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Corneal complication by anticancer chemotherapeutic drug

Short running title: Chemotherapy-associated corneal complication

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An 84-year-old woman presented with nodule in the left upper lobe of the lung, which was detected by mass screening. Examination of a transbronchial biopsy revealed the tumor to be lung adenocarcinoma, however, epidermal growth factor receptor (EGFR) mutation could not be performed because the specimens obtained was too small. As the patient had metastatic disease, she received outpatient chemotherapy using S-1, an oral fluoropyrimidine consisting of tegafur (a prodrug of fluorouracil), 5-chloro-2,4-dihydropyrimidine and potassium oxonate [1]. She received 7 courses of the chemotherapy (once a daily 100mg/day for 14 consecutive days followed by a 2-week rest period), and the response was evaluated as stable disease. She was in slowly progressive condition for 8 months since the initiation of chemotherapy and developed blurred vision. Best corrected visual acuity (BCVA) was 3/20 for the right eye and 6/20 for the left eye. Slit-lamp examination showed a hurricane-like irregularity of corneal epithelium in both eyes (Figure 1-A). Topical antibiotic, topical steroid, and artificial tears were administrated, but these findings were not improved during the S-1 therapy. However, considering her general condition, there was no alternative treatment option at that time, so S-1 therapy continued. As evaluation of EGFR mutation in circulating tumor DNA using plasma samples became feasible, the patient received this test and found to have Ex 19 deletion. As second-line therapy, the patient received 30 mg/day afatinib, a second-generation EGFR-tyrosine kinase inhibitors (TKI). A follow-up chest CT scan 1 month later showed decreases in both the size of primary site and pulmonary metastases. The patient had continued consultation with the ophthalmologist, but at 4 months after the initiation of afatinib therapy, the corneal findings improved markedly (Figure 1-B). The BCVA improved to 6/20 for the right eye and 10/20 for the left eye. The patient is currently doing well and is now, 4 months after the initiation of erlotinib, able to work.

Corneal injury associated with cancer chemotherapy is one of the complications that cannot be overlooked. Management by ophthalmologists is essential in disease condition.
Besides S-1 [2], corneal complications have also been reported to occur in patients receiving first generation EGFR-TKIs, gefitinib [3] or erlotinib [4], although all publications were only case reports or case series [3, 4]. Afatinib, a second-generation EGFR-TKI, is widely used in patients with advanced NSCLC and its clinical utility is now highly evaluated [5]. It is interesting that corneal complications due to S-1 improved by treatment change to afatinib. However, the mechanism why the S-1-induced corneal complication improved was beyond our knowledge. This observation suggests that afatinib may be a therapeutic option for EGFR mutated patients with corneal complication during S-1 or first-generation EGFR-TKIs. We report on a rare case with improvement of S-1-induced corneal complication by treatment change to afatinib. It should be noted that there is a possibility of corneal complication when complaining of blurred vision during anticancer treatment with some anticancer drugs such as S-1 or EGFR-TKIs.

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References


Figure 1. Slit-lamp examination showed a hurricane-like irregularity of corneal epithelium in both eyes (A). Slit-lamp photographs of the patient at 4 months after the initiation of afatinib therapy. The corneal findings improved markedly (B).