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Case Report

# Corneal Perforation Associated with the Oral Anticancer Drug S-1 : A Case Report

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**SUMMARY**

**Purpose** : S-1 is an oral anticancer drug containing tegafur, a prodrug of 5-fluorouracil (5-FU). We present a patient who experienced corneal perforation that appeared to be caused by S-1 administration.

**Case** : A 67-year-old woman was presented to our hospital because of corneal perforation in her left eye. She had been administrated S-1 for 17 months from gastroenterological surgeon at another hospital for treating pancreatic cancer. The best-corrected visual acuity was 0.4 in the right eye and 0.1 in the left eye at the initial visit. Convoluted subepithelial opacity was present in the cornea of the right eye, and corneal perforation was observed in the left eye. Anterior chamber formation was very poor, and iris incarceration was present in the left eye. Although anterior chamber formation was attempted with the use of soft contact lens wear, the condition remained unchanged. We requested to discontinue S-1 administration to gastroenterological surgery at another hospital. The patient was presented to the department of ophthalmology at another hospital because her eye condition and pancreatic cancer could be treated at the same institution.

**Conclusion** : Patients treated with S-1 should be carefully followed up for ocular complications because corneal perforation may occur.

**Key Words** : S-1, corneal perforation, ocular complication, 5-FU

## INTRODUCTION

S-1, an oral anticancer drug containing tegafur, gimeracil and oteracil potassium was approved for manufacturing in 1999[1]. Compared with the conventional intravenously administered drug 5-fluorouracil (5-FU), the novel drug S-1 is more effective and is associated with less toxicity and fewer gastrointestinal side effects. Therefore, it is presently prescribed for cancers of gastric, colorectal, head and neck, non-small cell lung, inoperable or recurrent breast, pancreatic, and biliary tract, and has become a key drug in chemotherapy. However, there have been many reports on ophthalmic complications by S-1 administration[2～12].

To the best of our knowledge, there is only one report mentioning of corneal perforation caused by S-1 administration[9]. Therefore, this adverse effect by S-1 seems to be less known and warrants for further attention.

We present a case of corneal perforation in the left eye while receiving adjuvant chemotherapy with S-1 for pancreatic cancer for 17 months. This case should

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**Fig. 1**
Corneal perforation with iris incarceration in the left eye of a 67-year-old Japanese woman receiving S-1 for pancreatic cancer.

raise awareness of the potentially vision-threatening side effect of S-1 and highlight the importance of co-management by gastroenterological surgeons and ophthalmologists.

## CASE REPORT

A 67-year-old woman presented with a 4-day history of ophthalmalgia and watering owing to corneal perforation in her left eye. She had received S-1 for 17 months for the treatment of her pancreatic cancer from the department of gastroenterological surgery at another hospital. Additionally, the patient had mild diabetes mellitus. She had been prescribed with topical levofloxacin 1.5% , fluorometholone 0.1% , and sodium hyaluronate 0.1% when she previously visited an eye clinic. At the initial visit, her best-corrected visual acuity was 0.4 in the right eye and 0.1 in the left eye. A slit-lamp examination using fluorescein stain revealed an irregular corneal epithelium, opacity of the cornea, involving the visual axis of the right eye, and corneal perforation with iris incarceration in the left eye (Fig. 1). Simple diabetic retinopathy was observed in the right eye ; however, checking the retinal condition was impossible in the left eye.

We informed about the corneal perforation in the left eye to gastroenterological surgeon and requested to discontinue S-1 administration. Although the patient continuously wore a soft contact lens in the left eye for 2 days, anterior chamber did not form. The patient wanted to move to another hospital because there was a department of ophthalmology in the same institution. The patient was presented to another hospital and had both medical follow-ups.

## DISCUSSION

To the best of our knowledge, this is the second reported case of corneal perforation caused by S-1 administration ; the first such case was reported by Yokogawa et al[9]. In such cases, discontinuation of S-1 administration appears to be the first step of treatment. Inoue et al. reported that corneal and conjunctival disorders are significant adverse effects of S-1 administration, and the only effective treatment is discontinuing S-1 administration and switching to other anticancer drugs[8]. However, compared with intravenous 5-FU, S-1 is more effective, less toxic, and is associated with fewer side effects. Therefore, its discontinuation is difficult.

Kobashi et al. reported that 5-FU was still present in the tear fluid after 1 week discontinuing S-1 administration[7]. Because elimination of 5-FU from tear fluid may take some time, corneal perforation should be followed up for a few weeks after S-1 discontinuation with careful attention to the risk of infectious diseases and surgery should be considered according to the patients condition. Tachibana et al. reported that after discontinuation of S-1, corneal epithelial damage improved after 1 month and was cured after 6 months[10]. In case of corneal perforations, S-1 will have to be discontinued for a longer period and corneal perforation sometimes accompanies infectious disease. It is very difficult for ophthalmologist to treat such condition.

Yamada et al. reported that older patients were at a greater risk of S-1-related ocular complications, with the age of the ocular complication group being 71.6±6.8 years and that of the non-ocular complication group being 63.5±7.3 years ($P=0.0077$)[11]. In this report, although the age of the patient was 67 years, severe corneal perforation occurred. Yamada et al. had prescribed preservative-free artificial tears to wash out the ocular surface tears along with 0.1% fluorometholone to reduce conjunctivitis[11]. We believe that this preservative method was worth trying. The patient had been prescribed 0.1% fluorometholone at an eye clinic she visited previously ; such measures

might be useful for conjunctivitis.

Yamada et al. and Moriya et al. had reported ocular complications in 33.3%[11] and 10.7%[12] of cases, respectively, after S-1 administration. Although Yamada et al. reported that ocular complications were not associated with total days or total dose of S-1 administration[11], Moriya et al. reported that ocular complications were associated with the male sex as well as total days and total dose of S-1 administration[12]. The patient reported here was a female, and the total period of S-1 administration was 17 months, which was believed to be too long by Moriya et al.[12] ; however, the total dose was not calculated.

In summary, this case report highlights the importance of carefully monitoring patients receiving S-1 to prevent any adverse effects, such as corneal perforation in rare cases.

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None of the authors reports any conflict of interest in this work.

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