Aim: 5-FU is metabolized by thymidine phosphorylase and orotate phosphoribosyl transferase and is principally degraded in the blood or liver by dihydropyrimidine dehydrogenase (DPD). DPD, the catalyzing enzyme in the first and rate-limiting step of the degradation process, degrades approximately 85% of the administered 5-FU. DPD activity in peripheral blood mononuclear cells has been reported to correlate inversely with 5-FU clearance. In reports of DPD deficiency, the prognosis is poor, and approximately 60% patients die. With a reported high mortality rate, chemotherapy is generally contraindicated for patients with DPD deficiency, and there have been no reports of continued chemotherapy in patients with a DPD activity level of <10%. Here we report the new findings of DPD-deficient patient in whom continuing chemotherapy through the dose-escalation method is successful.

Methods: Chemotherapy for a 73-year old man with jejunal cancer was initiated. Capecitabine was administered in incrementally increasing doses, beginning with a single pill (dose-escalation method), while monitoring plasma 5-FU concentration, leukocyte, neutrophil, and platelet counts.

Results: DPD protein measurement in the peripheral blood mononuclear cells yielded a level of 2.35 U/mg using the ELISA method (the same method yielded DPD measurements ranging from 33.6 to 183.6 U/mg in peripheral blood mononuclear cells from 10 healthy individuals). Ultimately, after increasing the Capecitabine dose to 1800 mg, oxaliplatin and bevacizumab were added and XELOX+bevacizumab treatment was initiated. Subsequent DPD protein measurement showed that the level had increased to approximately 10-fold the level before chemotherapy. Furthermore, the peritoneal metastases disappeared following chemotherapy.

Conclusions: Because of serious adverse events, the chemotherapy-associated mortality rate among DPD-deficient patients is high, and there have been no reports of continuous chemotherapy in patients with DPD activity levels of <10%. This report is the first of its kind worldwide and has indicated that DPD activity can be inducible. These findings may provide early indications of a new treatment method for DPD deficiency and will be reported in detail.

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