The Reliability of Histopathologic Angiolymphatic Invasion in Mobile Tongue Squamous Cell Carcinoma

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Abstract

Objective: To determine the reliability of identifying angiolymphatic invasion in histopathologic specimens of mobile tongue squamous cell carcinoma (SCCa).

Introduction: Evidence of angiolymphatic invasion on histopathologic surgical specimens of head and neck SCCa is often regarded as an indicator for increased tumor aggressiveness and/or poorer prognosis. Adjuvant treatment (i.e., radiation therapy and/or chemotherapy) is oftentimes based in part on these findings. Trained head and neck pathologist, however, admit to sampling error of focus specimen and, specifically, difficulty in definitively identifying angiolymphatic invasion, thereby, questioning the reliability of angiolymphatic invasion in certain histopathologic specimens. Methods: Retrospective chart review identifying 15 patients with mobile tongue SCCa with evidence of "angiolymphatic invasion" on permanent histopathologic surgical specimen. Additional histologic specimens were obtained from each patients' original tumor block for additional review for angiolymphatic invasion.

Results: To date, data collection from 6 of 15 patients has been completed. Two of 6 patients' histologic sections showed a change in the absence/presence of angiolymphatic invasion upon further review, while 4 of 6 patients showed no change. Conclusion: Evidence, or lack thereof, of angiolymphatic invasion on histologic section may lack reliability even when examined by trained head and neck pathologists. Further studies must be performed to determine if additional histopathologic tests are necessary to confirm such findings.

Discussion

The presence of angiolymphatic invasion in head and neck SCCa continues to be viewed as a poor prognosticator. Such findings, may even lead to early stage tumors being treated with adjuvant treatment not typically recommended in the absence of such findings. This study does not aim to determine if angiolymphatic invasion is a poor prognosticator, but rather questions whether it can be reliably identified by experienced head and neck pathologists in the known setting of sampling error.

In our 6 patients studied to date, 4 of the patients' original tumor blocks were further examined and showed consistent evidence of angiolymphatic invasion. In addition, there was no change in the tumor block status for each specimen. Two of the six patients, however, did show changes. Patient #4 showed a loss of angiolymphatic invasion upon deeper sectioning of tumor blocks. Whereas originally, 2 of 5 sections were positive, subsequent review showed only 1 of 15 slides positive. Had 5 different slides been sectioned during the original read, the presence of angiolymphatic invasion may have been lost.

Patient #14 showed an increase in angiolymphatic invasion upon further tumor block sectioning. Areas of the tumor distant from the original slide showing angioinvasion were positive on later sectioning. This patient's report originally read, "microfocus of angioinvasion." Upon further review, however, angiolymphatic invasion was present much more than originally noted.

Based on our small patient base to date, it is difficult to determine if indeed a lack of reliability exists when labeling a tumor with angiolymphatic invasion. More importantly, it is difficult to determine if a lack of reliability would significantly affect treatment algorithms and survival. Further studies with larger numbers of patients would be needed to determine this.

Introduction

Histologic examination and ultimately the grading of tumors seeks to characterize the biologic behavior of neoplasms. Several studies aimed at identifying certain histologic traits as prognostic indicators in tumors of the thyroid, breast and colon note evidence of angiolymphatic invasion as a poor prognosticator. Likewise, similar studies examining and/or siting histologic indicators for increased tumor aggressiveness and poorer prognosis in head and neck squamous cell carcinomas note angiolymphatic invasion as such an indicator.

At our institution, evidence of angiolymphatic invasion on permanent histopathologic specimen, regardless of tumor stage, warrants discussion at a multidisciplinary tumor board with head and neck surgeons, pathologists, radiation oncologists and medical oncologists. Based on these findings, adjuvant treatment (i.e., radiation and/or chemotherapy) is often recommended. Similarly, a recent study by Argiris et al. noted angiolymphatic invasion as a "highrisk histopathologic feature and warranted inclusion in a study examining the role of single agent carboplatin in addition to radiation for adjuvant treatment for head and neck SCCa."

Unfortunately, it is oftentimes difficult to definitively label angiolymphatic invasion to a tumor specimen during histologic analysis for several reasons related to artifact, cell flattening, and section sampling error. To the authors' knowledge, no study to date examines the reliability of angiolymphatic invasion in histologic specimens. This study, therefore, aims to test the reliability of histologic angioinvasion in mobile tongue SCCa and determine if changes in "finals reads" occur upon further review.

Methods

A database of head and neck cancer patients from the Cleveland Clinic between 2003-2007 was queried with specific criteria including: mobile tongue, SCCa, non-T4, primary tumor, primary surgery, angiolymphatic invasion. Fifteen patients were identified meeting the above criteria. Retrospective chart review was performed collecting demographic data, TNM tumor stage, adjuvant treatments, disease free survival (DFS) and overall survival (OS). Subsequently, original tumor blocks were re-sectioned looking for the presence or absence of angiolymphatic invasion. Each original slide was examined to confirm the original read, and subsequently three additional sections were obtained from each tumor block (e.g., One surgical specimen originally may have 3 blocks of preserved tumor with one slide from each block. Subsequent analysis in most cases involved obtaining 3 additional slides from each block for a total of nine new slides requiring review). All histologic analysis was done by one head and neck pathologist in a non-blinded fashion.

This study was approved by the Cleveland Clinic IRB protocol # 07-186.

Table 1: Presence / Absence of Angiolymphatic Invasion

<table>
<thead>
<tr>
<th>Patient #</th>
<th>Original Slides (all slides / total)</th>
<th>Study Slides (all slides / total)</th>
<th>TNM</th>
<th>Adjuvant Treatment</th>
<th>DFS (yr)</th>
<th>OS (yr)</th>
<th>Alive</th>
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<td>2 out of 2 / 5</td>
<td>2 out of 3 / 5</td>
<td>T2N2Mo</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
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<td>2</td>
<td>2 out of 5 / 15</td>
<td>1 out of 15 / 5</td>
<td>12kM</td>
<td>None</td>
<td>5.4</td>
<td>5.4</td>
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<tr>
<td>3</td>
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<td>3 out of 9 / 9</td>
<td>T2NM</td>
<td>XRT + CTx</td>
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<td>1.8</td>
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</tr>
<tr>
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<td>3 out of 12 / 12</td>
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<td>2</td>
<td>Yes</td>
</tr>
<tr>
<td>5</td>
<td>1 out of 12 / 9</td>
<td>3 out of 9 / 9</td>
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<td>XRT + CTx</td>
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<td>2</td>
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<td>9 out of 21 / 21</td>
<td>T2kM</td>
<td>None</td>
<td>3.7</td>
<td>3.7</td>
<td>No</td>
</tr>
</tbody>
</table>

Figure 1: Patient 10 Unequivocal angiolymphatic invasion

A focus of unequivocal angiolymphatic invasion with endothelial cells covering the tumor (arrows) (H&E section, 400x).

Figure 2: Patient 14: Equivocal angiolymphatic invasion

There is a space next to the carcinoma with some flattened cells (arrows) of the periphery. On routine H&E-stained sections it is difficult to determine if this space is truly a endothelial-lined vessel or merely a retraction artifact with adjacent fibrinoid (H&E section, 400x).

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References


Figure 3b: Patient 14: Gain of unequivocal angiolymphatic invasion

(a) On the original section a vascular lumen is occluded by carcinoma (H&E section, 200x); (b) the first deeper section shows a sinusus relationship between the vessel, possibly a small vein (black arrow), and the carcinoma (white arrows) (H&E section 100x); (c) a deeper (approximately 100 microns) section no longer shows a connection between the vessel (black arrow) and the carcinoma (white arrow) (H&E section, 100x).

Figure 4b: Patient 14: Gain of unequivocal angiolymphatic invasion

(a) The initial section demonstrates carcinoma with perineural invasion (arrows), but no angiolymphatic invasion (H&E section, 200x); (b) a deeper section now shows angiolymphatic invasion with carcinoma attached to the vessel wall (arrow) in this area (H&E section, 200x).

Conclusion

Evidence, or lack thereof, of angiolymphatic invasion on histologic section may lack reliability even when examined by trained head and neck pathologists. Further studies must be performed to determine if additional histopathologic tests are necessary to confirm such findings.