Case Report

Gastroparesis as a significant gastrointestinal adverse event during intensive chemotherapy for solid caner: a case report

Tomohiro Nakayama^, Koji Haratani, Takashi Kurosaki, Kaoru Tanaka, Kazuhiko Nakagawa^

Department of Medical Oncology, Kindai University Faculty of Medicine, Osaka-Sayama, Osaka, Japan

Correspondence to: Koji Haratani, MD, PhD. Department of Medical Oncology, Kindai University Faculty of Medicine, 377-2 Ohno-higashi, Osaka-Sayama, Osaka 589-8511, Japan. Email: haratani_k@med.kindai.ac.jp.

Background: Proper management of chemotherapy-related gastrointestinal toxicities is essential to maximize therapeutic outcome for malignancies. Gastroparesis is an onerous syndrome characterized by delayed gastric emptying without gastrointestinal obstruction, but this has not been recognized as chemotherapy-related complication in solid malignancies. Here, we describe a case of gastroparesis possibly caused by neurotoxicity of taxane and platinum-based high-intensity chemotherapy against solid cancer.

Case Description: A 73-year-old male was diagnosed with stage IVA oropharyngeal cancer (cT4N2bM0) as a cause of swallowing difficulty. As a curative treatment of the oropharyngeal cancer, induction chemotherapy with the regimen of docetaxel, cisplatin and fluorouracil (TPF) was initiated with nutritional support by nasogastric tube feeding. Then, this case was complicated with late-onset gastric dysmotility as evidenced by abnormally dilated stomach even after cessation of feeding for more than a few days. After a careful exclusion of other diseases that could cause gastric dysmotility, we eventually diagnosed chemotherapy-induced gastroparesis as a cause of his symptom. Notably, this refractory gastroparesis was successfully controlled with 5-HT4 agonist, mosapride, resulting in recovery of gastric motility and safe completion of the subsequent curative treatment.

Conclusions: Despite its rarity in patients with solid cancers, it is important to note chemotherapy-induced gastroparesis because delay in its management can be detrimental to their survival outcome. Thus, oncologists should consider gastroparesis in evaluating persistent upper abdominal symptoms after neurotoxic chemotherapies for solid cancer.

Keywords: Gastroparesis; solid cancer; chemotherapy; adverse event; case report

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Introduction

Gastrointestinal toxicity is a common adverse event during chemotherapy (gastrointestinal adverse event, GIAE), leading to an undesirable delay or dose reduction of chemotherapy which potentially results in questionable curability of comorbid malignancies. A major example of GIAE is chemotherapy-induced nausea and vomiting (CINV), and its management has been well established (1). However, other diseases are not fully characterized as causes of GIAE. Here, we report a case of gastroparesis as a significant GIAE during platinum and taxane-based intensive chemotherapy for solid cancer. We present the following case in accordance with the CARE reporting checklist (available at https://tcr.amegroups.com/article/view/10.21037/tcr-21-2776/rc).

^ ORCID: Tomohiro Nakayama, 0000-0003-4035-4658; Kazuhiko Nakagawa, 0000-0003-1284-9776.

Table 1 Laboratory data at the onset of symptoms

Variable	Reference, range†	At the onset of symptoms
Hemoglobin (g/dL)	13.7–16.8	10.6
Hematocrit (%)	40.7–50.1	32.4
Platelet count (per μL)	15.8–34.8	41.6
White-cell count (per μL)	3,300–8,600	9,350
Differential count (%)		
Neutrophils	38–77	72.8
Lymphocytes	20.2–53.2	15.5
Monocytes	2.7–9.3	8.2
Eosinophils	0.2–4.1	3.2
Basophils	0.2–1.3	0.3
C-reactive protein (mg/dL)	0–0.14	3.5
Alanine aminotransferase (U/L)	13–30	15
Aspartate aminotransferase (U/L)	10–42	8
Alkaline phosphatase (U/L)	106–322	359
Albumin (g/dL)	4.1–5.1	2.7
Sodium (mmol/L)	139–145	138
Potassium (mmol/L)	3.6–4.8	4.5
Chloride (mmol/L)	101–108	102
Urea nitrogen (mg/dL)	8–20	9.1
Creatinine (mg/dL)	0.65–1.07	0.88
Plasma glucose (mg/dL)	60–109	104

†, reference values are affected by many variables, including the patient population and the laboratory methods. The ranges used at Kindai University Hospital are for adults who are not pregnant and do not have medical conditions that could affect results. They may therefore not be appropriate for all patients.

Case presentation

A 73-year-old male was diagnosed with human papilloma virus (HPV)—negative stage IVA oropharyngeal cancer (cT4N2bM0) as a cause of swallowing difficulty. He had experienced distal subtotal gastrectomy with Billroth I reconstruction for duodenal ulcer at 33 years of age. As a curative treatment of the oropharyngeal cancer, induction chemotherapy with the regimen of docetaxel, cisplatin and fluorouracil (TPF) was initiated with nutritional support by nasogastric tube feeding. The TPF regimen consisted of docetaxel at a dose of 75 mg/m^2 followed by cisplatin at a dose of 75 mg/m^2 on day 1, and fluorouracil at a dose of 750 mg/m^2/day on days 1 to 5.

Approximately two weeks after starting this chemotherapy, he presented with upper abdominal distention, resulting in a complete interruption of the enteral nutrition. He was alert and afebrile. He did not have any medical histories and symptoms suggesting psychiatric disorders or neurodegenerative disorders such as parkinsonism. The only medication, which can impair gastrointestinal motility, that he took before this clinical course was short-acting opioid, and this was completely discontinued for more than two weeks. Blood examinations did not show any abnormalities including acute kidney injury, liver injury, electrolyte disturbances, endocrinopathies as well as hyperglycemia (shown in *Table 1*). Abdominal computed tomography (CT) scans showed abnormally dilated stomach without intestinal dilation (shown in *Figure 1A*,*1B*). An esophagogastroduodenoscopy (EGD) after discontinuation of enteral feeding for three days showed significant impairment of gastric emptying characterized by a large amount of gastric content, although mechanical obstruction and mucosal damage were not shown (shown in *Figure 1C*). CINV could be excluded because it rarely occurs one week after the start of chemotherapy (1). Thus, we diagnosed chemotherapy-induced gastroparesis as a cause of his symptom according to clinical practice guideline (2), and started oral mosapride 15 mg/day. Immediately after the initiation of mosapride, his symptom dramatically improved and repeated abdominal CT scans showed normal gastric emptying (shown in *Figure 1D*).

After this treatment course, a concurrent chemoradiotherapy with triweekly high-dose cisplatin (100 mg/m^2 on day 1) and definitive radiotherapy with 70 Gy in 35 fractions was started, under continuous support with mosapride. This curative treatment was successfully completed without recurrent gastrointestinal symptoms, and this patient remains alive with no disease progression at six months after the treatment.

All procedures performed in this study were in accordance with the ethical standards of Kindai University and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

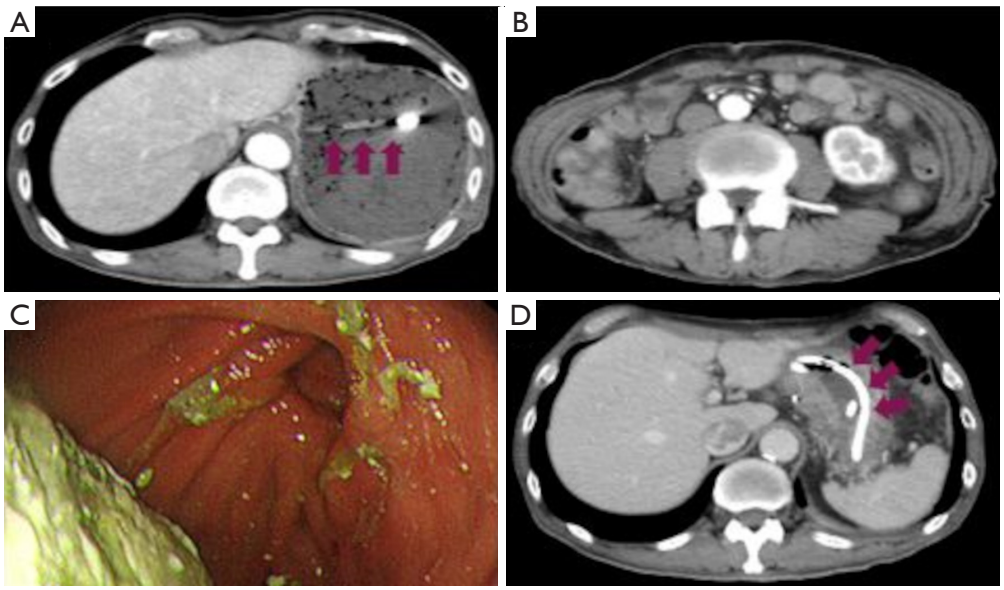

Figure 1 Computed tomography (CT) scans and an esophagogastroduodenoscopy image as evidences of gastroparesis. (A,B) Contrast-enhanced CT scans performed three days after discontinuation of enteral feeding through nasogastric tube (arrows) showed abnormally dilated stomach (A) without intestinal dilation (B). (C) Esophagogastroduodenoscopy showed a large amount of gastric content despite the discontinuation of tube feeding for more than three days, without any findings suggesting gastric outlet obstruction and mucosal impairment. (D) Complete resolution of delayed gastric emptying was achieved with mosapride, even after resumption of enteral feeding by nasogastric tube (arrows). These images are published with the patient's consent.

Discussion

We presented a characteristic case of gastroparesis during a course of intensive cytotoxic chemotherapy for curative treatment of solid cancer. We immediately diagnosed this disease which could lead to proper induction of mosapride with a resultant prompt and complete recovery of gastric motility and safe completion of subsequent definitive radiotherapy with high-dose cisplatin. Gastroparesis has not been well noted thus far as a chemotherapy-induced adverse event at least in solid cancers, therefore our report should be valuable for many oncologists.

Gastroparesis is a syndrome characterized by delayed gastric emptying in the absence of a mechanical obstruction (3). This is generally associated with diabetes mellitus, prior gastric surgery, antimotility medications, neurologic disorders, endocrine disorders, collagen vascular disorders, and viral infection, all of which were not regarded as causes of gastroparesis in this case. This case experienced distal subtotal gastrectomy, but very long duration after such surgery should exclude the possibility of this prior history as a main cause of his gastroparesis. Most cases of postsurgical gastroparesis occur within one year after surgery, and the occurrence after a few years is very rare (4). The fact that this case was disease-free for more than four decades could deny the gastric surgery to be a cause of gastroparesis although this can be only very partially associated with his clinical course. Opioids can cause delayed gastric emptying, but the discontinuation of the drug for more than two weeks should exclude this medication as a cause of gastroparesis in this case (2). Gastric scintigraphy was not approved for the diagnosis of gastroparesis in our country, but we should consider that severe delayed gastric emptying could be clinically confirmed by both CT scan and EGD after complete discontinuation of enteral feeding for three days in our case, as also reported in a recent report of gastroparesis in European country (5).

Chemotherapy-induced gastroparesis has been well recognized as a rare but careful complication with high-dose chemotherapy such as myeloablative regimens prior to bone marrow transplantation in blood cancers by several case reports (6,7). However, there is an only one case report of this disease in chemotherapy for solid cancer, which was published in 1980s (8). This report also suggested that gastroparesis might be an adverse event as a cumulative toxicity of platinum-based chemotherapy. The total dose

of cisplatin before the occurrence of his gastroparesis was more than 500 mg as a result of very aggressive regimen for germ cell tumor, although such dose is never used in the current standard practice. Therefore, the current case is very unique in developing gastroparesis in the phase after a single dose of cytotoxic chemotherapies which are presently used against certain types of solid cancers. Our report is thus notable and educational in alerting modern oncologists to this unfamiliar event as a possible complication of intensive chemotherapy even in the current era.

Peripheral neuropathy is a major adverse event of several types of chemotherapies such as taxanes, vinca alkaloids as well as platinum-compounds. This usually presents as sensory neuropathy, although autonomic neuropathy is possible (9). Gastroparesis is caused by a disruption of coordination of multiple systems required for gastric motility including gastric smooth muscles, autonomic nerves and specialized pacemaker cells, the intestinal cells of Cajal (3). Therefore, in the current case, taxane and platinum-based high-dose intensive chemotherapy should be suspected as a main contributor to induce gastroparesis because of their potential to cause autonomic neuropathy. It is difficult to determine whether cisplatin or docetaxel was more associated with the development of gastroparesis in the current case. A previous study evaluating the neurotoxicity of cisplatin and docetaxel indicated that the severity of the drug-induced neuropathy was higher in the combination than in either drug as single agent at similar doses (10). Accordingly, we presumed that synergistic toxicity for autonomic nerve system by both drugs is a rational mechanism of gastroparesis.

Management of gastroparesis often requires pharmacologic therapies including macrolide antibiotics and 5HT4 agonists in addition to dopamine or dopamine receptor antagonists (2). Refractory cases may require further interventions such as tricyclic antidepressants, serotonin reuptake inhibitors, and gastric electrical stimulation. This is distinct from that of CINV in which 5-HT2 antagonists and benzodiazepines as well as dopaminergic antagonists are generally used (1). Therefore, oncologists should note gastroparesis as a differential diagnosis of chemotherapy-induced GIAE especially when the patient receives multiple neurotoxic agents.

We reported a case of gastroparesis caused by intensive neurotoxic chemotherapies against solid cancer even in the current standard practice, which was successfully treated with a proper management with 5HT4 agonist. Although gastroparesis during chemotherapy for solid cancer is rare, it is important to note this complication because the delay in its management can be detrimental to treatment outcome of such concomitant malignancy. Thus, we should consider a possibility of gastroparesis when patients present persistent upper abdominal symptoms after neurotoxic chemotherapies for solid cancer.

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Footnote

Reporting Checklist: The authors have completed the CARE reporting checklist. Available at https://tcr.amegroups.com/article/view/10.21037/tcr-21-2776/rc

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study were in accordance with the ethical standards of Kindai University and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

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