Successful Treatment of Irinotecan-Induced Muscle Twitching: A Case Report

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ABSTRACT: Irinotecan, a topoisomerase I inhibitor, is commonly used in the treatment of advanced colorectal cancer. Its adverse effects include delay diarrhea, severe myelosuppression, and cholinergic-like symptoms. Though 2 cases of irinotecan-induced muscle twitching were reported but the successful treatment of this adverse event still not shown. We present a 24-year-old female patient with advanced colorectal cancer received bevacizumab and FOLFIRI (irinotecan + calcium leucovorin + 5-fluorouracil) treatment. Her right pectoralis major muscle presented with involuntary muscle twitching during the infusion of irinotecan at the sixth cycle of chemotherapy. The muscle twitching was slowly dissipated about 4 hours after the halted of irinotecan infusion. Then lorazepam 2 mg iv was injected before administration of irinotecan in an attempt to prevent the muscle twitching in the seventh cycle of chemotherapy. The patient did not report further muscle twitching. After that, lorazepam was routine administered before each cycle of FOLFIRI regiment. No any muscle twitching was observed after the use of lorazepam. This case provides valuable insight that muscle twitching can occur as rare irinotecan-related adverse effect. Benzodiazepine agonists, such as lorazepam, is the potential treatment of choice.

KEYWORDS: Irinotecan, colorectal cancer, muscle twitching, lorazepam

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Introduction

Irinotecan, a topoisomerase I inhibitor, has been used extensively in the treatment of advanced colorectal cancer since approved by the US Food and Drug Administration in 1996.[1] In addition, irinotecan combined with 5-fluorouracil, leucovorin, and oxaliplatin are considered as the standard therapy for metastatic pancreatic cancer.[2] Irinotecan is a prodrug that is converted in the liver by carboxylesterase to the active metabolite 7-ethyl-10-hydroxycamptothecin (SN-38). Then SN-38 is inactivated by microsomal uridine diphosphate glucuronosyltransferase enzymes (UGT1A1 and UGT1A9).[3] Typical side effects related to this agent include delay diarrhea and severe myelosuppression, which are known to be dose-limiting toxicities of irinotecan. Less frequent cholinergic-like symptoms are also observed during or after infusion of irinotecan. The cholinergic-like symptoms include bradycardia, sweating, lacrimation, abdominal pain, and diarrhea.[4] To the best of our knowledge, there has only 2 cases regarding irinotecan-induced muscle twitching been reported,[5,6] management of this adverse event. At the present time, there was no successful treatment or control of this adverse event confirmed. Here, we demonstrate a case report of irinotecan-induced muscle twitching and the successful treatment of muscle twitching by benzodiazepine.

Case Report

A 24-year-old female admitted to the emergency department due to acute left lower quadrant pain, her abdominal computed tomography image revealed a descending colon tumor with perforation that caused peritonitis. Subsequently, the patient underwent series examinations and the pathological diagnosis was colorectal adenocarcinoma with a stage T4aN2bM1. After surgical resection, she received systemic chemotherapy for stage IV KRAS-mutant colon cancer with FOLFIRI plus bevacizumab.

Consisting of bevacizumab 5 mg/kg IV over 2 hours on day 1, irinotecan 180 mg/m^2 IV over 2 hours on day 1, leucovorin 200 mg/m^2 IV over 2 hours on day 1, and day 2, 5-fluorouracil (5FU) 1200 mg/m^2 as a continuous IV infusion over 23 hours on day 1 and day 2 cycled every 14 days.

Premedication was given with diphenhydramine 30 mg iv, palonosetron 0.25 mg iv, dexamethasone 10 mg iv, and atropine 0.5 mg iv prior to infusion. This patient had no any history of neuro-muscular disease. Following the fourth cycles of chemotherapy, the patient tolerated the bevacizumab infusion well. But in the fifth cycle, she complained about epigastric pain after the infusion of irinotecan. The symptom can be relieved after administration of hyoscine butylbromide, aprepitant, and fluid hydration. Her upper GI endoscopy examination showed mild gastric ulcer. During the sixth cycle, infusion time of irinotecan was prolonged from 2 to 4 hours for attempting to improve chemotherapy-associated abdominal discomfort occurred during previous cycle. However, about 3 hours after the irinotecan infusion, she developed noticeably visible muscle twitching in the right pectoralis major muscle

(see Supplemental Video, which demonstrates the muscle twitching in the right pectoralis major muscle). The muscle twitching was slowly dissipated about 4 hours after the infusion ended. Consequently, lorazepam 2 mg injection was given before administration of irinotecan in an attempt to prevent the happen of irinotecan-induced muscle twitching in the seventh cycle of FOLFIRI regimen. We found that the patient did not report any muscle twitching. Since then, lorazepam was pre-medicated in the rest of each cycle of FOLFIRI regimen. Muscle twitching hasn't occurred anymore after lorazepam use.

Discussion

Involuntary muscle twitching, also known as muscle contraction or myoclonus, refers to sudden, brief, lightening-like muscle jerks arising from the nervous system. Treatment of muscle twitching is guided by anatomic/physiologic type, of which there are 5 major groups: cortical, cortical-subcortical, subcortical nonsegmental, segmental, and peripheral. However, there is no singularly effective drug, and treatment often proceeds sequentially using a trial-and-error approach. Benzodiazepines (such as clonazepam) and antiseizure medications (such as valproate, piracetam, levetiracetam, and topiramate) are often used to treat myoclonus. The possible mechanism of action of benzodiazepines for myoclonus is facilitation of gamma-aminobutyric acid (GABA) signaling and a decrease in 5-hydroxytryptophan utilization in the brain.[7] A retrospective study carried out in Turkey examined myoclonic seizures induced by antipsychotic drugs in 10 patients. Valproate (500-100 mg/day) was added in 8 of the patients, benzodiazepine (lorazepam 2 mg/day, clonazepam 1 mg/day) in 2 patients for the treatment of the myoclonic states.[8]

On the other hand, irinotecan is the drug of choice for patients with advanced colorectal cancer. Until now, the irinotecan-induced muscle twitching has remained unclear and is not explained by 2 published case reports to date.[5,6] To our knowledge, this case is the first report describing that muscle twitching induced by irinotecan can be successfully controlled by lorazepam. Among the chemotherapy medication, a published case series revealed 3 cases of prednimustine-induced myoclonus were efficiently suppressed by iv or oral diazepam and received prophylactic diazepam in subsequent courses of therapy.[9] Another case of prednimustine-induced myoclonus have also been reported and myoclonia gradually decreased after introduced clonazepam.[10] Collectively, these above study findings and clinical observation of our case might suggest that benzodiazepine can be considered as a choice in managing irinotecan-induced muscle twitching.

Conclusion

We report a case of 24-year-old woman with advanced colorectal cancer who received bevacizumab and FOLFIRI. This case highlights the rare side effect of muscle twitching caused by irinotecan and demonstrates the effectiveness of lorazepam in alleviating irinotecan-induced muscle twitching. However, further studies on the use of benzodiazepine in symptomatic relief are warranted.

Author Contributions

Conceptualization: H-FL; Data curation, investigation, and writing—original draft: Y-TS; Validation and visualization: H-FL; Writing—review & editing: H-FL, H-YL, and Y-TC.

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Supplemental Material

Supplemental material for this article is available online.

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