

1. Please explain the relationship between clopidogrel resistance and intestinal ulceration and the possible mechanism more detailed?

--> Thank you for valuable comment. We added a paragraph for this in Discussion(8~9 page).

("The mechanisms of clopidogrel resistance are not fully elucidated but there are several opinions on the mechanism for clopidogrel resistance. First opinion includes inappropriate dosing or underdosing of clopidogrel and drug–drug interactions between clopidogrel and other drugs. Second opinion may be hepatic conversion of the active metabolite by cytochrome CYP2C19. Third opinion could include variable intestinal absorption of the prodrug or clearance of the active metabolite. Otherwise, ABC1 activity, increased release of ADP and platelet receptor polymorphisms have been suggested.[18] In this case, these mechanisms might cause inappropriate concentration and action of active metabolite of clopidogrel and lead to ulceration and bleeding of small bowel.").

2. Is there any difference of intestinal ulceration risk/rate between patients with and without clopidogrel resistance?

--> Thank you for comment. We added a sentence for this in Discussion(7 page). Several studies of lower gastrointestinal tract disease(including bleeding, ulcers) with antiplatelet agents have been reported, but studies about small intestine ulcers with or without clopidogrel resistance have yet been reported. Through our case, it seems necessary to proceed with clopidogrel resistance related research.

("There is no mention of clopidogrel resistance, so the difference in intestinal ulceration with or without clopidogrel resistance is unknown.")

Angel Lanas, Carla J. Gargallo. Management of low-dose aspirin and clopidogrel in clinical practice: a gastrointestinal perspective. J Gastroenterol (2015) 50:626–637.

3. Did this patient suffer a history of ulcerative disease of the small intestine before clopidogrel oral-take?

--> Thank you for comment. We added a sentence for this in "History of past illness".

("And he had never complained of gastrointestinal(GI) symptoms prior to taking clopidogrel.")

**4. How can you make sure there is still intestinal ulceration existence after surgery?
Because it was mentioned that ulcers were improved in capsule endoscopy.**

--> Thank you for comment. After the operation, our patient did not complain of any symptoms. During follow-up in the outpatient clinic, the patient and patient's son requested confirmation that the small bowel ulcers was completely cured, and we agreed to this demand and performed a capsule endoscope. As a result, it was confirmed that the small intestine ulcers was completely healed. We added a sentence for this in "OUTCOME AND FOLLOW-UP".

("There were no complaining symptoms. One year after discharge, capsule endoscopy was performed and the small bowel ulcers were improved")

*** Additional modifications**

--> Additional sentences and references have been added for the flow of the text.

"It became possible to examine the small intestine through as double balloon endoscopy(DBE) and capsule endoscopy (CE). [8,9] "

8 Iwamoto J, Mizokami Y, Saito Y, Shimokobe K, Honda A, Ikegami T, Matsuzaki Y. Small-bowel mucosal injuries in low-dose aspirin users with obscure gastrointestinal bleeding. World J Gastroenterol 2014; 20: 13133-13138 [PMID: 25278707 DOI: 10.3748/wjg.v20.i36.13133]

9 Koffas A, Laskaratos FM, Epstein O. Non-small bowel lesion detection at small bowel capsule endoscopy: A comprehensive literature review. World J Clin Cases 2018; 6: 901-907 [PMID: 30568944 DOI: 10.12998/wjcc.v6.i15.901]