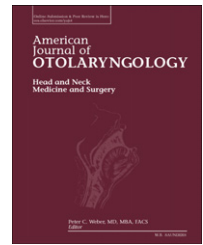


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Current review

Collision tumors of the larynx: A critical review ☆, ☆, ☆, ☆



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ABSTRACT

Problems related to definition of collision tumors are briefly examined in conjunction with etiology and natural history. Examples of genuine collision tumors in larynx are rare in the literature and are herein identified and tabulated. Aspects related to diagnosis and therapeutic strategies are also explored.

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1. Introduction

Coexistence of two morphologically distinct tumors in the same anatomical area is an example of double pathology and established in the literature. When the coexisting tumors become contiguous without admixture at their interface, a “collision” tumor develops. Although often regarded as clinical and/or pathological curiosities, collision tumors may result in diagnostic and therapeutic difficulties. Due to a lack

of characteristic clinical features, they are difficult to diagnose prior to representative biopsy or surgical resection. Diagnosis is based on routine histology though immunohistochemistry and other ancillary studies may be of help. Ratios between the morphologically distinct components of a collision tumor may increase difficulties, particularly when the inherent errors in sampling tissues are considered. For instance, a prominent/large benign tumor may overshadow any contiguous inconspicuous/small malignancy. Collision

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tumors have been reported in many areas of the human body, including head and neck where thyroid examples seem established [1]. Less attention has been paid to collision tumors of the larynx and the present review aims to explore controversies in their diagnosis and treatment implications. The latter seem of particular significance in larynx, where concerns about organ and function preservation influence therapeutic strategies.

2. Definition

“Collision tumors” are variously defined in the literature and a consensus may be difficult to achieve. Meyer’s classical definition [2], which regards a “collision tumor” as the meeting and eventual intermingling of two malignant neoplasms arising at independent topographical sites, seems satisfactory. Clarification is, however, needed as what is meant by “independent” topographical sites and the definition should be expanded to include benign tumors as a contiguous component. Later, Dodge [3] suggested that “in order to accept a tumor of mixed structure as a collision tumor, the concrescence of two independently-arising neoplasms, there should be separated tumor areas of two quite distinct histological patterns and, if both types of tumor metastasize, the two types of growth should be clearly separated in the metastasis also. Furthermore, there should be no areas of transitional pattern, intermediate in structure between the two types of tumor.” Spagnolo and Heenan [4] endorsed the notion of distinct, topographically separate, though not obligatorily distant (see below), sites of origin for the two components; they also emphasized that in spite of intimate mixing at the point of juxtaposition, the two components should preserve at least some degree of separation. However, the latter definition allows for transitional areas to be seen at the juxtaposition. For metastases, the same criteria would be applied.

Collision tumors may be composed of two primary tumors originating from the same organ, or a primary tumor and a metastasis. They should be distinguished from tumors that although show phenotypic differentiation suggestive of different cell lineages, they actually arise from a common ancestor [5]. Carcinosarcomas do not qualify as collision tumors and are a typical example. Although they show an epithelial component corresponding to squamous cell carcinoma and a mesenchymal component of sarcomatoid appearances, it is likely that the latter derives via epithelial-mesenchymal transition or “dedifferentiation” of the former [6].

At an early, “pre-collision” stage, two adjacent tumors of distinct morphology may be separated by a limited, though precisely undefined, zone of normal tissues and dual, non-colliding carcinomas are a typical example. With continuous growth such tumors would be expected to collide and eventually intermingle, though frank transition is lacking [4].

3. Etiology

Several hypotheses have been considered. Firstly, two primary tumors fortuitously develop in the same location. Secondly, two morphologically distinct tumors may develop contiguously

because the region is affected by the same carcinogenic factor, for example radiation. Thirdly, the presence of the index tumor may alter the microenvironment, allowing thus a second, primary or metastatic, contiguous tumor to develop or successfully anchor therein, respectively [7].

Particular collision tumors appear more common than others; for instance, gastric adenocarcinoma with lymphoma [8] or hepatocellular carcinoma with cholangiocarcinoma [9]. Collision thyroid tumors have already been mentioned. They include combinations of papillary and/or follicular with medullary carcinoma [10–13], though the possibility of a common cell of origin cannot be excluded.

In the larynx, squamous cell carcinoma has been reported in combination with melanoma [14], thyroid cancer [15], adenoid cystic carcinoma [16] or pleomorphic adenoma [17]. Metastases of squamous cell carcinoma in cervical lymph nodes affected by lymphomas/leukaemias [18,19] may be difficult to qualify as collision because those malignancies are rather intimately intermingled, which seems inconsistent with the requisite of initial contiguity.

4. Review of the literature

Collision tumors affecting the larynx appear rare. We undertook a literature search of the PubMed (including Medline) using the search strategy “collision tumor head neck” and “collision tumor larynx”. This identified 42 articles, which were hand-searched for pertinent articles. Their reference lists were also searched for additional cases. We excluded cases without a definitive diagnosis of collision tumor. To the best of our knowledge, only 7 cases reported in the literature satisfy strict criteria. Their clinicopathologic features are summarized in the Table [14–17,20,21] and in all cases the authors have interpreted the underlying pathology as “collision tumor”. Other observations [18,19,22–24] could be differently interpreted. For example, metastases of squamous cell carcinoma in cervical lymph nodes affected by lymphomas/leukaemias [18,19] could be regarded as cancer metastasizing in cancer; development of different phenotypic clones within the main mass or “satellite” tumor nodules should also be considered [22–24].

As squamous cell carcinoma is the most common primary laryngeal malignancy [25], it would be expected that it could combine with other tumors (adenoid cystic carcinoma, pleomorphic adenoma, malignant melanoma and papillary thyroid carcinoma) and effect the collision phenomenon.

5. Discussion

While secondary malignancies are relatively common among long-term survivors following treatment of the index tumor, collision tumors of the larynx are reported only sparsely in the literature. In terms of classification, collisions tumors need to be distinguished from a composite tumor, where two different histologic types are totally intermingled. For example, Gianoli et al. [26] published a case of a composite tumor described as a mixed squamous cell and oat cell carcinoma originated in the larynx.

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