Outcome of Observing the N0 Neck Using Ultrasonographic-Guided Cytology for Follow-up

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Objective: To assess the outcome of patients who underwent transoral tumor excision and a wait-and-see policy for the N0 neck, using ultrasonographic-guided fine-needle aspiration cytology (US-FNAC) of the neck for both selecting patients for neck treatment or observation and for follow-up.

Design: Retrospective outcome analysis of a patient cohort without palpable or US-FNAC detectable nodal metastases undergoing transoral tumor excisions. Patients were followed up for 1 to 4 years using palpation and US-FNAC.

Setting: Academic center.

Patients: A consecutive sample of 77 patients mainly with oral carcinomas. Excluded were patients who had neck dissections, radiotherapy, or no US-FNAC during follow-up.


Outcome Measure: The recurrence rate in the neck, without failure at the primary site and the salvage rate of these neck recurrences were the most important measures. Treatment delay and histopathologic findings were assessed as well.

Results: Fourteen patients (18%) had occult lymph node metastases and neck failures. Of the 14 neck failures, 9 were detected within 7 months of which 6 were not palpable. Ten (71%) of these 14 patients were successfully salvaged, and 4 died of uncontrolled disease. Three of the 4 patients also had distant metastases.

Conclusions: The low recurrence rate (18%) can be attributed to the initial US-FNAC. The high salvage rate (71%) indicates that strict US-FNAC follow-up enables early detection of recurrence in the neck. A wait-and-see policy thus seems warranted, provided regular US-FNAC examinations during follow-up can be guaranteed.


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PATIENTS AND METHODS

Seventy-seven patients treated by transoral tumor excision between 1991 and 1997 were studied. Inclusion criteria were that an initial ultrasonography showed no abnormalities or US-FNAC findings were negative, no elective neck dissection nor radiotherapy was performed and at least 1 follow-up US-FNAC was performed while no lymph nodes were palpable. Minimum follow-up was 1 year (mean follow-up, 31 months). Population consisted of 44 men and 33 women, with an average age of 61 years. Since 2 patients had 2 carcinomas, 79 squamous cell carcinomas were present: mobile tongue, 34; floor of mouth, 24; lip and buccal mucosa, 8; palate, 5; alveolar process, 3; oropharynx, 3; and supraglottic carcinomas (carbon dioxide laser resection), 2. One patient had both an upper jaw and lower lip carcinoma and another had both a soft palate and floor-of-mouth carcinoma. There were 43 T1, 33 T2, 2 T3, and 1 T4 tumors. All patients were treated surgically with a transoral excision of the primary tumor.

Real-time, B-scan ultrasonographic examinations were performed using a 7-MHz linear array transducer. The most suspicious lymph nodes in the first or second echelon were aspirated. A maximum of 3 lymph nodes per side were aspirated. All initial US-FNAC examination results were negative. In 70 neck sides the aspirate was negative, in 5 neck sides the aspirate was nondiagnostic and was repeated and negative after surgery, whereas in 79 neck sides no enlarged lymph nodes were seen and thus no aspirate was obtained. During the follow-up period, varying from 1 to 4 years, in the first 2 years US-FNAC examinations were performed as well. Follow-up visits were performed at 4- to 8-week intervals in the first year, gradually increasing the interval thereafter. The US-FNAC was performed every 2 to 5 visits, depending on the surgeon involved and the estimated risk of occult metastases. The number of US-FNAC examinations during follow-up varied from 1 to 6 per patient.

RESULTS

Of the 77 patients, 14 (18%) failed in the neck exclusively. The T stage of the primary tumor in these 14 cases in T2 tongue carcinomas. As a consequence, the arguments to refrain from elective neck treatment gain strength for patients treatable by transoral excisions or laryngectomies for their primary tumors.

In our clinic, since 1992 we gradually changed our policy for patients treatable by transoral excisions without evidence of lymph node metastases at palpation and US-FNAC. In the past these patients frequently had an elective neck dissection, now we mostly refrain from elective treatment of the neck while the patients are followed up at regular intervals with palpation and US-FNAC. In the past these patients frequently had an elective neck dissection, now we mostly refrain from elective treatment of the neck while the patients are followed up at regular intervals with palpation and US-FNAC. Our study describes the outcome in this patient group in terms of survival and characteristics of the failures.

Of the 77 patients, 14 (18%) failed in the neck exclusively. The T stage of the primary tumor in these 14 cases was similar to the whole group: 8 T1, 5 T2, and 1 T3 tumor. Six regional failures of the neck were found with US-FNAC, whereas 8 were detected clinically. In 6 of these 8 patients, US-FNAC was used to confirm clinical suspicion whereas for the other 2 no cytologic confirmation was obtained. Most metastases were detected in level 2 (Table 1). Four neck failures were detected within 3 months after treatment of the primary tumor, 5 between 4 and 7 months, and 5 after more than 7 months (Table 1).

Of these 14 patients, 12 were treated with a neck dissection of whom 10 also received postoperative radiotherapy, 1 had only 1 metastasis without extranodal spread (case 14) and 1 patient refused postoperative radiotherapy and eventually died (case 3) (Table 1). One patient with one 8-mm metastasis was only treated with curative intent radiotherapy and did well and another patient with distant metastases underwent radiation therapy for palliation only. In the 12 salvaged neck dissection specimens there were 32 histologically positive lymph nodes found in levels 1 through 4 (Table 1). Of these 32 nodes, 13 showed extranodal spread in 9 patients. Of these 14 patients who failed in the neck, 5 died (Table 1). Four died of uncontrolled cancer, whereas 1 died of another cause, free of disease, 5 months after neck dissection. In this group of 4 patients who died of their tumor, 2 neck recurrences were detected within 4 months, 1 after 8 months, and 1 after 19 months (Table 1). The size of the lymph node metastases in the 4 who eventually died was larger than 14 mm, whereas it was smaller in the 10 patients salvaged. Three of these 4 patients died of distant metastases. Two were free of disease locoregionally and 2 had uncontrolled neck disease. Ten (71%) of the 14 patients with regional failure were salvaged. Of this salvaged group, 1 patient developed a second primary tumor in the lung and he underwent a successful lobectomy. The disease-free survival in the 10 patients salvaged varied from 5 to 48 months (mean, 26 months).

Of the 77 patients, a local recurrence occurred in 5 of whom 4 also had a recurrence in the neck. All these patients died. Three more patients developed a secondary primary in the lung and died. In total, 17 patients died and 60 patients are alive. Five patients died of nontumor-related causes whereas 12 died of cancer. Of these 12 patients, 3 had a presumed second primary in the lung without local or regional tumor recurrence, 5 had a locoregional recurrence, and 4 had a regional recurrence.

COMMENT

The key question in the decision making between elective neck treatment or observing the neck is whether there is a difference in prognosis between these 2 policies. There have been many retrospective studies,9-11 most of which have shown an advantage of elective treatment. Only 3 randomized prospective studies12-14 have been performed and none of these showed a statistically significant difference in survival.

The failure rate in the neck of 18% compares favorably with the incidence of occult metastases quoted in the literature for patients treated with transoral tumor excision and a wait-and-see policy for the neck.15-17
(Table 2). In all these studies, in which only palpation is used to initially stage the neck, the recurrence rate in the neck is between 24% and 57% (mean, 32%) (Table 2). Our low recurrence rate can be explained by the initial use of US-FNAC that diminishes the risk of occult metastases. If we estimate our initial risk (N0 neck) as found in our earlier studies and is higher than the sensitivity of 44% found by Takes et al as commented by van den Brekel or the 50% found by Righi et al. This again shows the interindividual variability in the accuracy of this technique.

An important issue for the prognostic impact of a wait-and-see policy is the salvage rate in case of neck recurrences. Our results show that with US-FNAC during follow-up it is possible to detect a significant percentage of neck recurrences in an early stage. However, although most of the detected lymph node metastases were small, the incidence of extranodal spread in these nodes was high. It is striking that the size of the lymph nodes in the 4 patients who died of their tumor was 14 mm or larger whereas the size was smaller for all other patients (Table 1). This once again stresses the importance of a strict follow-up regimen. In the literature, the reported salvage rate varies from as low as 27% to 82% (average, 50%) after a regional recurrence (Table 2). In this study we found a salvage rate of 71%, although our follow-up period is still limited. As the prognosis is closely related to the metastatic burden in the neck as well as to the presence of extranodal spread, the delay between the treatment of the primary tumor and the neck is probably crucial. To keep this delay as short as possible, the intervals between follow-up visits should be kept short, especially in the first and second years. Although this implies an extra workload in the outpatient clinic, it is mandatory if a wait-and-see policy for the neck is conducted. In our series of patients, US-FNAC was used during follow-up. However, it was not used at regular intervals in all patients and some found it uncomfortable. The first year, all patients were palpated by the surgeon every 4 to 8 weeks whereas US-FNAC was used at every 2 to 5 follow-up visits. In the second year, and thereafter, the interval was gradually increased. In total, 6 of the 14 neck recurrences were detected before being palpable, and most of these nodal metastases were smaller than 1 cm. This strict follow-up, also using US-FNAC, enabled an early detection rate in case of neck recurrences was 41%, the sensitivity of the US-FNAC in this study can be calculated to be 68%. This figure of 68% for the palpably N0 neck is in the same range as found in our earlier studies and is higher than the sensitivity of 44% found by Takes et al or the 50% found by Righi et al. This again shows the interindividual variability in the accuracy of this technique.

Table 1. Characteristics of 14 Patients Who Failed in the Neck

<table>
<thead>
<tr>
<th>Case</th>
<th>Positive at US-FNAC</th>
<th>No. of Metastases</th>
<th>Levels Involved</th>
<th>Neck Treatment</th>
<th>Delay</th>
<th>Follow-up, mo</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>2 (12 and 8)</td>
<td>2 (1)</td>
<td>2 and 3</td>
<td>ND-RT</td>
<td>5</td>
<td>NED, 19</td>
</tr>
<tr>
<td>2</td>
<td>2 (12 and 6)</td>
<td>2 (1)</td>
<td>2 and 3</td>
<td>ND-RT</td>
<td>5</td>
<td>NED, 23</td>
</tr>
<tr>
<td>3</td>
<td>3 (14)</td>
<td>5 (5)</td>
<td>2 and 3</td>
<td>ND</td>
<td>8</td>
<td>DOD, 6</td>
</tr>
<tr>
<td>4</td>
<td>2 (9 and 7)</td>
<td>3 (1)</td>
<td>2</td>
<td>ND-RT</td>
<td>3</td>
<td>NED, 8</td>
</tr>
<tr>
<td>5</td>
<td>2 (8)</td>
<td>2 (0)</td>
<td>1 and 2</td>
<td>ND-RT</td>
<td>7</td>
<td>NED, 17</td>
</tr>
<tr>
<td>6</td>
<td>2 (12 and 10)</td>
<td>4 (1)</td>
<td>1-3</td>
<td>ND-RT</td>
<td>3</td>
<td>NED, 16</td>
</tr>
<tr>
<td>7</td>
<td>2 (8)</td>
<td>2 (0)</td>
<td>RT</td>
<td>ND-RT</td>
<td>3</td>
<td>NED, 29</td>
</tr>
<tr>
<td>8</td>
<td>1 (30)</td>
<td>6 (0)</td>
<td>1-4</td>
<td>ND-RT</td>
<td>2</td>
<td>DOD, 14</td>
</tr>
<tr>
<td>9</td>
<td>2 (10)</td>
<td>3 (1)</td>
<td>1-3</td>
<td>ND-RT</td>
<td>5</td>
<td>DOD, 8</td>
</tr>
<tr>
<td>10</td>
<td>2 (20)</td>
<td></td>
<td></td>
<td>RT</td>
<td>19</td>
<td>DOD, 2</td>
</tr>
<tr>
<td>11</td>
<td>2 (9)</td>
<td>1 (1)</td>
<td>2</td>
<td>ND-RT</td>
<td>13</td>
<td>DOD, 5</td>
</tr>
<tr>
<td>12</td>
<td>No US-FNAC</td>
<td>2 (1)</td>
<td>1 and 2</td>
<td>ND-RT</td>
<td>11</td>
<td>NED, 41</td>
</tr>
<tr>
<td>13</td>
<td>No US-FNAC</td>
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<td>1</td>
<td>ND-RT</td>
<td>10</td>
<td>NED, 15</td>
</tr>
<tr>
<td>14</td>
<td>2 (5)</td>
<td>1 (0)</td>
<td>3</td>
<td>ND</td>
<td>6</td>
<td>NED, 27</td>
</tr>
</tbody>
</table>

*Ultrasonographic-guided fine-needle aspiration cytology (US-FNAC) indicates the levels and sizes of the metastatic lymph nodes as detected at the final positive US-FNAC; number of metastases and extranodal spread (ENS) found at histopathologic examination of the neck dissection specimen; ND, neck dissection; RT, radiotherapy; delay, delay between surgery of the primary tumor and the neck failure in months; follow-up, outcome and duration of follow-up or death in months after treatment of the neck; ellipses, not applicable; NED, no evidence of disease; DOD, dead of disease; and DOC, death of other cause.

Table 2. Summary of Results in Several Series of Clinically N0 Patients in Whom a Wait-and-See Policy for the Neck Was Conducted and the Primary Tumor Was Treated by Transoral Excision

<table>
<thead>
<tr>
<th>Source, y</th>
<th>No. of Patients Observed</th>
<th>Neck Recurrences, No. (%)</th>
<th>Salvaged, No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kligerman et al, 1994</td>
<td>33 11 (33)</td>
<td>3 (27)</td>
<td></td>
</tr>
<tr>
<td>Ho et al, 1992</td>
<td>28 10 (36)</td>
<td>3 (30)</td>
<td></td>
</tr>
<tr>
<td>Fakih et al, 1989</td>
<td>40 23 (57)</td>
<td>7 (30)</td>
<td></td>
</tr>
<tr>
<td>Cunningham et al, 1986</td>
<td>43 18 (42)</td>
<td>9 (50)</td>
<td></td>
</tr>
<tr>
<td>McGuirt et al, 1995</td>
<td>103 37 (36)</td>
<td>22 (59)</td>
<td></td>
</tr>
<tr>
<td>Khalfi et al, 1991</td>
<td>396 90-95 (24)*</td>
<td>53 (59)</td>
<td></td>
</tr>
<tr>
<td>VandenBrouck et al, 1980</td>
<td>36 17 (47)</td>
<td>14 (82)</td>
<td></td>
</tr>
<tr>
<td>Total (average)</td>
<td>679 211-216 (32)</td>
<td>111 (52)</td>
<td></td>
</tr>
<tr>
<td>This study</td>
<td>77 14 (18)</td>
<td>10 (71)</td>
<td></td>
</tr>
</tbody>
</table>

*Of 95 patients, only 90 were available for follow-up.
a combination of sentinel node detection and US-FNAC and/or molecular detection of tumor cells in the aspirate.18,19 We recently started to use this sentinel node detection technique in combination with US-guided aspiration and were able to specifically aspirate from the sentinel node in the first 7 patients tested. We are currently developing molecular biological techniques to increase the tumor cell detection rate in the aspirate.

**CONCLUSIONS**

A wait-and-see policy of the N0 neck after transoral tumor excision only seems feasible if a strict and accurate follow-up regimen can be provided. The moderate rate of occult metastases and high rate of neck salvage in this study warrant further use of this policy. Prognosis in these patients is comparable with that reported for patients treated with elective neck dissection whereas in our series most patients did not need neck treatment. A strict follow-up with US-FNAC requires motivation and good instruction to the patient, as well as the skill of a well-trained ultrasonographer dedicated to do repeated examinations and aspirations of small lymph nodes.

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18. Klutmann S, Bohuslavizki KH, Hoft S, et al. Lymphoscintigraphy in double tracer sentinel node detection and US-FNAC: a combination of sentinel node detection and US-FNAC and/or molecular detection of tumor cells in the aspirate.18,19 We recently started to use this sentinel node detection technique in combination with US-guided aspiration and were able to specifically aspirate from the sentinel node in the first 7 patients tested. We are currently developing molecular biological techniques to increase the tumor cell detection rate in the aspirate.

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