A Case of Non-occlusive Mesenteric Ischemia with Massive Hepatic Portal Venous Gas Treated Conservatively

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Non-occlusive mesenteric ischemia (NOMI) is caused by ischemia and necrosis of the intestinal tract without organic obstruction of the main mesenteric artery. Accordingly, in many cases, resection of the ischemic intestinal tract is performed to save the life of the patient. However, conservative treatment has also been reported in some cases. Arterial vasodilator therapy using angiography is considered the gold standard for NOMI treatment. However, for facilities without capacity for angiography, conservative management is needed. Herein, we report a case of NOMI in an 85-year-old woman hospitalized for an odontoid process fracture. On post-admission day 14, the patient developed acute onset of epigastric pain, with evidence of hepatic portal venous gas (HPVG) on computed tomography (CT) abdominal imaging. In the absence of peritoneal irritation and findings suggestive of intestinal necrosis on blood tests, combined with the risk of cervical cord injury with intubation for surgery, we initiated continuous intravenous administration of prostaglandin E1 (PGE1, 0.01 μg/kg/min) on the same day of symptom onset, achieving resolution of epigastric pain on the next day. PGE1 administration was continued to day 5 after symptom onset, with no worsening of symptoms after PGE1 discontinuation. Blood tests showed no deterioration **(Fig. 1)**. The patient was discharged on day 63. Continuous intravenous infusion of PGE1 for NOMI may be an option for the conservative treatment of early onset or no intestinal necrosis-associated NOMI.
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Ⅰ Introduction

Non-occlusive mesenteric ischemia (NOMI) is a progressive disease, which is fatal, and therefore requires prompt treatment. The accepted gold standard treatment for NOMI is intra-arterial vasodilator infusion using angiography[1)2)]. However, angiography is not available in all medical facilities. Continuous intravenous prostaglandin E1 (PGE1) therapy, which obviates the need for angiography capacity, has been proposed as an alternative, and its efficacy for NOMI has been demonstrated in recent years[3)]. Herein, we describe a case of NOMI treated with continuous intravenous PGE1 therapy at our center, which is a regional hospital.

Ⅱ Case Presentation

An 85-year-old woman was admitted to our hospital for an odontoid process fracture. On post-admission day 14, the patient reported acute onset of epigastric pain. Accordingly, NOMI with hepatic portal venous gas (HPVG) was diagnosed on abdominal computed tomography (CT) imaging and the patient was referred to the department of surgery for treatment.

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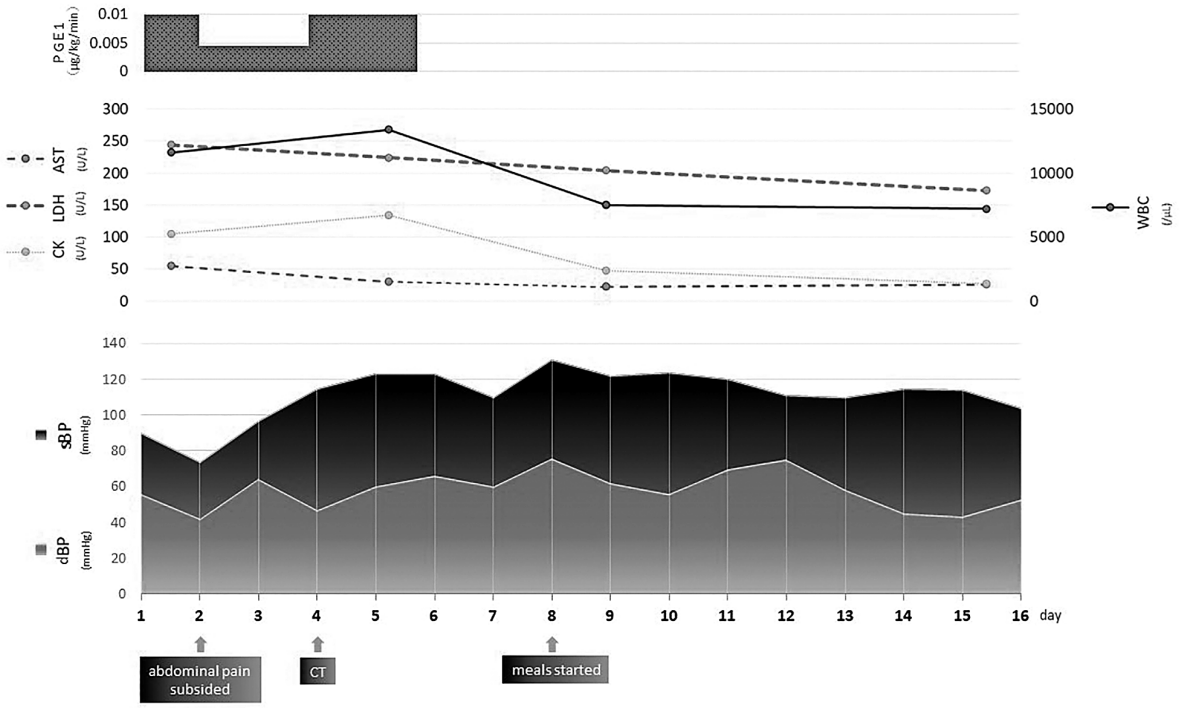

Fig. 1 Treatment and clinical course. Top panel, PGE1 doses and schedules of drug therapies. Middle panels, clinical findings. WBC, white blood cell ; CK, creatine kinase ; LDH, lactate dehydrogenase ; AST, aspartate transaminase. Bottom panels, blood pressure and clinical progress.

The prior history of the patient included systemic scleroderma, interstitial pneumonitis, and surgery for a subarachnoid hemorrhage. She was on prednisone (5 mg daily) for systemic scleroderma. Her blood pressure was 90/56 mmHg, heart rate was 74 /min, and SpO_2 was 96 %. She also had tenderness in the upper abdomen, with no recurrent pain or muscular defense on palpation. Blood levels were within normal limits, with no findings suggestive of intestinal necrosis : white blood cell count, 11600/μL ; AST, 55 U/L ; ALT, 45 U/L ; LDH, 244 U/L ; ALP, 281 U/L ; CK, 105 U/L ; and CRP, 0.66 mg/dL. In addition, no metabolic acidosis was observed (pH, 7.48 ; HCO3, 21.1 mmol/L ; base excess, −1.5 mmol/L). Unfortunately, our facility does not have the ability to measure lactate levels. Abdominal CT revealed severe intrahepatic portal venous gas **(Fig. 2a)**, with discontinuity and segmental loss of contrast effect in the small intestinal wall **(Fig. 2b)**. Moreover, evidence of gas in the superior mesenteric vein and intestinal pneumatosis were observed **(Fig. 2c–d)**. On chest CT, interstitial and emphysematous changes were visible in the lower lung fields, bilaterally **(Fig. 3)**. Based on the above, the diagnosis of NOMI with HPVG and intestinal pneumatosis was confirmed. The consulting anesthesiologist identified the risk of exacerbation of the odontoid process fracture with tracheal intubation during surgery, with interstitial pneumonitis associated with systemic scleroderma being an additional risk. In the absence of peritoneal irritation symptoms, conservative treatment was initiated with the possibility of transferring the patient to a more advanced medical institution in the event of exacerbation of abdominal symptoms. We started continuous intravenous administration of PGE1 (dose, 0.01 μg/kg/min) on the day of symptom onset **(Fig. 1)**. Due to a temporary decrease in blood pressure (71/45 mmHg), the dose was reduced to 0.004 μg/kg/min. Abdominal pain resolved on the next day. Repeat abdominal CT on day 4 after symptom onset revealed resorption of the portal venous gas and intestinal pneumatosis **(Fig. 4)**. Continuous intravenous administration of PGE1 was maintained to day 5 after symptom

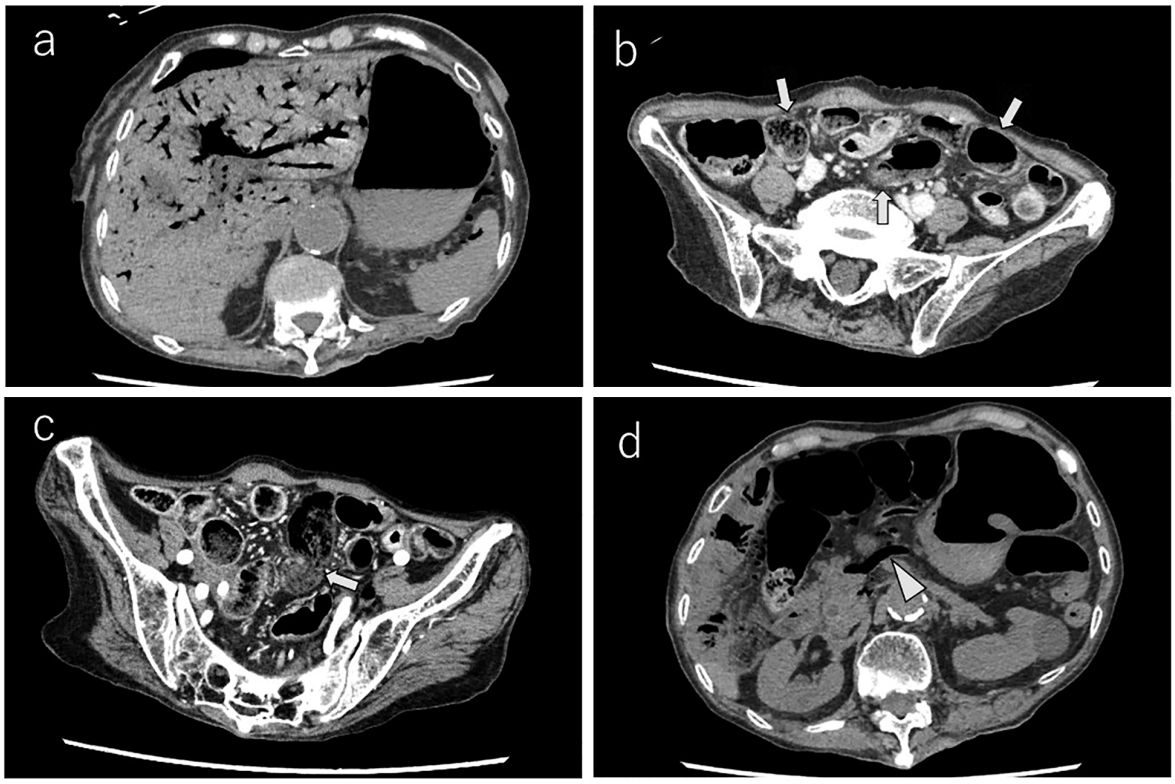

Fig. 2 Abdominal computed tomography (CT) at the time of symptom onset
(a) Intrahepatic portal venous gas observed in the liver.
(b, c) Discontinuity and segmental loss of contrast effect in the small intestinal wall (arrows).
(d) Intestinal pneumatosis and gas in the superior mesenteric vein (arrowheads).

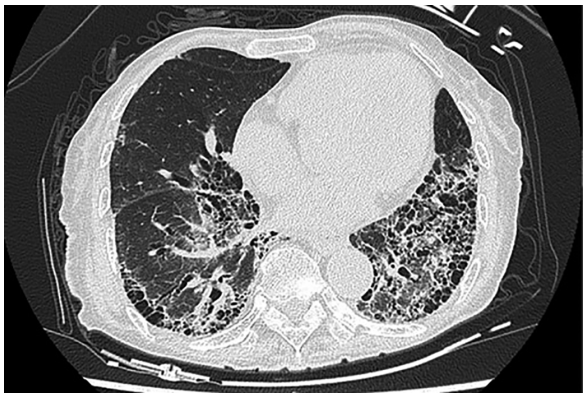

Fig. 3 Chest computed tomography (CT), showing interstitial and emphysematous changes in the lower lung fields, bilaterally.

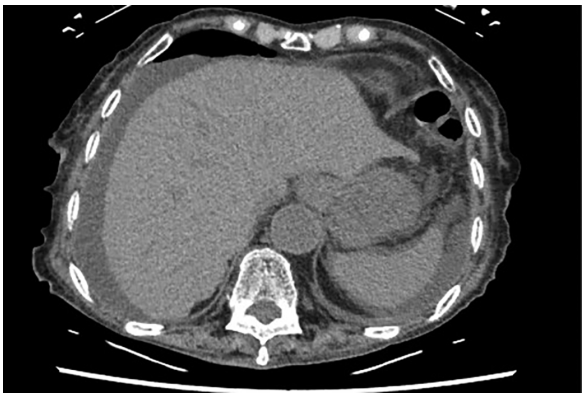

Fig. 4 Abdominal computed tomography (CT) on day 4 after symptom onset. Although ascites were observed, but without symptomology, resolution of the intrahepatic portal venous gas was achieved.

onset. After treatment discontinuation, no exacerbation in abdominal symptoms was observed. The patient started eating on day 8 after symptom onset and was transferred to the orthopedic department on day 20 and discharged on day 63. On discharge, the patient walked independently. Of note, off-label PGE1 was used after urgent review by the Ethics Committee.

Ⅲ Discussion

NOMI is an acute intestinal circulatory disorder with poor initial symptoms, often resulting in intestinal necrosis and shock by the time symptoms become apparent[1]. This disorder is thought to be caused by physical stress, dehydration, or septic shock, which leads to a state of low return flow to the intestinal tract due to constriction of mesenteric vessels. Risk factors for NOMI include cardiovascular disease (heart failure, aortic insufficiency, arrhythmia, and arteriosclerosis), decreased blood volume (dehydration and bleeding), sepsis, dialysis, and administration of vasoconstrictive drugs[4)5)]. In the case presented herein, a cervical corset was placed around the neck of the patient to stabilize the odontoid process fracture. We postulated that stress from the physical restraints caused sympathetic dominance, release of catecholamines, and spasm of the mesenteric vessels, resulting in the development of NOMI.

According to the treatment algorithm for NOMI[2], the gold standard for diagnosis and treatment is abdominal angiography and intra-arterial vasodilator therapy, with surgery recommended in the presence of peritoneal signs[2] . Frequently, NOMI results in an unstable circulatory status, requiring angiography, an alternative to surgical treatment, for patient safety. However, the implementation rate of conservative treatment is low[6]. Moreover, angiography is not available in all hospitals. In fact, our hospital is located in Kiso County, which has a population of approximately 25000, and has no radiologists or facilities for performing angiographic examinations. This underlines the importance of a conservative approach for NOMI. Of note, we were prepared to transport the patient to an advanced medical institution if the treatment was not successful in resolving the condition of the patient. We opted to begin with the conservative treatment approach as the required transport time of 1-2 h may have allowed progression of the NOMI status, with the possibility of irreversible intestinal necrosis. Moreover, in this case, the possibility of worsening of the odontoid fracture needed to be considered.

The increasing use of multidetector CT has improved the diagnosis of NOMI without requiring angiography[7]. However, for treatment purposes, the alternative to angiography remains a challenge. Some studies have reported on the conservative treatment of NOMI using intravenous fluids for hydration and antibiotics[8]. For instance, Mitsuyosi et al.[3] reported on the effectiveness of continuous intravenous PGE1 therapy for the treatment of NOMI. PGE1 relaxes vascular smooth muscles, improving vasospasm and, thus, improving intestinal blood supply[9)10)]. Of note, Mitsuyosi et al. implemented continuous intravenous PGE1 treatment in 9 cases of suspected NOMI, with the treatment initiated prior to the confirmation of diagnosis. Of these 9 cases, recovery was achieved in 7 cases, with patients discharged without lasting effects. No abdominal angiography was performed in any of the cases. The mean duration of PGE1 administration was 4.8 d, administered as per recommended guidelines. By comparison, symptom resolution was achieved in our patient on the day following the initiation of PGE1 therapy, with blood parameter levels remaining within normal limits. The normal blood parameter levels in our case were a key difference compared with the cases reported by Mitsuyoshi et al.[3]. In their study, the blood tests of patients showed elevated levels of AST and ALT. Moreover, our patient was able to communicate clearly as she did not require sedation for her odontoid fracture. Early detection of NOMI in our case may have greatly contributed to the positive clinical outcomes of continuous intravenous PGE1 therapy. Of note, Oshikata et al.[11] reported on the effectiveness of continuous PGE1 in combination with steroids in a case of NOMI, whereas Kurita et al.[12] used PGE1 in combination with papaverine.

In our case, NOMI was associated with massive HPVG, which is a highly lethal condition that develops with critical illnesses, such as intestinal ischemia. intestinal obstruction, enteritis, and peptic ulcer, and is associated with a mortality rate of 14-100 %[8]. Therefore, HPVG requires emergency surgical management. HPVG results from the rapid absorption of carbon dioxide and, therefore, its identification is highly dependent on the timing of diagnostic imaging[13]. There-

fore, the treatment should be responsive to the pathology and severity of the underlying disease[13]. In our case, resolution of the HPVG was confirmed on abdominal CT on day 4 after treatment initiation, which was consistent with the findings by Seike et al.[8] who reported resolution of HPVG at 20 h after treatment initiation.

The patient in our case had a history of long-term use of oral steroids for systemic scleroderma. Steroids decrease the number of lymphocytes in the gastrointestinal wall, especially in Peyer's patches, contributing to the impairment of the intestinal defense barrier system, causing weakening of the intestinal wall, decreased bowel movements, and excessive production of intestinal air[14)15)]. Impaired blood flow to the intestinal wall due to steroid administration is likely to result in intestinal wall damage and hypervolemia. Therefore, we considered that the massive HPVG that developed concomitant to the NOMI in our patient was not clinically serious, with abdominal findings, blood tests, and imaging studies not providing any evidence of intestinal necrosis. In making decisions about patient management, we also needed to consider the effect of treatment, including surgery, on the neck fracture and severe pneumotitis.

In summary, our case showed that initiation of continuous intravenous PGE1 therapy early after the onset of NOMI symptomology, is a feasible conservative treatment that could serve as a main treatment option in medical institutions that do not have abundant resources, such as the capacity for angiography. For patients who are vitally stable, have mild abdominal pain, no signs of intestinal necrosis on CT, and no findings of intestinal necrosis on blood test, but for whom NOMI cannot be ruled out, PGE1 continuous intravenous treatment may be considered acceptable in clinical practice. In contrast, for cases of NOMI with unstable vitals, severe abdominal pain, or worsening, this option should not be considered.

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Consent for publication

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Conflicts of interest

There are no conflicts of interest to declare.

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