Surgical Treatment of Canalicular Stenosis in Patients Receiving Docetaxel Weekly

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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.


OCETAXEL (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
patients (50%) had moderate canalicular stenosis and 5 (50%) had severe canalicular stenosis. The interval between initiation of docetaxel therapy and surgery to correct canalicular stenosis ranged from 14 to 44 weeks (mean, 24 weeks). The mean interval between initiation of docetaxel therapy and surgery was 17.8 weeks for patients who required bicanalicular silicone intubation and 30 weeks for patients who required DCR (P = .04).

The mean cumulative dose of docetaxel at the time of surgery was higher in patients who required DCR (246 mg/m²) than in patients who required silicone intubation (210 mg/m²) but this difference was not statistically significant. Eight of the 10 patients in this study received docetaxel doses of 35 mg/m²; the other 2 patients received 25 mg/m² and 40 mg/m² of docetaxel at each infusion, respectively. Every patient received dexamethasone at an average dose of 16 mg prior to each infusion. All 10 patients had complete resolution of epiphora immediately after surgery. Four patients continued to receive docetaxel weekly after surgery. The follow-up time after surgery ranged from 7 to 14 months (mean, 9 months).

In 12 eyes (7 patients) treated with bicanalicular silicone intubation, the silicone tubes were removed 6 weeks after discontinuation of docetaxel. All 7 patients (12 eyes) have remained asymptomatic after removal of the silicone tubes. All patients who underwent a DCR remain asymptomatic at the time of this report with the exception of 1 patient (1 eye) who had a canaliculo DCR; after removal of the silicone tube, this patient’s epiphora returned. Probing and irrigation in this patient revealed blockage at the level of the proximal lower canalicus. There were no surgical or anesthesia-related complications in this cohort.

We recently reported that canalicular stenosis is the underlying mechanism for epiphora in patients receiving weekly docetaxel. 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.

**COMMENT**

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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 canaliculi. 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 canaliculi 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.

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REFERENCES