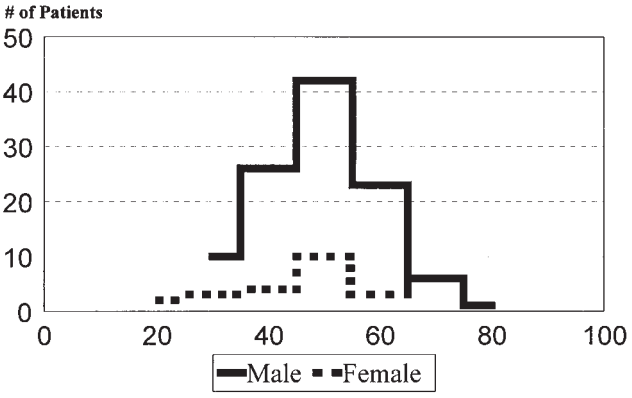


FIGURE 1. The age distribution of patients (in years) is shown.

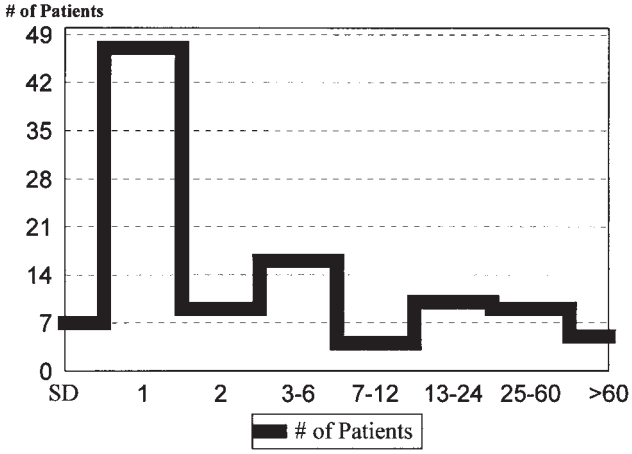


FIGURE 2. The intervals (in months) to discovery of the primary tumors are shown. SD: same day.

been considered branchiogenic carcinomas or SCC arising in a branchial cleft cyst.

Micheau and other authors[1–14] concluded that so-called branchiogenic carcinomas are actually cystic metastases in the neck from a tonsillar primary, and presented reports on 71 such cases in aggregate. The purpose of our study was to examine a larger number of similar cases at a single institution, with the aim of attempting to confirm these authors' conclusion, while also better quantifying the behavior of this type of carcinoma so that therapy can best be tailored to this specific type of cancer. Because not absolutely all cystic carcinomas in the neck are from primaries in the tonsil, we aim to describe, as well as possible, the histologic features that might predict a tonsillar origin, determine the reliability of such a prediction, and delineate any relevance to therapy and prognosis.

MATERIALS AND METHODS

One hundred thirty-six cases of cervical cystic SCC were identified in the files of the Otorhinolaryngic–Head & Neck Tumor Registry of the Armed Forces Institute of Pathology from the years 1971 to 1991. We added additional follow-up material to these files. Follow-up information included information regarding the identification of a primary site and the type of treatment received by the patients. One of our cases has been previously reported.[15] Hematoxylin and eosin–stained slides for all cases were reviewed.

Five criteria were established to define the typical histologic features of the cystic SCCs in the neck: 1) formation of a large cyst or cysts, as opposed to multiple small or comedo-like cysts; 2) predominantly a cystic lesion with only focal areas of solid growth; 3) cystic spaces lined by a squamous epithelium arranged in a ribbonlike configuration, maintaining a relatively uniform thickness and orderly polarity throughout the cyst (approximately the thickness of a normal mucosal stratified squamous epithelium), with occasional areas of either endophytic or irregular papillary exophytic proliferations; 4) epithelium that is generally of a transitional nature, with the cells demonstrating a high nuclear-to-cytoplasmic ratio, no appreciable degree of surface maturation, and limited (if any) keratinization, with suggestions of squamous pearl formation; and 5) no prominent degree of anaplasia, but instead a recapitulation of the normal tonsillar crypt epithelium, with variable mitotic activity.

The overwhelming majority of our cases presented as masses in the upper neck, involving the jugular digastric lymph nodes. Because the lymphatic drainage of Waldeyer's tonsillar ring courses behind the styloglossus, the stylohyoid, and the posterior belly of the digastric muscles to drain primarily into the jugular digastric lymph nodes in the upper deep cervical chain (intimately associated with the external carotid artery and the internal jugular vein),[16–18] the site of metastatic disease is relevant to our hypothesis.

The cases in which disease did not demonstrate the five histologic characteristics, nor was found in the typical jugular digastric lymph nodes, were categorized as ''atypical,'' as described below.

RESULTS

Clinical

The patients included 28 females and 108 males. Their ages ranged from 23 to 82 years, with an overall

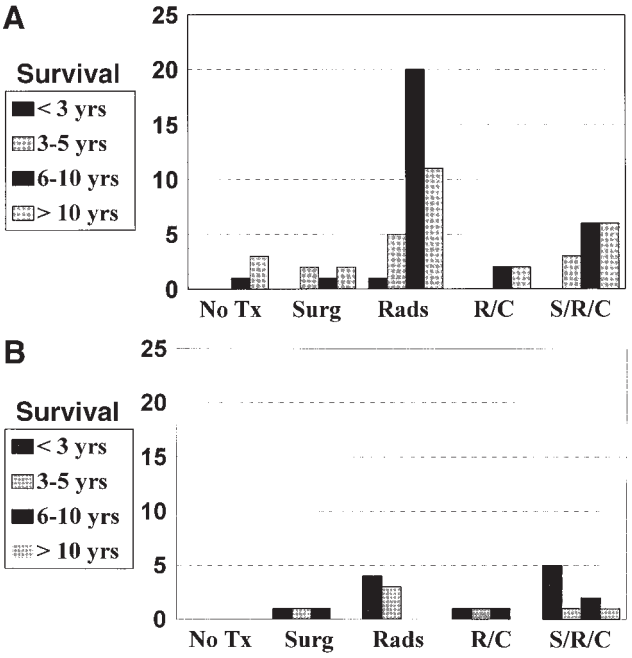


FIGURE 3. Prognoses are shown for 85 patients with tonsillar primaries, (A) alive with no evidence of disease (NED) or (B) dead of disease, who received no therapy (No Tx); surgery (Surg); radiation therapy (Rads); radiation and chemotherapy (R/C), and surgery, radiation, and chemotherapy (S/R/C).

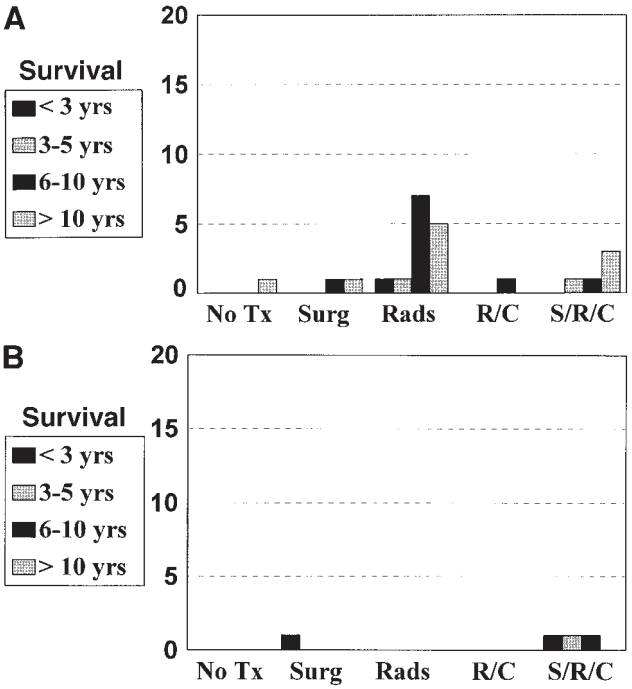


FIGURE 4. Prognoses are shown for 27 patients with unknown primaries, (A) alive with no evidence of disease (NED) or (B) dead of disease, who received no therapy (No Tx); surgery (Surg); radiation therapy (Rads); radiation and chemotherapy (R/C), and surgery, radiation, and chemotherapy (S/R/C).

TABLE 1
Disease at Time of Death for Each Primary Site, by Treatment Modality

Disease status	Surgery only	Radiation only	Combination therapy
Local	0	0	0
Regional	N(1) T(1) U(1)	O(1) T(3)	O(1) N(1) T(2)
Widely metastatic	T(3)	T(6) N(2)	O(3) T(5) U(3)

N: nasopharynx; T: tonsil; U: unknown primary; O: other.

average age at presentation of 54.2 years. The median age at presentation was 54 years, with a mode of 51 years. The female patients had a median age at presentation of 55 years, but the difference was not statistically significant (Fig. 1). One hundred thirty-three patients were white and three were African American.

The lesions presented as masses in the upper to mid-lateral neck, and they had been present for 2 weeks to 84 months. The average duration of symptoms was 4.5 months, with a mode of 1 month. There were 57 tumors on the right and 44 on the left, and tumors were bilateral or unspecified in the remaining 35 patients.

Follow-up was available in all 136 cases. During the follow-up period, 87 primaries (63%) were identified at the base of the tongue, the lingual tonsil region, or the faucial tonsil region (histologically of the transitional type, tonsillar crypt epithelium, rather than the usual SCC, which can occur at the base of the tongue); 11 primaries were in the nasopharynx; 11 primaries were in the larynx, palate, or sinuses; and 27 primaries were of unknown location or as yet undiscovered.

The primaries were found on the day of the initial surgery, or up to 132 months later (11 years) (Fig. 2). The average time to discovery of the primary was 12.4 months, whereas the median and mode were 1 month each, with primaries discovered within 1 month of the initial presentation of the cystic mass in the lateral upper neck in 54 patients.

Thirty-seven of the patients used to or still continued to smoke cigarettes and consume alcohol, 25 patients used to or still continued to smoke cigarettes only, and 2 patients used to or still continued to consume alcohol only. Thirty-one patients denied

TABLE 2
Neck Cystic Squamous Carcinoma Survival Predicted by Histology

Primary location	No. of patients (%) alive		Total (alive or dead)
	Typical	Atypical	
Tonsil	47 (78%)	8 (80%)	85
None found	15 (83%)	6 (75%)	27
Nasopharyngeal	4 (80%)	4 (57%)	11
Other	3 (100%)	5 (50%)	13
Total			136

ever having used tobacco or alcohol products. Alcohol and tobacco use was unknown for 41 patients.

Survival

Eighty-five patients had primary tumors identified at the base of the tongue (the lingual tonsil area was presumed), the lingual tonsil, or the faucial tonsil. Of these patients, 65 were alive at the time of follow-up and were treated with radical neck dissection (n = 5); radiation therapy (n = 37); a combination of radical surgery, radiation, and chemotherapy (n = 15); or no additional therapy (n = 4) (Fig. 3A). Of the patients who died of their disease, 15 of the 20 died within 5 years of initial treatment, with only 5 dying 6–11 years after the initial diagnosis (Fig. 3B). Of the 20 patients who died of their disease, 4 were treated by surgery alone: 1 died of regional disease and 3 of widely metastatic disease; 9 were treated with radiation only: 3 died of regional disease and 6 of widely metastatic disease; and 7 were treated by combination therapy: 2 died of regional disease and 5 of widely metastatic disease (Table 1).

The survival statistics were quite similar for the 27 patients in whom no primary has been found to date. Of these patients, 23 were alive at the time of follow-up and were treated with radical neck dissection (n = 2); radiation therapy (n = 14); a combination of radical surgery, radiation, and chemotherapy (n = 6); or no additional therapy (n = 1) (Fig. 4A). Three of the 4 patients who died of their disease also died within 5 years of the initial treatment, with only 1 dying 6–11 years after the initial diagnosis (Fig. 4B). Of the 4 patients who died of their disease, 1 died of regional disease after being treated with surgery only, and 3 patients died of widely metastatic disease after receiving combination therapy (Table 1).

Seven of the 11 patients with nasopharyngeal primaries were alive at the time of follow-up; all were treated with radiation therapy, and 3 were also treated with radical surgery. Four of the patients died within 5 years of recurrence of their disease; 2 patients died of regional disease, 1 treated with surgery only and the other with combination therapy; and 2 patients died of widely metastatic disease after being treated with radiation therapy only (Table 1).

Eight of the 13 patients with other primaries (including primaries of the larynx, palate, and sinuses) were alive, 7 of whom were treated with radical surgery, radiation, and chemotherapy. Two patients had died of regional disease, 1 treated with radiation therapy only and 1 with combination therapy. Three patients had died with widely disseminate disease, after being treated with combination therapy (Table 1).

Using the five histologic criteria that we estab-

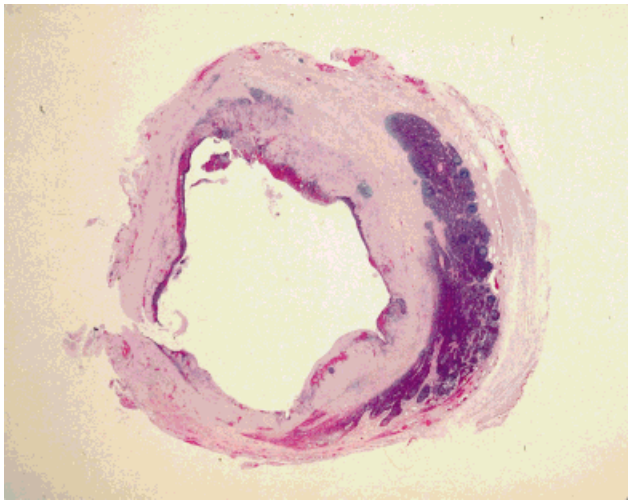


FIGURE 5. The macroscopic appearance of a cystic metastasis is shown. A narrow band of epithelium is intimately associated with the underlying lymphoid component.

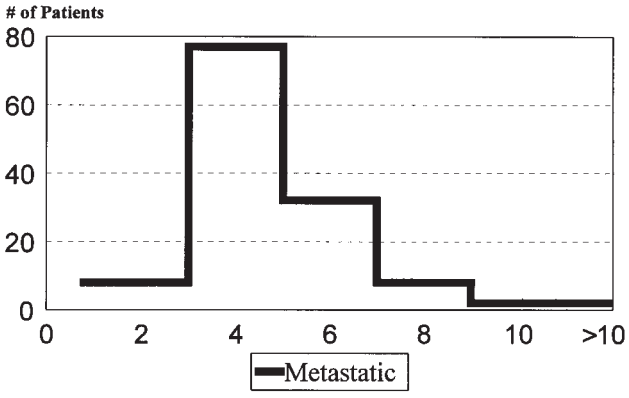


FIGURE 6. The sizes (in cm, horizontal axis) of metastatic cystic lesions found in the neck are shown.

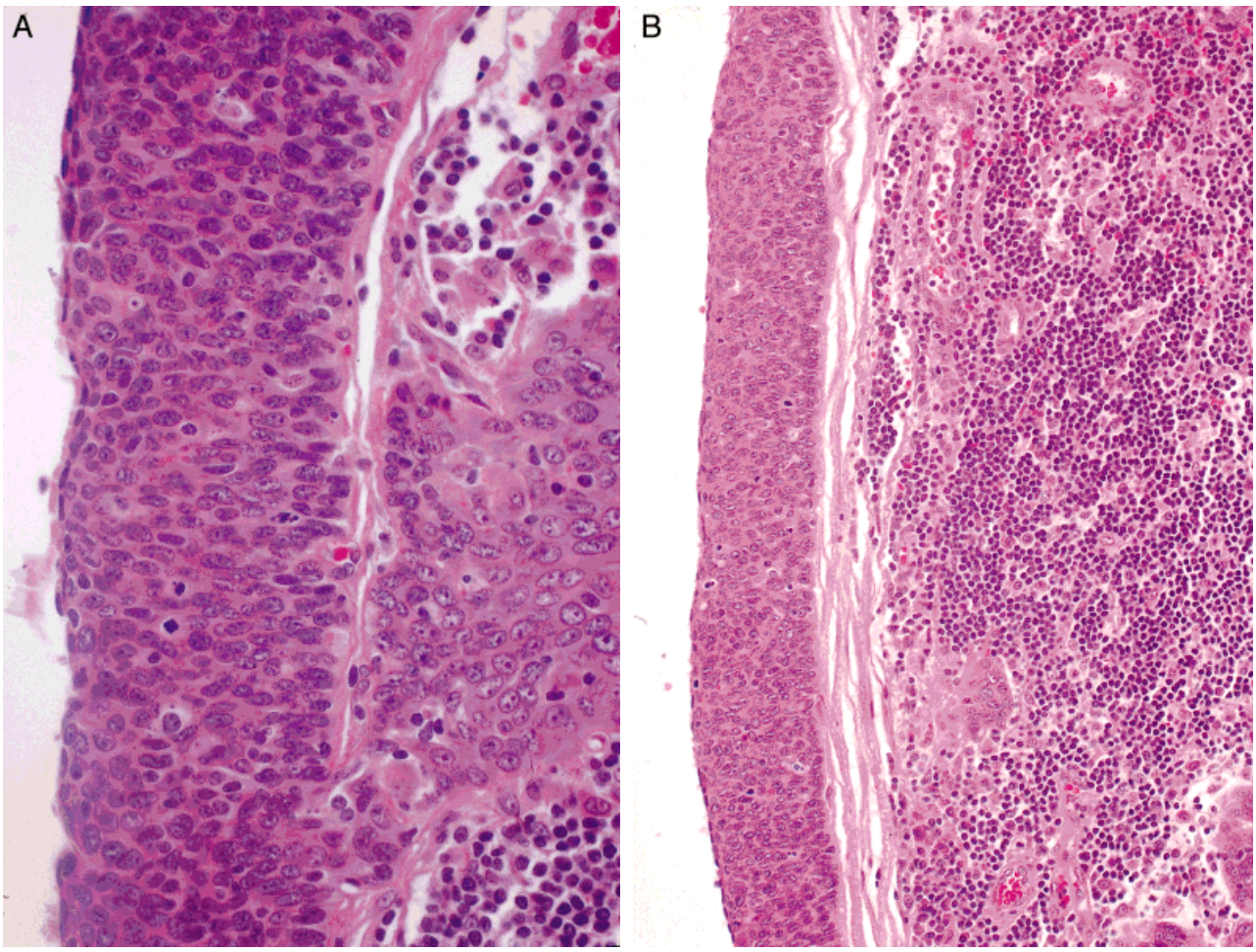


FIGURE 7. (A) Squamous cell carcinoma is shown growing along the cystic cavity created by the metastatic focus to the lymph node, benign in overall appearance. (B) The uniform thickness of the ribbonlike growth along the cyst cavity is shown.

lished to identify what we felt were the cases of tonsillar or base of tongue primary, we believe that a marked similarity can be identified between the cases of tonsillar or base of tongue primary and those in which there is an unknown primary, when compared with the cases in which another primary was identified (nasopharyngeal or laryngeal) (Table 2). The lesions that had an atypical histologic appearance were often from a nontonsillar primary, whereas those with typical histology were from the tonsil in 88% of cases.

Pathologic Features

Macroscopically, the neck lesions were generally well circumscribed, usually surrounded by a thick fibrous capsule, that was most probably generated from the capsule surrounding the lymph node (Fig. 5). The neck masses ranged in size from 1.5 to 13 cm, with an average size of 3.9 cm (Fig. 6). The cut surface was predominantly cystic and filled with grumous, granular, thick, tenacious, and purulent yellow, brown, and/or hemorrhagic fluid. The cystic space was generally unilocular, although multiple cystic spaces were occasionally identified. The primary tumors in the Waldeyer's tonsillar ring region were often too small to be identified clinically and were only identified on histologic examination.

Histologically, the lesions met the criteria stated above for the typical cases. There was a predominantly cystic space that was generally empty on the hematoxylin and eosin-stained slides, as the contents had been washed away. The spaces were lined by a ribbonlike growth of transitional-type epithelium, generally of a uniform thickness, as the cells covered the inside of the cystic space (Fig. 7A and B). There were a number

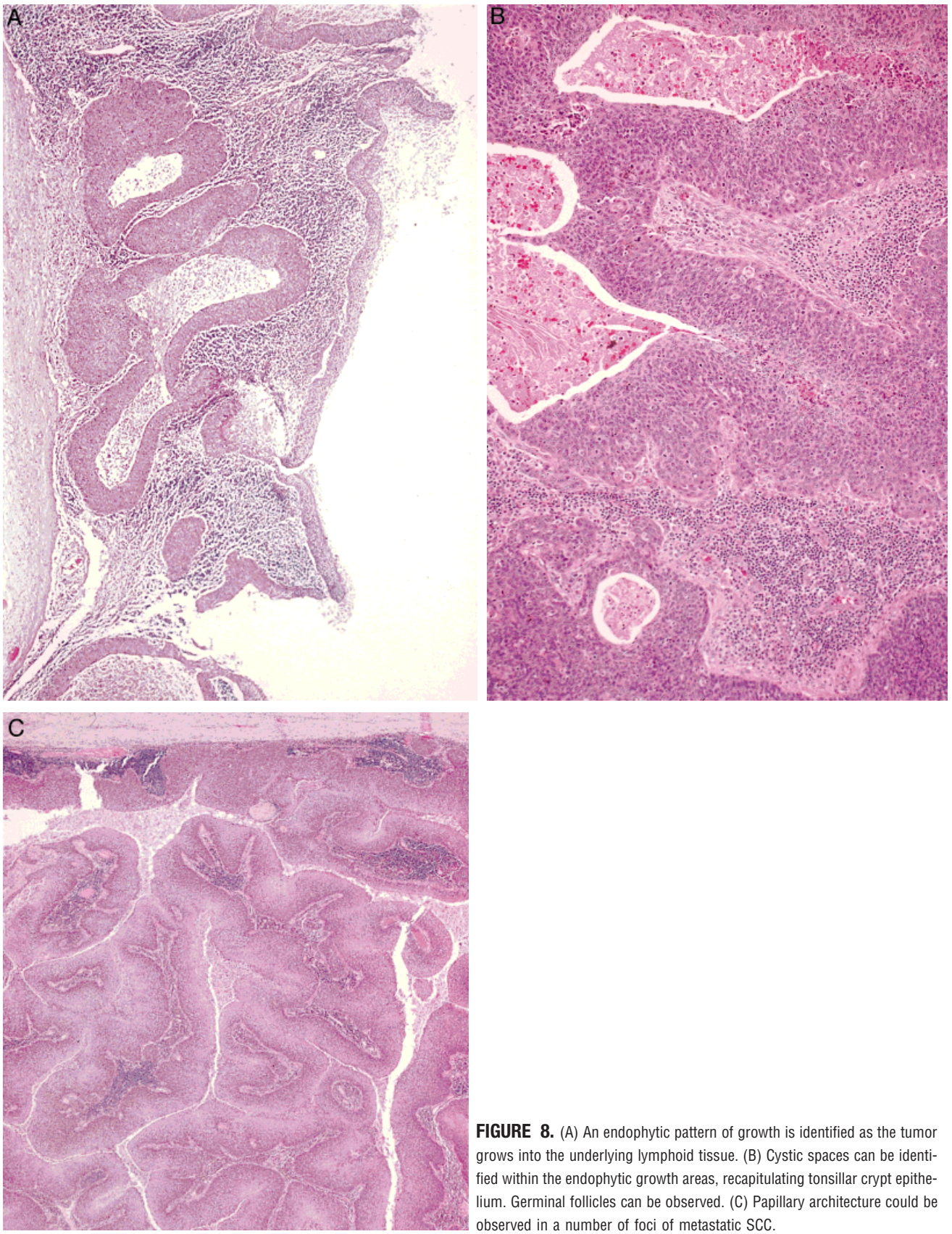
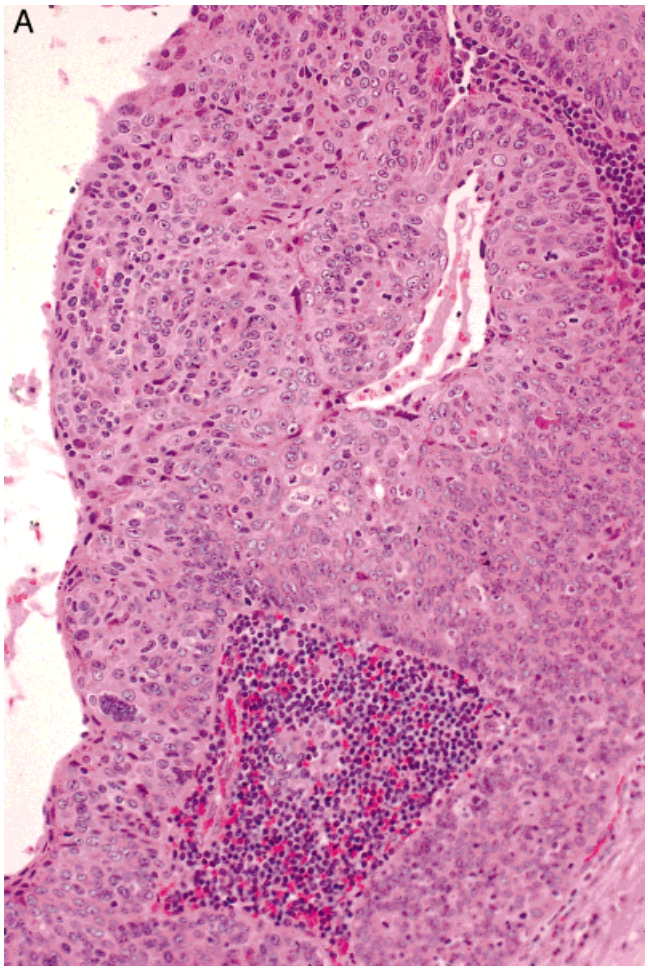


FIGURE 8. (A) An endophytic pattern of growth is identified as the tumor grows into the underlying lymphoid tissue. (B) Cystic spaces can be identified within the endophytic growth areas, recapitulating tonsillar crypt epithelium. Germinal follicles can be observed. (C) Papillary architecture could be observed in a number of foci of metastatic SCC.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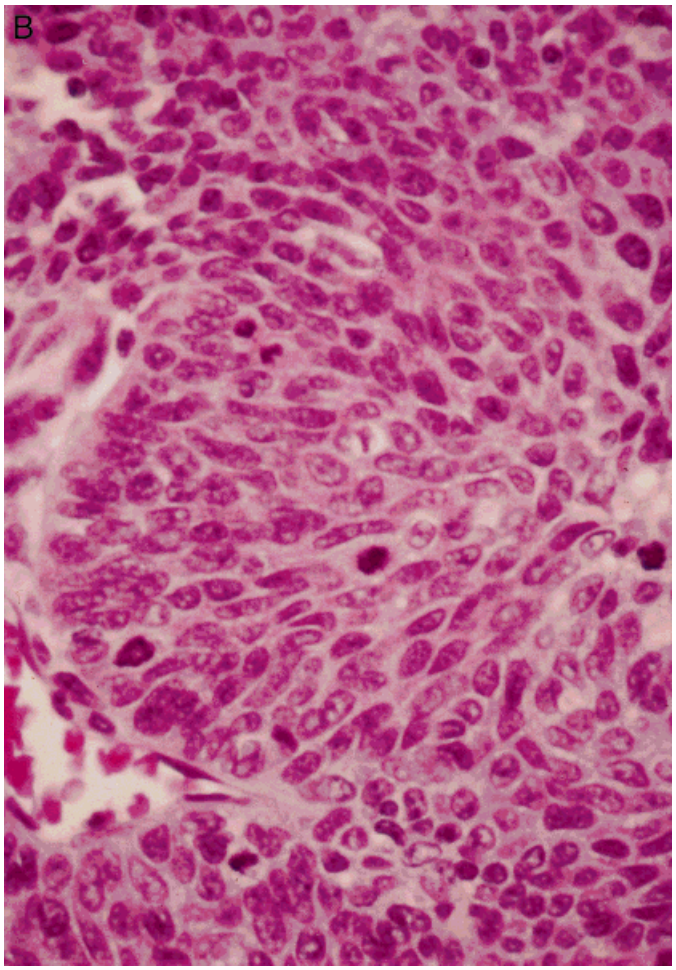
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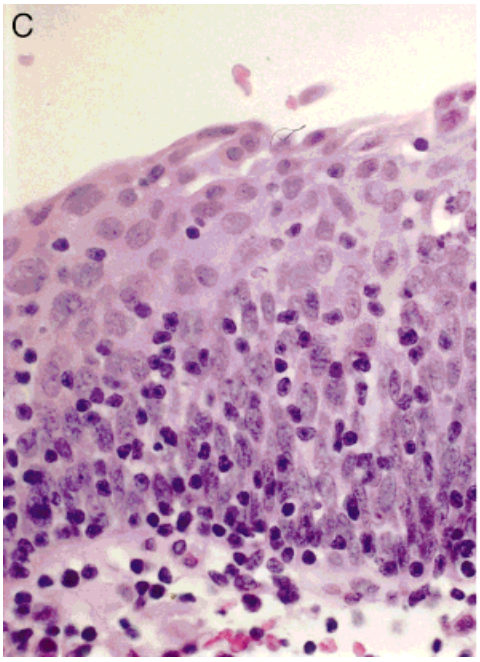
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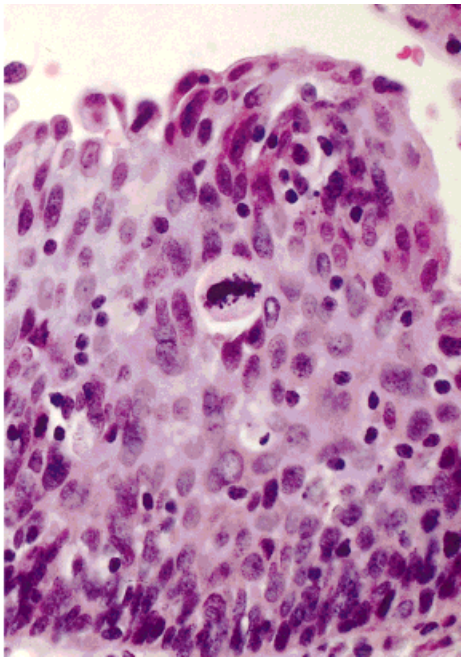

of places in which the lining of the cystic spaces grew downward into the underlying lymphoid elements, creating an endophytic growth pattern (Fig. 8A and B), whereas in other areas a papillary architecture was noted (Fig. 8C). A dense, fibrous connective tissue response was often present, limiting any comment regarding ''extranodal extension'' of the tumor (Figs. 5 and 8C). The cells were slightly enlarged with a high nuclear-to-cytoplasmic ratio, very little maturation towards the surface, and at least a few areas of loss of polarity (Fig. 9A–C). The overall histologic appearance in many areas was very bland, recapitulating the normal squamous to transitional-type epithelium identified in the tonsillar crypts or occasionally identified in a branchial cleft cyst (Fig. 5, 9C, 10). There was seldom anaplasia in these typical cases, nor were there more than 5 mitotic figures per 10 high-power fields.

The primary tumors were small (as logically follows from the need for random biopsies or tonsillectomy to identify the tumors), demonstrating a histologic appearance similar to that of the metastatic foci described above. The lymphoepithelium of the tumors was frequently very well differentiated, but still with a certain degree of atypia that was beyond what one can accept in a benign reactive or hyperplastic response.

The atypical cases included lesions in which the primary site was identified as the larynx, sinuses, palate, esophagus, or nasopharynx, in addition to a few cases originating in the tonsil. These cases demonstrated a squamous-type epithelium, with intercellular bridges, squamous pearl formation, and squamous eddies. There was a loss of polarity as well as areas of surface maturation and keratinization. The cells were frequently anaplastic, with many mitotic figures identified, including atypical forms. The lumen was often filled with keratinaceous and granular debris, frequently arranged in a comedo-type growth pattern. There were other cases in which the cells were arranged in syncytial sheets, with large, vesicular nuclei, open chromatin and prominent nucleoli, richly invested with lymphoid cells. These cases were usually of nasopharyngeal origin.

DISCUSSION

The majority of cystic SCC described in this report that ultimately were proved or considered to be of tonsillar origin presented clinically as moderately large cystic metastases in lymph nodes of the upper neck, whereas the primary carcinomas in the tonsils were relatively small. Indeed, many of the primaries were occult and very small when eventually discovered; some tumors were diagnosed only on microscopic examination ($<$0.1 cm). Some remained undiscovered for many years. It is important to clarify that this type of tonsillar SCC does not comprise all tonsillar SCCs. Many tonsillar carcinomas are large primary lesions[16,19,20] at the time of initial presentation and at that time may or may not be associated with clinically manifest metastases. When metastases from these other tonsillar carcinomas occur, they usually are not cystic. Thus, the tonsillar carcinomas described in this report comprise only a subtype of tonsillar SCC, and their histologic and clinical features cannot be used to describe the features of tonsillar SCCs in general. However, the description of this subtype of SCC is useful because of the diagnostic difficulties in accurate interpretation it presents to pathologists, and also because its behavioral features entail some special considerations from a clinical standpoint.

Just as not all tonsillar SCCs form cystic metastases, cystic SCC metastases in the neck do not always come from the tonsillar tissues. However, the very well-formed or ''typical'' cystic metastases, which are almost always the ones mistaken for branchiogenic carcinoma or carcinoma arising in a branchial cleft cyst, are almost always from primary carcinomas somewhere in the tonsillar tissue of Waldeyer's ring (such typical cases in this study, wherein the primary was stated as being in the base of the tongue, were almost surely in lingual tonsil tissue). The histologic features of typical tonsillar cystic metastases were described in the ''Materials and Methods'' section of this article. If these previously described histologic features of a cervical cystic SCC are typical and the primary carcinoma is not located after a thorough clinical search has been done, it is still reasonable to assume that the primary origin is the inferior portion of Waldeyer's tonsillar ring, for purposes of treatment. The percentage of these typical cystic SCCs arising in the nasopharyngeal tonsillar (adenoid) tissue is small (only 4.7% of the primary cases in this study demon-

FIGURE 9. (A) The ribbon of neoplastic cells demonstrates a loss of polarity, limited maturation towards the surface, and keratin pearl formation, although limited in extent. There is an invasive quality to the proliferation. (B) Enlarged cells with an increased nuclear-to-cytoplasmic ratio and mitotic figures can be observed. (C) The left side demonstrates a bland epithelium with limited nuclear disorganization, whereas the right side demonstrates loss of polarity, mitotic figures, and an increased nuclear-to-cytoplasmic ratio of the epithelium in an adjacent area of the same specimen.

strated typical histology, and were from the nasopharynx), and the very large majority of these prominently cystic SCCs arise from lingual or faucial (oropharyngeal) tonsillar tissue. Thus, the above-mentioned authors' assertion that these are oropharyngeal tonsillar carcinomas[1–14] is, in our view, correct. However, although the correlation between the histologically typical cystic SCC and the tonsillar origin is high, because the predictability in an individual case is not perfect (partly because of some biologic variability in tissue appearances from case to case), it is probably in the best interests of the patient for the physician to do everything feasible to try to find and document the primary site, so that the best treatment can be rendered more confidently. If the primary is located in the oropharyngeal tonsillar tissue as opposed to the nasopharynx, irradiation ports can be reduced to some extent. For example, the roof of the nasopharynx would not have to be included in the irradiation field, and this would reduce the chance of any injury to the pituitary gland. Although radiation therapy of tonsillar carcinoma would usually entail the relatively wide-field irradiation of retropharyngeal lymph nodes,[16,18] because the crypt epithelial carcinomas that produce highly cystic metastases seem to be relatively reduced in aggressiveness, the chance of retropharyngeal lymph node involvement might be ameliorated enough that it might be feasible in selected instances (i.e., instances of very small primary tumor and apparently unicystic neck metastasis with ''typical'' histologic features) to elect to reduce the irradiation field below what usually would be performed. This conceivably could reduce the extent of postirradiation mucositis and troublesome symptoms of xerostomia.[4,8,12,14,17,21–23]

The first important step in trying to determine the origin of a cervical cystic SCC for which the primary origin has not been discovered is to realize that the lesion is indeed metastatic and there is definitely a primary carcinoma somewhere, however small or occult in clinical presentation. SCC arising from a branchial cleft cyst is a hypothetical entity that, from a practical clinical standpoint, does not exist (in our opinion). Many other authors have also expressed strong doubt about the existence of branchiogenic SCC[1–14,24] and have implied that, at best, it must be a very rare entity. However, there are still many reports in the recent literature (1970 to present) of primary branchiogenic carcinoma,[15,25–43] one even claiming in 1992 to be the first such description.[38]

In analyzing these reported cases, a number of discrepancies or deficiencies were noted: no tonsillectomy was performed;[15,25,26,28,30,31,34,36,39–41,43] no random biopsies noted;[25,26,39,40,43] no biopsy of the tonsillar bed performed[35] (cases in which there has been a previous tonsillectomy have been reported in which a primary is still found in the bed of the previous tonsillectomy site[9]); insufficient follow-up or no follow-up period given;[25,27,30,31,36,39,40,43] treatment with radiation therapy given, effectively treating the possible primary[15,28–31,36,40,41,43] (the Sandiford case[15] is included in our series, and the patient is now 23 years out, without evidence of disease after radiation therapy); multiple recurrent, metastatic foci to other lymph nodes and distant sites documented;[15,27,28,41] a previous tumor of similar histology reported;[29,34,37,42] a mucoepidermoid carcinoma or an atypical histologic appearance described;[29,33,34,36,42] disease not occurring in the correct anatomic location;[38,40] and/or illustrations not furnished.[32] Therefore, we do not believe that any of these reported cases truly meet the original criteria of Martin et al.[4] or the criteria that we have set forth herein.

Admittedly, we cannot formally ''prove the negative,'' i.e., prove that carcinoma might not very rarely arise in a branchial cleft cyst. However, we have hundreds of cervical cystic SCCs in the Otorhinolaryngic–Head & Neck Pathology Registry files (most thought by the contributors to represent branchial cleft carcinomas), along with many cases in the literature; and in no case have the findings supported such an interpretation. Areas thought to be portions of a previously benign cyst are, on careful examination, still atypical in subtle ways, such that they are consistent with very well-differentiated, nonkeratinizing SCC. In many cases, the primary tonsillar carcinoma has been found, demonstrating that the extraordinary bland appearance of the epithelium is in fact from a malignant tumor. Our experience indicates to us that branchiogenic SCC must be so rare that to consider it in the differential diagnosis becomes untenable.

Indeed, because tonsillar carcinoma cystic metastases can have areas lining the cyst that are practically benign in appearance, if one should (theoretically) encounter SCC arising in a branchial cleft cyst, it could probably not reliably be diagnosed as such. The only way we can imagine that such a lesion might confidently be recognized is in a case in which the cystic lesion is associated with a well-defined sinus tract with a course documented to indicate a branchiogenic developmental anomaly (based on embryologic knowledge of the development of the branchial cleft region). Not only have we not encountered such a case, but we are not aware of such a case in the literature that is convincing.[38]

Our discussion would not be complete without consideration of the single case in our study, and

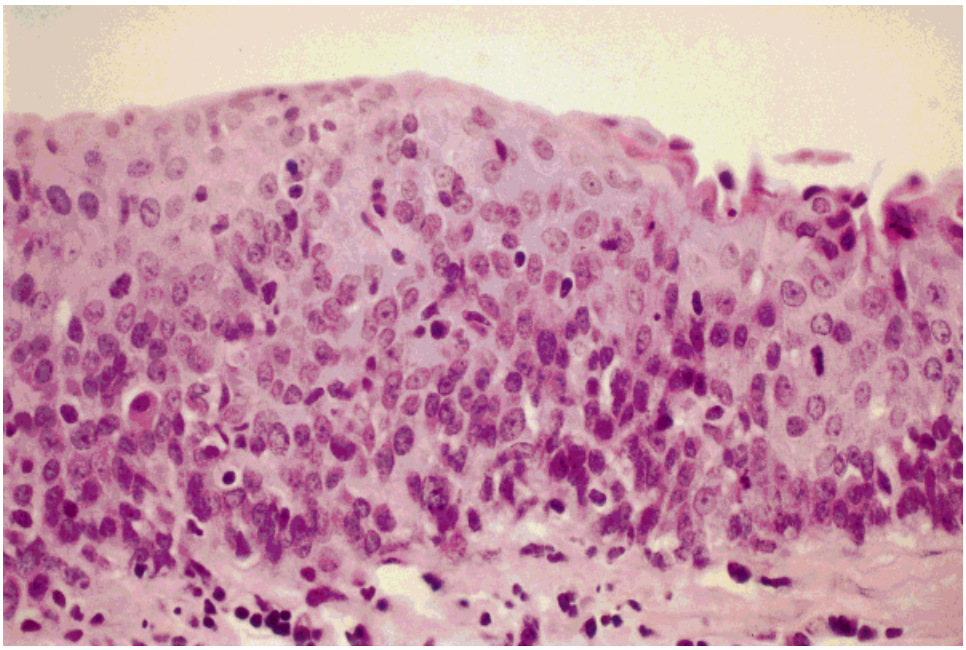

FIGURE 10. The epithelium had a bland appearance in one case, simulating a branchial cleft cyst. In other areas, more atypical regions were identified.

those reported in the literature,[3,26,34,35] in which the patient received no treatment other than excision of the neck mass and did well for a long period (e.g., over 5 years), with no tonsillar or other mucosal primary ever being discovered. Doesn't this ''prove'' a branchiogenic (or at least nonmucosal) origin for the carcinoma? Our data (as well as the data of Micheau et al.[1,2]) include cases in which the primary was not discovered for periods longer than 5 years (up to 11 years) but then was discovered after these prolonged intervals. One might reasonably claim that this was a second unrelated primary because of the very prolonged time period. However, some of the primaries discovered within a year or two were amazingly small but had produced a large metastasis, indicating that this type of primary can be indolent in its growth. If such a primary can be indolent for 1 year, or 2, 3, or 4 years, why could an occasional primary not be indolent for several more years? Our data indicate a relatively smooth incidence curve for the time periods to discovery of the primary carcinomas (Fig. 2). When, therefore, and on what basis, would one determine a cutoff point for such a lesion to be considered the primary source, and determine when it should be considered a second primary? No matter what time period one chose, it would be arbitrary and without compelling justification. After all, if we explain the data on the basis of one neoplastic process rather than hypothesizing two separate tumors, we are following the principle of striving for simplicity in hypotheses.

The indolent (or even ''suppressed'') growth of the primary tumor and the histologically well-differentiated areas that may occur in the metastases can be partially explained by the nature of the tonsillar crypt lymphoepithelium from which they arise. Lymphoepithelium is generally thought of as epithelium overlying lymphoid tissue.[1,2,22,44,45] We, however, believe there is a difference between surface tonsillar mucosal epithelium and the crypt epithelium. A morphologic difference can certainly be appreciated, rather strikingly emphasized by an immunostain for keratin (CK1 and AE1/AE3, mouse monoclonal, 1:2 dilution [Dako, Carpinteria, CA], with enzyme digestion). With such a stain, one can clearly see the irregularity of the basal zone, which is intimately admixed with lymphocytes and dendritic reticulum cells. This is what we consider the ''true'' lymphoepithelium, as it is the immunoresponsive site for tonsillar epithelium.[44,45] The intimate functional relationship of lymphocytes with crypt lymphoepithelium might explain the apparently slow-growing, indolent nature of many of the crypt epithelial carcinomas. It is a well-known fact that patients with primary tumors that develop a marked inflammatory response in the head and neck have a better outcome.[22] A tumor-suppressive (or at least tumor-hindering) immunologic reaction might be

engendered because the epithelium from which these primaries arise is normally a site of immunocytologic reaction involving immunocompetent cells and epithelium.[44,45] Furthermore, because crypt epithelium is normally so intimately associated with lymphoid cells, the metastatic epithelium is right at home in the microenvironment furnished by the lymph node. This interaction may account for the well-developed cystic formations as the carcinoma recapitulates the parent crypt epithelium that normally invaginates into lymphocytic tissue. This epithelium is often relatively benign in appearance in some areas of the metastatic foci.

In addition, Martin et al.[4] reported three cases in which a metastatic tumor and a primary tumor had been discovered, in which the primary tumor underwent involution without additional therapy. By analogy, could not cases in which the primary has as yet been undiscovered undergo involution, thereby never being discovered? We believe that the immunologic response coupled with the size of the tumor may allow this phenomenon to occur.

Once it is accepted that a cervical cystic SCC of unknown primary origin (after comprehensive examination—radiographic, endoscopic, and biopsy—of the upper airway) is definitely metastatic and not branchiogenic, efforts to provide for maximally efficient and efficacious therapy with minimum morbidity can be instituted. First, the location of the lesion and its histologic features should be rescrutinized. Up to 95% of metastases from a tonsillar primary or an unknown head and neck primary will present in the jugular digastric lymph nodes, the first drainage site for the lower portion of Waldeyer's tonsillar ring.[16–18] If the metastatic lesion is not located in the jugular digastric area, the farther away it is from this area, the greater the chance that it may not be from the faucial or lingual tonsil. Therefore, the search for a primary will need to include areas outside of Waldeyer's tonsillar ring. Moreover, if the metastasis is not histologically ''typical,'' as denoted in this discussion, then it may very well not be from Waldeyer's tonsillar ring. Other tumors can metastasize to the lateral neck or other cystic lesions can be present, i.e., metastatic papillary carcinoma of thyroid origin,[46–48] lymphangioma, and thymic cyst. The histologic features of these tumors or benign developmental anomalies is so characteristic that histologic examination would exclude metastatic SCC. If the tumor is both locationally and histologically typical, the main search efforts should be directed toward Waldeyer's tonsillar ring, specifically the lower portion. In addition to extensive physical examination under anesthesia with panendoscopy, detailed radiographic studies should be performed, as they can sometimes uncover the occult primary site.[8,17,49] If these studies do not provide evidence of the primary, then prophylactic lingual and faucial tonsillectomy, specifically on the ipsilateral side, should be considered. Tissue from such a procedure should be very thoroughly examined, because, as already mentioned, the primary may be undetectable to the unaided eye. As the tumor can often be well differentiated and obscured by lymphocytes, a tiny primary can easily be overlooked.[1,2,8,9,13,50] We have been able to identify the primary tumor after completely embedding all of the tissue in some cases of cystic metastases, in which tonsillectomies were performed and the tissue reported to be free of tumor.

If the primary site is found to be the faucial or lingual tonsil, or if the cervical cystic SCC is judged to be locationally and histologically typical for such a metastatic tonsillar carcinoma, further treatment decisions can be based on our patient follow-up data and that of other authors.[1–3,5–7,11,12,21,51–54] This type of carcinoma appears to have a more indolent growth behavior compared with most SCCs. This is based on the information that some of the cystic metastases were present for up to 84 months (an average of 4.5 months) with little clinical growth and that many of the primary carcinomas remained small and undiscovered for up to 11 years. This type of carcinoma has a better prognosis than does the average metastatic SCC in the neck. In cases of the latter type, 5-year survival is approximately 6–55%,[12,19,20,53,55] whereas the survival at 5 years in our series is 86 of 112 (77%), with 34 of these patients surviving longer than 10 years. These data suggest that radiotherapy alone provided a good prognosis and that combination therapy with additional modalities is probably not needed. This confirms the findings of others,[4,12,16,21,51–54,56] which suggest that radiation therapy provides the best clinical outcome for patients with tonsillary primaries or for initially unknown primaries (see Figs. 3A, 3B, 4A, and 4B). The initial surgical excision of the neck mass probably removed all of the metastatic disease. Many of these cystic metastases are solitary. If additional surgery in the form of a neck dissection is performed (only for metastatic foci that are greater than 3 cm or in multiple lymph nodes[16,51,53]), it is recommended that the dissection be as limited and conservative as is feasible.

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