Surgical Treatment of Canalicular Stenosis in Patients Receiving Docetaxel Weekly

M. Amir Ahmadi, MD; Bita Esmaeli, MD

Objective: To describe the surgical treatment and outcomes in patients with metastatic breast cancer and canalicular stenosis caused by weekly treatment with docetaxel.

Methods: This case series included 10 patients with persistent epiphora due to weekly docetaxel treatment, who were evaluated by probing and irrigation of the tear drainage apparatus and were found to have significant canalicular stenosis. The severity of canalicular stenosis was graded clinically. Each patient underwent bicanalicular silicone intubation or dacryocystorhinostomy (DCR) with placement of either a silicone tube (canaliculo DCR) or a pyrex glass tube (conjunctivo DCR).

Results: Seven patients (12 eyes) underwent bicanalicular silicone intubation. Three patients (5 eyes) required canaliculo DCR with the placement of a silicone tube. In 2 patients (3 eyes), the degree of canalicular stenosis was severe enough to require conjunctivo DCR with the placement of a pyrex glass tube. All 10 patients had complete resolution of epiphora immediately after surgery. Four patients continued to receive docetaxel after surgery. In patients who underwent bicanalicular silicone intubation, the silicone stent was kept in place for the duration of docetaxel therapy. There were no surgical or anesthesia-related complications. At a mean follow-up time of 9 months after surgery, all but 1 patient (1 eye) remained asymptomatic. The interval between initiation of docetaxel therapy and surgery was significantly higher in patients who required DCR compared with those who had silicone intubation. The mean cumulative dose of docetaxel at the time of surgery was higher in patients who required DCR than in patients who had silicone intubation, but this difference was not statistically significant.

Conclusions: Canalicular stenosis secondary to weekly treatment with docetaxel should be treated with bicanalicular silicone intubation early in the course of docetaxel therapy. Failure to treat this adverse effect early may likely lead to severe and irreversible canalicular stenosis, which may necessitate conjunctivo DCR with the placement of a permanent pyrex glass tube.


DOCETAXEL (Taxotere; Aventis, Collegeville, Pa) is an effective chemotherapeutic agent against metastatic breast cancer.1-3 In women with metastatic disease, docetaxel is usually administered as a 1-hour intravenous infusion every 21 days. With this standard administration schedule, the dose-limiting adverse effect is myelosuppression.4 Weekly administration of docetaxel has been studied in phase I and II trials and has proven to be a less myelosuppressive regimen.5,6 Excessive tearing (epiphora) is a common adverse effect of weekly docetaxel treatment, occurring in up to 77% of patients treated with this regimen7,8 (also B.E., unpublished observations, 2000). Canalicular stenosis has been established as the underlying mechanism for epiphora in patients receiving weekly docetaxel8 (also B.E. unpublished observations, 2000). In this report we describe the surgical management and outcomes in patients who had significant canalicular stenosis due to weekly administration of docetaxel, with emphasis on the effects of the timing of surgical intervention.

RESULTS

Ten patients with metastatic breast cancer receiving docetaxel weekly were diagnosed with canalicular stenosis during the study period and underwent surgery to correct the problem. Patient characteristics and surgical procedures are listed in the Table. All patients in this study received docetaxel as a single agent or in combination with trastuzumab. Five

From the Ophthalmology Section, Department of Plastic Surgery, The University of Texas M. D. Anderson Cancer Center, Houston.
PATIENTS AND METHODS

This case series included all patients who were referred to the Ophthalmology Clinic at The University of Texas M. D. Anderson Cancer Center (Houston) between March 2000 and November 2000 for evaluation of epiphora that occurred during weekly docetaxel therapy for metastatic breast cancer. These patients were found to have canalicular stenosis and underwent surgery to correct the problem. In each patient, epiphora was severe enough to disrupt daily activities, such as driving or reading. Each patient underwent a comprehensive ophthalmologic examination, including evaluation of the tear drainage apparatus by probing and irrigation. Severity of canalicular stenosis was graded based on clinical observations during in-office probing and irrigation. In a few patients, a nuclear lacrimal scan was done to confirm the presence of canalicular stenosis. Depending on the extent and severity of canalicular stenosis, patients were treated with bicanalicular silicone intubation or dacryocystorhinostomy (DCR) with placement of either a silicone tube (canaliculo DCR) or a pyrex glass tube (conjunctivo DCR). All patients were treated by the same surgeon (B.E.).

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Age, y/Race</th>
<th>Severity of Stenosis</th>
<th>Duration of Docetaxel Therapy, wk†</th>
<th>Cumulative Dose, mg/m²</th>
<th>Surgical Intervention</th>
<th>Right Eye</th>
<th>Left Eye</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>43/White</td>
<td>Moderate</td>
<td>17</td>
<td>105</td>
<td>SI</td>
<td>SI</td>
<td>SI</td>
</tr>
<tr>
<td>2</td>
<td>39/Hispanic</td>
<td>Moderate</td>
<td>24</td>
<td>420</td>
<td>SI</td>
<td>SI</td>
<td>SI</td>
</tr>
<tr>
<td>3</td>
<td>55/White</td>
<td>Severe</td>
<td>24</td>
<td>305</td>
<td>Canal DCR</td>
<td>Canal DCR</td>
<td>Canal DCR</td>
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<tr>
<td>4</td>
<td>59/White</td>
<td>Moderate</td>
<td>15</td>
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<td>SI</td>
<td>SI</td>
<td>SI</td>
</tr>
<tr>
<td>5</td>
<td>36/White</td>
<td>Severe</td>
<td>19</td>
<td>210</td>
<td>SI</td>
<td>SI</td>
<td>SI</td>
</tr>
<tr>
<td>6</td>
<td>40/Black</td>
<td>Moderate</td>
<td>14</td>
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<td>SI</td>
<td>SI</td>
<td>SI</td>
</tr>
<tr>
<td>7</td>
<td>43/White</td>
<td>Moderate</td>
<td>16</td>
<td>210</td>
<td>Canal DCR</td>
<td>Canal DCR</td>
<td>Canal DCR</td>
</tr>
<tr>
<td>8</td>
<td>60/White</td>
<td>Severe</td>
<td>36</td>
<td>110</td>
<td>Conj DCR</td>
<td>Conj DCR</td>
<td>Conj DCR</td>
</tr>
<tr>
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<td>Severe</td>
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<td>160</td>
<td>Canal DCR</td>
<td>Canal DCR</td>
<td>Canal DCR</td>
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<tr>
<td>10</td>
<td>47/White</td>
<td>Severe</td>
<td>30</td>
<td>410</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*SI indicates silicone intubation; canal DCR, canaliculo dacryocystorhinostomy; and conj DCR, conjunctivo dacryocystorhinostomy.
†Duration of docetaxel treatment before surgical intervention.

We recently reported that canalicular stenosis is the underlying mechanism for epiphora in patients receiving weekly docetaxel.8 In the present study, we observed that surgical treatment—bicanalicular silicone intubation or DCR—resulted in complete resolution of epiphora in patients with moderate or severe canalicular stenosis due to weekly docetaxel treatment.

In this series, the severity of canalicular stenosis and thus the type of surgical intervention required correlated with the duration of treatment with docetaxel; patients with longer treatment had more severe canalicular stenosis. In patients with more severe stenosis, a canaliculo DCR or a conjunctivo DCR was necessary to overcome the blockage of tear outflow. Our observations suggest that in advanced cases, canalicular stenosis secondary to weekly administration of docetaxel does not spontaneously resolve after cessation of treatment and may require conjunctivo DCR in symptomatic patients.
Our observations underscore the importance of timely management of canalicular stenosis in patients receiving docetaxel weekly. Although mild epiphora has been observed in patients receiving docetaxel every 3 weeks, it is usually transient and responsive to in-office probing and irrigation and other conservative measures, such as the use of artificial tears and topical steroids (B.E., unpublished observations, 2001). However, in patients receiving docetaxel weekly, in-office probing and irrigation, artificial tears, or topical steroids are not enough to prevent complete closure of the canaluli. We believe this difference is due to the continuous exposure of the lacrimal drainage apparatus to docetaxel in patients who receive this drug once a week, albeit at a lower dose each time, compared with patients receiving docetaxel every 3 weeks. Studies are currently underway to measure the concentration of docetaxel in tears collected from patients receiving this drug to test the hypothesis that docetaxel secretion in the tears may be one mechanism for canalicular stenosis.

Given the recent widespread use of weekly docetaxel as an effective first- or second-line antineoplastic agent for the treatment of breast cancer and other common forms of cancer, it is crucial that ophthalmologists and oncologists be aware that canalicular stenosis is a common adverse effect of weekly treatment with docetaxel. We recommend prompt referral to an ophthalmologist (ideally, a lacrimal surgeon) as soon as epiphora is noted by a patient receiving docetaxel. If canalicular stenosis is diagnosed through careful probing and irrigation of the tear drainage apparatus, bicanalicular silicone intubation should be considered, especially in patients who need to continue receiving docetaxel weekly. Silicone tubes can remain in place for the duration of docetaxel therapy and removed in the office 4 to 6 weeks after cessation of chemotherapy, by which time all docetaxel will most likely be cleared from the body. If canalicular stenosis is not treated early, complete closure of the canaluli can occur. In advanced cases, a conjunctivo DCR and placement of a permanent pyrex glass tube (Jones tube) may become necessary to overcome the blockage of lacrimal outflow.

Corresponding author and reprints: Bita Esmaeli, MD, Ophthalmology Section, Department of Plastic Surgery, Box 443, M. D. Anderson Cancer Center, 1515 Holcombe Blvd, Houston, TX 77030 (e-mail: besmaeli@mdanderson.org).

REFERENCES