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Nasolacrimal Duct Stenosis after Oral Capecitabine Administration

Dear Editor,

Capecitabine is a prodrug of 5-fluorouracil (5-FU) and is converted to its active form within tumor cells. Although the selective activity of capecitabine significantly lowers systemic toxicity events, several side effects have been reported. The literature mentions common adverse effects associated with capecitabine, including hand-foot syndrome, gastrointestinal toxicity (diarrhea, nausea, and vomiting) and myelotoxicity. With regard to the ocular adverse effects, ocular surface irritation and symptoms of epiphora are commonly reported, but there is no report of nasolacrimal duct obstruction in a patient receiving capecitabine, except one case report in Japan [1]. This report describes the first two cases of nasolacrimal duct stenosis after oral administration of capecitabine in Korea.

A 71-year-old woman with recurrent metastatic breast cancer was referred to our clinic for tearing of the eyes. She was receiving oral capecitabine monotherapy (1,000 mg/m^2 every 12 hours for 14 consecutive days followed by a 7-day rest), and she developed epiphora in both eyes 7 months after initiation of chemotherapy. The height of the lacrimal lake was high in both eyes, and lacrimal irrigation fluid was passed to the nasal cavity. She showed a normal punctal opening and normal anterior segment in both eyes. On the fluorescein dye disappearance test, the dye remained unchanged in both eyes. On dacryocystography, contrast media refluxed through the upper puncta and focal stenoses of the distal nasolacrimal ducts were noted (Fig. 1A). She was diagnosed with partial nasolacrimal duct obstruction, and bilateral lacrimal silicone tube intubation was recommended.

A 72-year-old man with sigmoid colon cancer underwent low anterior resection and was receiving adjuvant oral capecitabine monotherapy (1,000 mg/m^2 every 12 hours for 14 consecutive days followed by a 7-day rest). One month after initiation of chemotherapy, he complained of epiphora and was referred to our clinic. The tear meniscus was very high in both eyes, and lacrimal irrigation fluid was passed to the nasal cavity. His punctal opening and anterior segment were normal in both eyes. The height of dye was unchanged in both eyes on the fluorescein dye disappearance test. Dacryocystography revealed that both nasolacrimal ducts were narrow and irregular (Fig. 1B). The patient was diagnosed with partial nasolacrimal duct obstruction, and he was offered the option of bilateral lacrimal silicone tube intubation. However, he declined to undergo any surgical intervention.

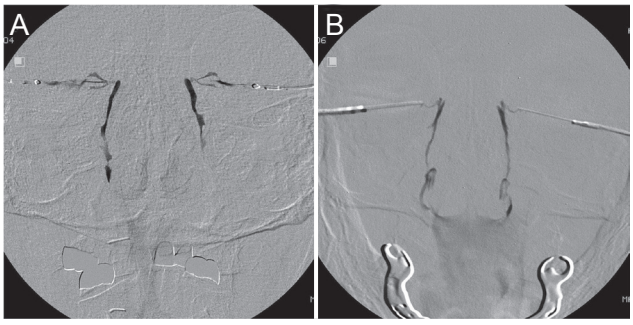

Fig. 1. (A) Dacryocystographic image of the patient in case 1 revealed focal stenosis of the distal nasolacrimal duct and mild dilatation of the nasolacrimal duct proximal to the stenotic site. Contrast media injected through the right and left lower puncta refluxed through the upper puncta. (B) Dacryocystographic image of the patient in case 2 demonstrated that the right and left nasolacrimal ducts were narrow and irregular. Contrast media injected through the lower puncta in both eyes almost passed to the nasal cavity. Informed consent was received from the patient.

We presented two cases of nasolacrimal duct stenosis, a rare side effect after capecitabine administration. Our patients complained of epiphora 7 and 1 months after initiation of chemotherapy, respectively. The literature is limited to only one case report, and the patient complained of epiphora 7 days after capecitabine was initiated [1]. Howev-

er, more studies have been done on lacrimal drainage abnormalities associated with S-1, another prodrug of 5-FU, and the onset of epiphora ranged from 2 to 8 months after the initiation of S-1 [2]. The mechanism by which capecitabine causes lacrimal drainage obstruction has not been previously discussed, but some studies suggested that 5-FU, one of the metabolites of capecitabine, can cause nasolacrimal inflammation and narrowing [1]. Noguchi et al. [3] reported the administration of topical antibiotics and corticosteroid drops to their capecitabine-induced epiphora patient, and the symptoms improved. Their patient visited the clinic very early, 7 days after symptoms developed. We did not recommend conservative management for the patients in our report because they visited our clinic at least 2 months after the onset of symptoms, and the long interval from onset to management usually indicates irreversible fibrotic changes in the nasolacrimal duct mucosa.

Capecitabine and 5-FU share several adverse effects, such as diarrhea and myelosuppression, and 5-FU administration-associated punctal, canalicular, and nasolacrimal ductal stenoses have been reported in several articles [4,5]. Therefore, capecitabine administration may be associated with nasolacrimal duct stenosis, despite its tumor-specific conversion. Ophthalmological referral is critical for early surgical intervention before the nasolacrimal duct is completely obstructed in these patients.

Yeonji Jang

Department of Ophthalmology, Seoul National University Hospital, Seoul National University College of Medicine, Seoul, Korea

Namju Kim

Department of Ophthalmology, Seoul National University Bundang Hospital, Seoul National University College of Medicine, Seongnam, Korea
E-mail: resourceful@hanmail.net

Keun-Wook Lee

Department of Internal Medicine, Seoul National University Bundang Hospital, Seongnam, Korea

Ho-Kyung Choung

Department of Ophthalmology, Seoul National University Boramae Hospital, Seoul National University College of Medicine, Seoul, Korea

Sang In Khwarg

Department of Ophthalmology, Seoul National University Hospital, Seoul National University College of Medicine, Seoul, Korea

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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