

CLINICAL REVIEW

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Diagnostically challenging lesions in head and neck pathology

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Abstract There are a variety of diagnostically challenging lesions in the head and neck region. Contact ulcer usually occurs within specific clinical parameters (vocal abuse, post-intubation and gastro-esophageal reflux), which should be documented in correlation with the granulation tissue-like response affecting the posterior vocal cords. Spindle squamous cell carcinoma (carcinosarcoma) presents a variably cellular spindle cell proliferation, often with surface epithelial ulceration. The clinical presentation of a firm, polypoid mass in the larynx, combined with the histomorphologic features of a spindle cell tumor, can be confirmed to be of epithelial origin when a portion of the overlying epithelium is seen to blend with the spindle cell component, or when ancillary studies authenticate the epithelial origin of the tumor. The diagnosis of a verrucous squamous cell carcinoma can only be made accurately with an accurate clinical history. The very well differentiated histologic appearance, a broad pushing border of infiltration, a bland epithelial proliferation with scant mitotic activity and “church-spire”-type keratosis coupled with the clinical presentation of a large, locally destructive lesion, can confirm the diagnosis of verrucous carcinoma. A wide variety of disorders can result in midline destructive disease clinically, but a specific etiology must be sought to provide appropriate clinical management. Angiocentric T/NK-cell lymphoma of the sinonasal tract is one such disease. The atypical lymphoid cells are usually angiocentric and angiodestructive in their growth pattern. Identification of the atypical cells in the early stages of disease may be difficult, often requiring multiple biopsies over time with the application of immunohistochemical stains or molecular studies to accurately identify the nature of the infiltrate. Cystic squamous cell carcinoma in

the neck is almost always a manifestation of metastatic tumor and not a branchiogenic carcinoma. When specific histomorphologic features are noted (a large, unfilled cyst lined by a ribbon-like or endophytic growth of a “transitional”-appearing squamous epithelium with a limited degree of anaplasia), most of these tumors demonstrate primaries in Waldeyer’s ring, often of a very small size. Adequate clinical work-up (pan-endoscopy, extensive radiographic imaging and random biopsies or prophylactic tonsillectomy) is mandatory in order to limit the radiation-therapy ports and to document the location of the primary, yielding an excellent long-term prognosis.

Key words Head and neck pathology · Contact ulcer · Spindle squamous cell carcinoma · Verrucous carcinoma · Angiocentric T-cell lymphomas · Midline reticulosis · Branchiogenic carcinoma

Introduction

A number of diagnostically challenging lesions occur in the head and neck region. These include contact ulcers, spindle squamous cell carcinoma and verrucous lesions in the larynx, as well as angiocentric T-cell lymphoma of the sinonasal cavity. Significant difficulty has also occurred in the last few decades in correctly diagnosing cervical cystic squamous cell carcinoma. These various lesions will be discussed in detail in this review, especially since confusion in their diagnoses can result in inappropriate clinical management. For the most part treatment considerations will not be discussed.

Contact ulcer

A contact ulcer in the larynx is considered to be a benign, somewhat tumor-like condition [19, 23, 26, 27]. This has also been described as a pyogenic granuloma and occurs most commonly along the posterior aspect of the vocal cords. This lesion is found most frequently in adult males

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and generally presents clinically with symptoms of sore throat, hoarseness and dysphagia. In some cases the lesion can be present for a number of years, especially in patients with gastroesophageal reflux disease due to regurgitation of gastric acid that is otherwise asymptomatic. In individuals who are public speakers or demonstrate vocal abuse, the nature of vocal cord lesion can be suggested by clinical history. In contrast, acid regurgitation commonly occurs while the patient is asleep, resulting in gastric fluid destroying the mucosal lining of the larynx during a period when patients are unaware of what is happening. As such, clinicians will need to elicit a careful history as well as perform appropriate studies [14]. Even so, documentation may be difficult.

An endoscopic view will demonstrate primary involvement of the posterior vocal cord, although advanced lesions can occur anywhere in the glottis. The actual appearance of the lesion can be bullous and in certain cases can almost completely obliterate the endolaryngeal lumen. In our experience gross endoscopic findings are very similar to findings of pyogenic granuloma in the nasal cavity.

The gross specimen of a contact ulcer is generally ulcerated, polypoid, nodular or fungating and can reach up to about 3 cm in maximum dimension. The surface will have a fibrinoid-type of necrosis covering an underlying granulation tissue that shows the full spectrum of both acute and chronic inflammatory elements (Fig. 1A). After the lesion has been present for a certain length of time, surface re-epithelization may develop from the immediately surrounding epithelium that was not involved by the lesion itself. With complete re-epithelization of the surface, a lesion may appear as if it is actually a keratotic or hyperplastic mucosal lesion that can be misconstrued as a preneoplastic or neoplastic epithelial lesion when in fact it is only a reactive condition (Fig. 1B).

Low-power light microscopy often demonstrates small fragments of epithelium at the lesion's periphery. The bulk of the lesion is composed of fibrinoid necrosis, which almost completely covers the surface of the polypoid structure (Fig. 1A). High-power examination (300–400× magnification) will illustrate reactive, plump endothelial cells lining vascular spaces. These spaces are often filled with red blood cells, with background acute and chronic inflammatory elements as well as myofibroblastic spindle cells (Fig. 1B and C).

The changes identified in contact ulcers can occur in other lesions resulting from reactive or neoplastic processes. Without appropriate clinical information noting a history of vocal abuse or possible acid regurgitation, the histologic appearance seen by a pathologist can be described as reactive granulation tissue or another equally non-specific diagnosis, while ignoring the diagnostic appellation of contact ulcer. Since an infectious agent can also be the etiologic cause of a similar histologic reaction, appropriate cultures may be required in addition to special histochemical or immunohistochemical studies in ruling out an infectious organism.

Fig. 1 **A** Surface epithelial ulceration of the vocal cord with fibrinoid necrosis covering a granulation-type tissue with inflammatory elements (hematoxylin and eosin stain, × 15). **B** Surface re-epithelization overlying the spindle cell proliferation in the granulation tissue of a vocal cord lesion. Hemorrhage and inflammatory cells are noted (hematoxylin and eosin stain, 150). **C** Contact ulcer of vocal cord. Numerous vascular channels are lined by plump, reactive endothelial cells, filled with blood, and surrounded by spindle cells and inflammatory cells (hematoxylin and eosin stain, × 150)

A spindle squamous cell carcinoma must also be included in the differential diagnosis of a contact ulcer, especially in cases in which the spindle cell component is somewhat atypical (as later discussed). A lobular capillary hemangioma is often used synonymously with pyogenic granuloma, and there is a similarity in histologic appearance. However, the lobular arrangement of a capillary hemangioma is not usually found in a contact ulcer. Considering that a hemangioma is a neoplasm, and a contact ulcer is a reactive condition, an etiologic distinction is important. Surgical excision will cure a hemangioma, but surgical excision alone without treating an underlying etiologic cause of a contact ulcer may result in recurrence and unnecessary repeated surgeries. Mucosal Kaposi's sarcoma is increasing in frequency in patients with acquired immune deficiency syndrome (AIDS), but it is still an infrequent neoplasm in the larynx or nasal cavity. As such, histologic criteria should be used to first exclude a contact ulcer. Similarly, angiosarcoma is sufficiently rare in the mucosal surfaces of the head and neck as to warrant only a catalogue entry in the differential diagnosis [26, 27].

Spindle cell squamous cell carcinoma (carcinosarcoma)

A sarcomatoid carcinoma or spindle cell carcinoma is thought to represent a conventional squamous cell carcinoma that has undergone a transformation or dedifferentiation into a malignant spindle cell histomorphology. The stromal component is usually identified deep to the mucosal surface, which can be ulcerated. A number of different names have been applied to this tumor, including carcinosarcoma, metaplastic carcinoma, "collision tumor" and the eponymic "Lane tumor" [2, 3, 7, 16, 21].

The tumor usually presents clinically in the 6th to 8th decades of life in male patients and can occur anywhere in the upper aerodigestive tract. The tumor presents most frequently in the oral cavity, followed by the true vocal cord. The presenting symptoms invariably match the anatomic location, with a mass lesion, hoarseness, dysphagia and airway obstruction the most frequent findings. Although an etiologic relationship with alcohol and tobacco use is well established for squamous cell carcinoma in general, no other risk factors have been identified in the development of a spindle squamous cell carcinoma [3, 12, 21].

The tumor is usually seen clinically as a polypoid mass, often with surface ulceration (Fig. 2A). The gross appearance can be quite variable, but the cut surface is usually gray-white to tan and has a firm or gritty texture. The histologic appearance depends upon the size of biopsy taken and the extent of surface ulceration. A dysplasia, carcinoma in situ or an invasive squamous cell carcinoma may be identified in the specimen. Careful examination is necessary to identify the squamous component which may be extremely limited or can be very poorly differentiated. If the surface component is present, malignant spindle cells can be seen invading from the basal layer,

with spindle cells composing the dominant histologic picture (Fig. 2B). There is often an imperceptible blending of the overlying epithelium with the stroma, eliminating a clear-cut epithelial to stromal junction. The spindle cell constituent varies from remarkably bland to markedly pleomorphic, arranged in a fascicular, pin-wheel, storiform or palisaded growth pattern (Fig. 2C). There is usually a marked increase in cellularity, although the deposition of a dense, collagenized stroma can obscure the malignant cells. Individual cells are usually spindle-shaped, with scant to abundant eosinophilic to amphophilic cytoplasm surrounding vesicular to hyperchromatic nuclei with variably present nucleoli. There is a very vague epithelioid appearance to the cells, but this feature is difficult to quantify. Mitotic activity is frequently brisk, with atypical forms easily identified. Necrosis can also be seen (Fig. 2D). Heterologous elements, such as cartilage or bone, can be present that may also become malignant, possibly creating a true malignant mixed tumor.

Immunohistochemical reactions can be used to help define the nature of the spindle cell component. While keratin will confirm the epithelial differentiation of the tumor (Fig. 2E), many of these tumors are so completely transformed that the expression of tonofilaments and other epithelial markers is completely lost. Therefore, a negative immunohistochemical reaction for keratin does not exclude the diagnosis.

The principle lesions to be differentiated from spindle cell carcinomas are other spindle cell neoplasms. Nodular fasciitis and fibrous histiocytoma do not usually have surface epithelial involvement, nor do they ulcerate. Although the histologic pictures of both latter lesions may include mitotic figures, no atypical forms occur. Both of these lesions are also extremely rare in the larynx. When present, each will demonstrate an immunohistochemical profile of mesenchymal lesions (i.e., no keratin or epithelial membrane antigen reactions).

A mucosal malignant melanoma (or a metastatic melanoma) can present with a surface component in addition to the spindle cell architecture. However, the overall growth pattern, intranuclear cytoplasmic inclusions, melanin pigment and S-100 protein and/or HMB45 immunopositivity will help to exclude this possibility [7]. Malignant fibrous histiocytoma (MFH), fibrosarcoma and synovial sarcoma can be included in the differential diagnosis of malignant spindle cell tumors, but are very uncommon in the larynx. If an MFH or fibrosarcoma does occur in this location, they are deeply seated lesions and do not usually ulcerate. There is also no connection to the surface epithelium and any immunoprofile would be different from a spindle squamous cell carcinoma. Metastatic foci from a spindle squamous cell carcinoma will frequently exhibit cell components of both squamous carcinoma and spindle cell carcinoma but without heterologous elements. If squamous cell carcinoma is present in a lymph node and only a spindle cell neoplasm is identified in the larynx, it probably represents an earlier manifestation of the carcinoma prior to de-differentiation.

Fig. 2 **A** Spindle cell carcinoma of larynx. Polypoid mass with small areas of surface epithelium visible in an otherwise denuded surface. Areas of spindle cell proliferation are identified in the stroma (hematoxylin and eosin stain, $\times 12$). **B** Spindle cell carcinoma. A small portion of dysplastic surface epithelium is seen on the left, while most of the tumor is composed of spindle cells, including atypical mitotic figures (hematoxylin and eosin stain, $\times 150$). **C** Spindle cell carcinoma. Bland-appearing spindled to epithelioid cells arranged in a haphazard growth pattern (hematoxylin and eosin stain, $\times 300$). **D** Spindle cell carcinoma. Marked nuclear pleomorphism with necrosis and mitotic figures (hematoxylin and eosin stain, $\times 300$). **E** Spindle cell carcinoma. Focal reactivity of the cytoplasm in neoplastic cells with keratin antibody (immunohistochemical keratin reaction, $\times 150$)

Verrucous squamous cell carcinoma

There has been considerable debate in the literature over the years regarding the nature of verrucous squamous cell carcinoma [8, 15, 18, 24]. Classically, these tumors are described as a highly differentiated variant of squamous cell carcinoma. The tumor in general tends to be more locally destructive than metastatic, but these findings would be expected with any very well differentiated tumor. This tumor type represents only about 1–5% of laryngeal carcinomas [8, 15, 24]. This tumor usually presents in men in the 6th to 7th decades of life and is more common in the oral cavity than in the larynx.

The clinical symptoms of this tumor duplicate those of any mass lesion in the larynx. The tumor is most frequent in the glottis. Various epidemiologic studies have shown there is an association with tobacco and human papilloma virus (HPV) [1, 15].

The clinical size of a lesion is often important in its definition, especially when separating verrucous hyperplasia from ordinary squamous cell carcinoma. The extent of any tissue destruction and the overall size of a lesion need to be conveyed to the pathologist, especially if the entire lesion is not able to be excised in toto.

The histology of the tumor demonstrates a broad pushing border of infiltration with a rich chronic inflammatory cell infiltrate (Fig. 3A). The rete pegs are slightly expanded

Fig. 3 **A** Verrucous carcinoma of larynx. Broad, pushing infiltration with inflammatory cells in the underlying stroma (hematoxylin and eosin stain, $\times 250$). **B** Verrucous carcinoma of larynx. Church-spire type keratosis with a bland cytologic appearance (hematoxylin and eosin stain, $\times 75$). **C** Verrucous carcinoma of larynx. Bland cytologic appearance with only slight nuclear enlargement and maturation towards the surface. Mitotic activity is inconspicuous (hematoxylin and eosin stain, $\times 150$)

Fig. 4 **A** Squamous papilloma demonstrating an exophytic growth pattern and fibrovascular cores (hematoxylin and eosin stain, $\times 30$). **B** Pseudoepitheliomatous hyperplasia with numerous islands of benign-appearing squamous epithelium. Squamous pearls are noted. This is a case of granular cell tumor, with the background cells containing small eosinophilic granules (hematoxylin and eosin stain, $\times 75$). **C** Papillary growth pattern in a squamous cell carcinoma. Comedo-type necrosis, marked nuclear pleomorphism and atypical mitotic figures are identified (hematoxylin and eosin stain, $\times 75$)

and are covered by a "church-spire" type keratosis with a bland cytologic appearance (Fig. 3B). The cells usually show a subtle disorganization, without a loss of maturation towards the surface or a loss of polarity. There is generally only a slightly increased nuclear to cytoplasmic ratio, inconspicuous nucleoli and an almost complete absence of mitotic activity (Fig. 3C). There may be a slight variability from one area to another within the tumor, but the overall histologic appearance is that of a benign growth.

In determining histopathology it is most important to be cautious about tangential sectioning, as this can give the impression of fingers of infiltration occurring in a papillomatous benign lesion rather than the broad based invasion seen in a verrucous squamous cell carcinoma. Thus, it is important to have a good perpendicular 90° angle to the cutting surface of any tissues sectioned.

The differential diagnosis includes squamous papilloma, keratosis, verrucous hyperplasia and pseudoepitheliomatous hyperplasia. A squamous papilloma usually has a narrow base, tends to lack keratosis and contains fibrovascular cores. There can also be a considerable degree of atypia (Fig. 4A). True verrucous hyperplasia exists, but may be difficult to prove. Although there may be a continuum from hyperplasia to verrucous carcinoma to well-differentiated squamous cell carcinoma, the distinction between each rests upon clinical information, especially related to the destructivity of the tumor. Pseudoepitheliomatous hyperplasia (PEH) histologically shows multiple finger or tongue-like projections into the underlying stroma, but there is generally only reactive atypia and no true dysplasia (Fig. 4B). PEH is usually associated with reactive conditions or infectious processes but can also be found in granular cell tumors or squamous cell carcinomas.

It is important to realize that a papillary or verrucous growth pattern can be seen histologically in a well-differentiated squamous cell carcinoma [25]. Although this latter tumor can have a verrucous or papillary growth, there is often considerable cytologic atypia, loss of polarity, epithelial disorganization and mitotic activity (Fig. 4C). Certain of these tumors can have a fibrovascular stalk containing multiple papillary or filiform fronds due to their unique growth patterns.

Verrucous carcinomas are believed by some clinicians to have a poor response to radiation therapy, as can occur with other well differentiated squamous cell tumors. Although some lesions have undergone dedifferentiation into more poorly differentiated tumors, this same phenomenon has been identified in other squamous cell carcinomas. Some verrucous carcinomas metastasize, but this occurs infrequently in actual practice due to the very well differentiated nature of the tumor and the limited degree of tissue invasion present. Tumors recur if incompletely excised. Since there can be difficulties in accurate histologic classification, multiple biopsies of multiple areas repeated over time may be necessary to achieve a correct diagnosis.

Angiocentric T-cell lymphoma of the sinonasal tract

Angiocentric T-cell lymphoma has been associated with as much controversy as spindle cell carcinoma and verrucous carcinoma. The exact nature and extent of the disease has been completely misunderstood, as typified by the various names used to encompass the disorder. These have included but are not limited to lethal midline granuloma, Stewart's granuloma, polymorphic reticulosis and atypical lymphoid hyperplasia [4, 6, 10, 11, 13, 17]. All of these disease entities represent a variation within the spectrum of what can be seen in malignant lymphoma, either T/NK- or B-cell immunophenotype malignant lymphomas, or in the Oriental or Western subtypes. This lesion is a neoplastic lymphoid proliferation that has a polymorphous composition of inflammatory elements in its early stage, in addition to atypical lymphoid cells. Lesions progress in later stages to a monomorphous (and monotypic) cellular population, often centered around blood vessels, causing local tissue destruction and ulceration. Destruction and infiltration around mucoserous glands can be seen.

Clinically, a lesion can present in any site in the upper aerodigestive tract and is frequently bilateral. Although it is most common in men in the 5th to 7th decades of life, it can occur at any age (as expected with malignant lymphoma). The patient will often present initially with nasal obstruction or discharge, progressing over time to facial swelling and ultimately producing significant tissue destruction. The disease can extend into the nasopharynx, orbit or base of the skull. As with any lymphoma, systemic manifestations are frequently present [4, 6, 10, 11, 13, 17].

The microscopic appearance is quite variable, depending upon the stage of development of the disease. In the early stage, there is a subepithelial population of a polymorphous cellular infiltrate which is composed of lymphocytes, histiocytes, immunoblasts, and plasma cells, as well as possible eosinophils or acute inflammatory elements. Due to the remarkable diversity of the infiltrate, the atypical lymphoid elements that are interspersed throughout the lesion are often missed and can be obscured by the rest of the cells. Unfortunately, the size of the biopsy and the cellular diversity of the infiltrate present may not immediately bring to mind the diagnosis of a malignant lymphoma [4, 6, 10, 11, 13, 17]. Immunohistochemical reactions are not helpful during the early stages of development, since the number of atypical cells is small. Overall immunohistochemical results will demonstrate a polymorphic population. However, as the disease progresses, atypical cells will begin to predominate, surrounding vessels (angiocentricity) or invading vessels to cause obstruction and infarction (angioinvasive). The atypical lymphocytes have enlarged nuclei, vesicular to hyperchromatic nuclear chromatin, irregular nuclear contours, uneven distribution of the nuclear chromatin and occasional nucleoli. There is usually scant cytoplasm surrounding these atypical nuclei. Mitotic activity is particularly prominent in the later stages of the disease (Fig. 5).

Fig. 5 Angiocentric T-cell lymphoma containing atypical lymphoid cells with increased nuclear to cytoplasmic ratio, nuclear chromatin condensation and nuclear contour irregularities. Mitotic figures are identifiable (hematoxylin and eosin stain, $\times 300$)

Fig. 6 Wegener's granulomatosis showing vasculitis, necrosis, foreign-body-type giant cells and epithelioid histiocytes in loose granuloma formation (hematoxylin and eosin stain, $\times 150$)

Fig. 7 **A** Papillary growth filling a cystic space of a lymph node that has been replaced by metastatic squamous cell carcinoma of tonsillar origin (hematoxylin and eosin stain, $\times 24$). **B** Ribbon-type growth lining a cystic space, composed of a neoplastic squamous epithelium infiltrating into the underlying lymphoid stroma. Nuclear variability can be seen along with mitotic figures (hematoxylin and eosin stain, $\times 150$). **C** Disorganized growth with limited maturation, loss of polarity and atypical squamous cells identified within a metastatic squamous cell carcinoma from the tonsil (hematoxylin and eosin stain, $\times 240$)

Although most of the atypical lymphocytes are of a T-cell phenotype ("Oriental type"), malignant lymphomas of a B-cell phenotype ("Western type") can be seen in the nasal cavity as well [4]. The B-cell phenotypes tend to be less angioinvasive and less angiodestructive, but this is often a subjective finding.

The differential diagnosis for this tumor includes a variety of non-specific inflammatory disorders, Wegener's granulomatosis, Churg-Strauss syndrome (allergic granulomatosis and angiitis), granulomatous inflammation and other types of malignant tumors [22]. Non-specific inflammation is the most frequently misdiagnosed lesion in this area, principally in the earlier stages of the disease.

However, careful examination combined with the clinical information of a destructive lesion with systemic symptoms should help to avoid an incorrect diagnosis. Wegener's granulomatosis does not contain atypical lymphoid cells, but will demonstrate a certain angiocentricity, especially with active vasculitis, foreign body type giant cells and vague granuloma formation (Fig. 6). Pulmonary disease and glomerulonephritis are common findings. Churg-Strauss syndrome can have associated nasal polyposis and pulmonary findings. Poorly differentiated squamous cell carcinoma and olfactory neuroblastoma can be included in the differential diagnosis, but the overall growth pattern, the lack of inflammatory ele-

ments and the immunohistochemical reaction patterns will help to exclude these tumors.

Cystic squamous cell carcinoma in the neck

On occasion a neck biopsy will uncover a squamous cell carcinoma in a mass lesion associated with lymphoid elements. A question then arises if this finding represents a branchial cleft cyst in which a carcinoma has developed or if the lesion represents a metastatic squamous cell carcinoma. The distinction is important in order to treat a primary tumor and to avoid unnecessary therapy [5, 9, 20].

These lesions most frequently occur in men in their 5th through 7th decades of life, although many tumors can present earlier. Patients frequently present with an enlarging, non-tender mass in the lateral neck, which is often located high in the anterior cervical triangle. Patients may have symptoms for as short as a few days to as long as many years. There is generally no antecedent event.

To date, we have obtained follow-up of 136 cases of cystic squamous cell carcinoma in the neck that were accessioned to the Armed Forces Institute of Pathology (AFIP) tumor registry. Of this group, 87 had primary cancers located in the base of the tongue, lingual or faucial tonsil areas (involving Waldeyer's ring). Eleven primaries were discovered in the nasopharynx and an additional 11 were found in other sites in the upper area of the aerodigestive tract, including the sinuses, palate or larynx. Twenty-seven cases have not yet had a primary tumor discovered. When primary neoplasms were found, this occurred at any time from the day of presentation up to 132 months later. Those tumors discovered the same day were found in patients treated by surgeons who did not believe that a cystic squamous cell carcinoma in the neck represented a primary branchial cleft carcinoma, but instead involved metastatic disease. The mode time for finding a primary tumor was 1 month, and this involved the turnaround time required to submit a case to the AFIP, evaluate carefully all tissue and then send back a report identifying the tumor type and the extent of work-up needed to find the primary. In all, tumors were discovered throughout the entire 132-month time frame from the day of initial presentation without a period in which no tumors were discovered. In other words, the interval to discovery did not stop with a possible "second" primary discovered later, but instead there was a continuous slope towards the longest interval to discovery. Given the number of cases discovered after a 60-month cut-off, it is important to stress the need for long-term follow-up in these patients. These findings also solidify the clinical impression of metastatic tumor causing squamous cell carcinomas in the neck and not a primary branchiogenic carcinoma.

Grossly, tumors were usually large, cystic structures expanding the size of the structure removed. Although the lymphoid component may be obscured, the intimate association with lymphoid elements in a number of cases should identify the site as a lymph node (and most fre-

quently involved a jugulodigastric node). The cyst was duplicated on histology, but the cyst was generally not filled with anything. There was generally no keratinaceous debris, no inflammatory elements nor blood. There was also usually no comedo-type necrosis. If a comedo-type necrosis was found, the primary tumors did not commonly originate in tissue from Waldeyer's ring. When cystic spaces are lined by an endophytic-type growth into underlying stroma or lymphoid elements or a papillary growth pattern, this recapitulated the growth pattern seen in tonsillar tissue with squamous crypt epithelium (Fig. 7A, B). In such cases, the neoplastic epithelium is arranged in a ribbon-type of configuration, has a uniform thickness and is composed of a generally bland appearing transitional type epithelium (Fig. 7B). A spectrum of histologic appearances can be identified, with some areas demonstrating an increased nuclear to cytoplasmic ratio, no surface maturation and loss of polarity. The overall appearance is not of an anaplastic or poorly differentiated epithelium, but instead can be almost identical to tonsillar crypt epithelium (Fig. 7C). Because the epithelium is so well differentiated, it is not difficult to see why a clinician can conjecture a squamous cell carcinoma arising in a branchial cleft cyst.

Several lesions can be confused in the differential diagnosis of a cystic cervical squamous cell carcinoma. These include a branchial cleft cyst, papillary carcinoma of thyroid origin metastasizing to a lymph node, a thymic cyst and a cystic hygroma. A true branchial cleft cyst usually has an epithelium that is not very thick, is generally without nuclear atypicality, is filled with keratinaceous debris, has no mitotic figures and demonstrates an intimate investment by inflammatory cells. Clearly there is a somewhat arbitrary and subjective component to this distinction, which can vary from case to case. However, the features of carcinoma will generally be obvious with careful examination. The growth pattern and composition of the cells are rather characteristic for a metastatic papillary thyroid carcinoma. The cells are arranged in papillary fronds or small follicles or line a cystic cavity, with colloid present in a number of foci. The nuclei are enlarged and there is an increased nuclear-to-cytoplasmic ratio. The nuclei also have irregular nuclear contours and can show nuclear grooves, chromatin clearing, nuclear membrane accentuation and nuclear overlapping. There are no features of squamous differentiation. A thymic cyst will demonstrate small foci of squamous pearl formation duplicating Hassall's corpuscles and can be associated with lymphocytes and often with adipose tissue. Cystic spaces are generally lined by a benign squamous epithelium. The possibility of a thymic carcinoma or thymoma in this setting should also be excluded, but these would be extraordinary events. A lymphangioma is a lateral neck lesion, but the vascular lined spaces are filled with lymph or serum and are completely different from a metastatic squamous cell carcinoma.

In our experience, the prognosis for primary cancers found in regions other than Waldeyer's ring or base of tongue has been dismal, while that for lesions found in Waldeyer's ring or for patients in whom a primary tumor

was not found, tended to be much better when treated with surgical excision of known primary tumor and adjuvant radiation therapy (to 600 Gy).

Of the 87 patients having primaries found in Waldeyer's ring area, tumors had a fairly distinctive histologic appearance that was different from those tumors found in the nasopharynx or other areas of the upper aerodigestive tract. This was similar to the patients who never had primaries found, while these later patients may well represent a similar patient population group. In many of the patients in whom a primary was found in the Waldeyer's ring region, the primary tumor was extremely small and was often less than 0.5 cm in maximum dimension. With tumors this small, it is not difficult to see how these can grow for a prolonged period of time without being discovered. Since the lymphoid tissue of the tonsil is involved in immune regulation and is constantly being bombarded by immunologic insults from the external environment, it is possible that it is so efficient in eliminating "foreign" material that a tumor a few millimeters in size may actually be destroyed by its lymphoid elements or even be completely eliminated prior to discovery. Alternately, the lymphoid component may just be sufficient enough to keep a tumor in check through immunologic mechanisms. Thus, radiographic imaging, pan-endoscopy, random biopsies or even tonsillectomy may not demonstrate a minute primary. As a consequence, a single section submitted from a biopsy specimen will not permit a tiny tumor to be detected. Obviously, when a lesion is of sufficient size to be detected, significant tumor may be present. The rich lymphatics present in the region of the tonsil will also account for early metastatic disease, especially to the jugulodigastric and upper cervical nodes as the closest lymph nodes.

Although one can never prove a "negative," for all practical intents and purposes, based on the findings in our study, it is best to think of a cystic squamous cell carcinoma in the lateral neck as a metastatic carcinoma and then try to document a primary site. If the primary is found, then appropriate management can be given. If it is not found, then perhaps prophylactic tonsillectomy followed by coned-down radiation ports (of appropriate clinical dose) would be in a patient's best interest. Again, close clinical follow-up is always necessary to exclude a primary lesion.

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ANNOUNCEMENTS

XXX Course on Temporal Bone Dissection 3-5 November 1997, Barcelona, Spain

Organized by Dr. Pedro Clarós (Hospital Universitari Sant Joan de Deu, Barcelona) and Prof. J.P. Bebear (University of Bordeaux II)

For further information, please contact: Clinica Clarós, Los Vergós, 31, E-08017 Barcelona, Spain; Tel.: (3) 203.12.12, Fax: (3) 280.33.32

8th International Course in Endonasal Sinus Surgery 1-4 December 1997, Bochum, Germany

For further information, please contact: Dr. H. Luckhaupt, ENT-Department, St. Elisabeth-Hospital, Bleichstraße 15, D-44787 Bochum, Germany; Tel.: 02 34/61 22 82, Fax: 02 34/61 22 79

Asia-Pacific Head and Neck Cancer Congress 11-14 December 1997, Bombay, India

Sponsored by International Federation of Head and Neck Oncologic Societies and Indian Society of Head and Neck Oncology

For further information, please contact: Dr. Ashkok Mehta, Chairman, Asia-Pacific Congress, Tata Memorial Hospital, Dr. E. Borges Road, Parel Mumbai - 400012, India; Tel.: 91-22-414-6750, Fax: 91-22-414-6937, e-mail: medimail@tmc.ernet.in

International Symposium on Metastases in Head and Neck Cancer 15-18 January 1998, Kiel, Germany

Chairman: Prof. Dr. H. H. Rudert, Kiel

For further information, please contact: PD Dr. J. A. Werner, Dr. B. M. Lippert, Department of Otorhinolaryngology, Head and Neck Surgery, University of Kiel, Arnold-Heller-Str. 14, D-24105 Kiel, Germany; Tel.: +49-431-597-23 21, Fax: +49-431-597-2272, E-mail: j.a.werner@t-online.de

Course on Education and Rehabilitation of Cochlear Implant 21 February 1998, Barcelona, Spain

Organized by Dr. Pedro Clarós and Dr. Andrés Clarós

For further information, please contact: Clinica Clarós, Los Vergós, 31, E-08017 Barcelona, Spain; Tel.: (3) 203.12.12, Fax: (3) 280.33.32

XXXI Course on Temporal Bone Dissection 20-22 April 1998, Barcelona, Spain

Organized by Dr. Pedro Clarós (Hospital Universitari Sant Joan de Deu, Barcelona) and Prof. J.P. Bebear (University of Bordeaux II)

For further information, please contact: Clinica Clarós, Los Vergós, 31, E-08017 Barcelona, Spain; Tel.: (3) 203.12.12, Fax: (3) 280.33.32

European Consensus Development Conference (ECDC) on Neonatal Hearing Screening 15-16 May 1998, Milan, Italy

For further information, please contact: Dr. F. Grandori, Centre of Biomedical Engineering, Polytechnic of Milan, Piazza Leonardo da Vinci 32, I-20133 Milan, Italy; Fax: +39-2-23993360, e-mail: ecdc@elet.polimi.it

Politzer Society Annual Meeting integrated with Mediterranean Society of Audiology and Otology Meeting 8-11 June 1998, Antalya, Turkey

For further information, please contact: O. Nuri Ozgirgin, Chairman, Baymdir Medical Center, 06520 Ankara, Turkey; Fax: 90-312-2850733, e-mail: ozgirgin@neuron.ato.org.tr, web page: <http://www.ato.org.tr/home/ozgirgin>

Combined meeting of the European Rhinologic Society and the International Symposium on Infection and Allergy of the Nose (ERS & ISIAN) 28 July-1 August 1998, Vienna, Austria

For further information, please contact: The Scientific Secretariat, 17th ERS and ISIAN Meeting, H. Stammberger, Department of General ENT, Head and Neck Surgery of the University Medical School, Auenbruggerplatz 20, A-8036 Graz, Austria; Fax: ++43-316-385-3425