

Nonocclusive Mesenteric Ischemia in a Patient on Maintenance Hemodialysis

Sang Youb Han, M.D., Young Joo Kwon, M.D., Jin Ho Shin M.D.
Heui Jung Pyo, M.D., Ae Ree Kim, M.D.*

*Division of Nephrology, Department of Internal Medicine, Department of
Anatomic Pathology*, College of Medicine, Korea University, Seoul, Korea*

Nonocclusive mesenteric ischemia (NOMI) is known to occupy about 25% to 60% of intestinal infarction. NOMI has been reported to be responsible for 9% of the deaths in the dialysis population and the postulated causes of NOMI include intradialytic hypotension, atherosclerosis and medications, such as diuretics, digitalis and vasopressors. Clinical manifestations, such as fever, diarrhea and leukocytosis, are nonspecific, which makes early diagnosis of NOMI very difficult. Case: A 66-year-old woman on maintenance hemodialysis for 5 years was admitted with syncope, abdominal pain and chilly sensation. Since 7 days prior to admission, blood pressure on the supine position during hemodialysis had frequently fallen to 80/50 mm Hg. Four days later, she complained of progressive abdominal pain. Rebound tenderness and leukocytosis (WBC 13900/mm³) with left shift were noted. Stool examination was positive for occult blood. Abdominal CT scan showed a distended gall bladder with sludge. Under the impression of acalculous cholecystitis, she was operated on. Surgical and pathologic findings of colon colon were compatible with NOMI. Because of recurrent intradialytic hypotension, we started midodrine 2.5 mg just before hemodialysis and increased the dose up to 7.5 mg. After midodrine therapy, blood pressure during dialysis became stable and the symptoms associated with hypotension did not recur. Conclusion: As NOMI may occur within several hours or days after an intradialytic hypotensive episode, abdominal pain should be carefully observed and NOMI should be considered as a differential diagnosis. In addition, we suggest that midodrine be considered to prevent intradialytic hypotensive episodes.

Key word : *Nonocclusive mesenteric ischemia (NOMI), dialysis, midodrine*

INTRODUCTION

Nonocclusive mesenteric ischemia (NOMI) was reported in a heart failure patient by Ende in 1958¹⁾. In dialysis patients, Dahlberg et al.²⁾ reported 6 patients with acute mesenteric ischemia, and 3 of them were NOMI. NOMI is the cause in at least 20% to 30% of cases of acute mesenteric ischemia³⁾, and the mortality rates of NOMI were reported from 71% to 100% (4). Diamond et

al.⁵⁾ reported that NOMI was the cause of mortality in 9% (5/56) of the deaths in the dialysis population. So, early recognition and prompt management is necessary to improve survival.

We describe NOMI in a patient with hypotensive episodes in dialysis therapy who was admitted with abdominal pain and who undertook colectomy. Hypotensive episodes decreased and related symptoms were improved after midodrine therapy.

CASE

A 66-year-old woman on maintenance hemodialysis for 5 years was admitted with syncope, abdominal pain

Address reprint requests to : Young Joo Kwon, M.D., Div. of Nephrology, Dept. of Internal Medicine, Korea University Guro Hospital, #80 Guro-Dong Guro-Gu Seoul, South Korea 152-050

and chilly sensation. She had been also diagnosed as having microvascular angina 3 years prior to admission. Hemodialysis was being done 3 times per week : her dry body weight was 46 kg and the interdialytic weight changes were about 3 kg. Her interdialytic, systolic and diastolic pressures had been 100 to 140 mmHg and 90 to 100 mmHg on the supine position, respectively. During hemodialysis, systolic pressures had been above 100 mmHg on supine position. However, interdialytic and intradialytic blood pressures had showed a tendency to decrease for several months prior to admission. So, she had not taken antihypertensive medication to prevent intradialytic hypotension.

Since 7 days prior to admission, blood pressure on the supine position during hemodialysis had frequently fallen to 80/50 mmHg. On admission, the blood pressure on the supine position was 80/50 mmHg, body temperature 38.8 , heart rate 104 per minute and respiratory rate 26 per minute. Abdominal examination showed mild abdominal tenderness without rebound tenderness.

Laboratory data were as follows: leukocyte count 5200/mm³ with normal differential count, hemoglobin 12.8 g/dL, platelet count 112000/ μ L, Bun 60 mg/dL, serum creatinine 7.3 mg/dL, calcium 9.8 mg/dL, phosphorus 7.3 mg/dL, AST 63 IU/L, ALT 64 IU/L, alkaline phosphatase 89 IU/L, -glutamyl transferase 55 IU/L, bilirubin 0.54 mg/dL, total protein 8.6 g/dL, albumin 5.7 g/dL, amylase 480 IU/L(normal, 60- 180), lipase 13 IU/L(normal, 30- 190), PT 11.6 second(INR 0.98 sec) and aPTT 40.1 second(control 30 sec). Simple abdominal x-ray and abdominal ultrasound did not reveal any abnormal findings. 2-D echocardiography showed diffuse left ventricular dysfunction with slightly decreased ejection fraction.

Four days later, she complained of progressive abdominal pain, and rebound tenderness and leukocytosis (leukocyte count 13900/mm³) with left shift were noted. Stool examination was positive for occult blood. Abdominal CT scan showed a distended gall bladder with sludge. Under the impression of acalculous cholecystitis, she was operated on. On operation, ischemic necrosis at the sigmoid colon and mesocolon in addition to acalculous cholecystitis were found, and Hartman's operation and cholecystectomy were undertaken. Pathologic findings of the colon were compatible with NOMI(Fig. 1).

After that, systolic blood pressures rose to 80 to 100 mmHg, but intradialytic hypotension(60/30 mmHg)

occurred recurrently. We started midodrine 2.5mg just before hemodialysis and increased the dose up to 7.5mg. After midodrine therapy, the blood pressure during dialysis became stable. Although hypotensive episodes occurred, the degree of hypotension was mild and the symptoms associated with hypotension did not occur(Fig. 2).



Fig. 1. Pathology of resected colon.

The wall of the colon shows superficial sloughing of the epithelium with preservation of the architecture. There are edema, congestion and an inflammatory exudate in the submucosa.(Hematoxylin and Eosin, $\times 40$)

DISCUSSION

In chronic renal failure, peptic ulcer and colonic dysfunction are the most common gastrointestinal manifestations. They may be complicated by perforation, bleeding, constipation and colonic pseudoobstruction. However, ischemic bowel disease is less frequently recognized in the dialysis population⁴. As a cause of acute mesenteric ischemia, NOMI has been emerging importantly. Bender et al.⁶ reported that 11 of 12 patients with acute abdomen undergoing hemodialysis were diagnosed as NOMI. Therefore, they insisted that NOMI be the most common cause of acute abdomen in dialyzed patients and should be the most probable diagnosis until proven otherwise.

Patients with ESRD have several risk factors for bowel infarction, which include advanced atherosclerosis, low cardiac output states, several medications and intradialytic hypotensive episodes.

Low cardiac output states such as heart failure,

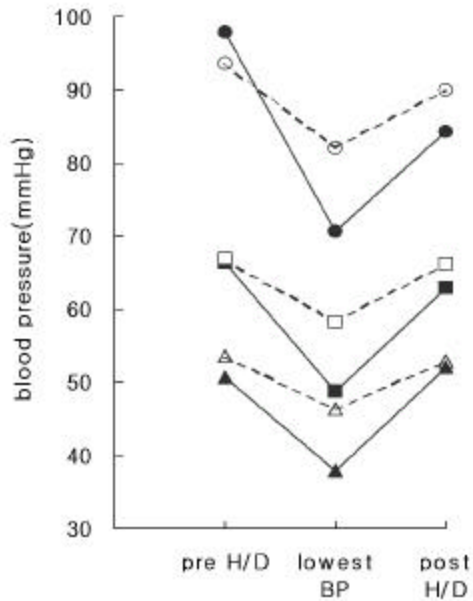


Fig. 2. Blood pressure(BP) without and with midodrine.

Each blood pressure was recorded for consecutive hemodialysis sessions before and after midodrine therapy. Each point is a mean value of 14 recorded values (hard line : before midodrine therapy, dot line : after midodrine therapy, ○ : systolic BP, □ : mean arterial pressure, ▲ : diastolic BP). There were significant differences between before and after midodrine therapy in the lowest blood pressure during hemodialysis by Student's t-test. (○ : p=0.012, □ : p=0.007, ▲ : p=0.047)

myocardial infarction, arrhythmia, sepsis and hypovolemia, may decrease splanchnic blood flow and cause vasoconstriction by excessive sympathetic activity that will eventually lead to NOMI⁷. Mesenteric vasospasm may represent a homeostatic mechanism to maintain cardiac and cerebral perfusion. Such splanchnic vasoconstriction is potentiated by a number of vasoactive agents. Reduced blood flow from vasoconstriction induces inadequate intestinal tissue oxygenation and results in vulnerability to tissue injury as well as reperfusion injury by oxygen radicals⁸.

Several medications such as diuretics⁹, β -blockers¹⁰ and digoxin¹¹ have been associated with NOMI

Symptomatic intradialytic hypotension has been described to occur in as many as 20% to 50% of patients³. This problem has been ascribed to multiple factors including excessively rapid ultrafiltration rate¹², autonomic dysfunction¹³, disturbance in cardiac function and vascular responsiveness¹⁴ and paradoxical withdrawal of sympathetic activity¹⁵.

In our case, the repetitive intradialytic hypotensive episodes may be the cause of NOMI. The cause of hypotensive episodes was not clear, but uremia-induced autonomic dysfunction might be considered. Head-up tilting test may be helpful in making a diagnosis of autonomic dysfunction.

Because symptoms and signs of NOMI are nonspecific, the diagnosis of this entity is very difficult. Charra et al.¹⁶ reported the clinical features of 13 bowel necrosis episodes in hemodialysis patients. All of them complained of abdominal pain. Although fever, ileus, diarrhea and leukocytosis were found, they were not constant manifestations. In contrast to Charra's report, Howard et al.¹⁷ reported the absence of abdominal pain in 20 to 25% of cases with NOMI. Our case also showed nonspecific manifestations such as abdominal pain, fever and leukocytosis.

Splanchnic vasospasm, which may develop in hours or days after the initial insult, results in a delayed appearance of the disorder⁷. Therefore, the diagnosis of this condition should be considered whenever dialysis patients with risk factors complain of severe and abrupt abdominal discomfort within several hours or several days after intradialytic hypotensive episodes. Four days after nonspecific abdominal pain, our case was diagnosed as NOMI by surgical and pathological findings.

After colectomy, this patient continued to show recurrent intradialytic hypotensive episodes. For the prevention of these episodes, a variety of maneuvers, including sodium modeling and cooling of the dialysate, have been used with no success before the trial of midodrine therapy.

Midodrine is an oral agent with selective α -adrenergic agonist activity that has been used successfully in the treatment of orthostatic hypotension secondary to autonomic dysfunction¹⁸. The efficacy of midodrine therapy in patients with intradialytic hypotension was reported by Blowey et al.¹⁹. Midodrine is a prodrug that is rapidly and almost completely absorbed from the gastrointestinal tract after oral

administration. The peak plasma levels of midodrine and its active metabolites, de-glymidodrine, were observed 60 and 90 minutes after the oral dose, respectively. De-glymidodrine was effectively removed by hemodialysis ($t_{1/2}$: 10 hrs without dialysis, 1.4 hr with dialysis)¹⁹. The effect of midodrine to increase blood pressure comes from its constrictive effect on the arterioles and venous capacitance vessels. In this way, it prevents venous blood pooling and augments venous return which will subsequently increase cardiac output²⁰. Generally, midodrine appears to be well tolerated. It has minimal cardiac and central nervous system effects by virtue of its α -1 receptor specificity and its inability to cross the blood-brain barrier, respectively. Adverse effects such as piloerector reactions, scalp pruritus, urinary urgency and headache were observed but they were usually mild²⁰.

In our case, midodrine has decreased intradialytic hypotensive episodes without adverse effects for six months. The blood pressure became more stable after a trial of midodrine than before (Figure 2). We compared the frequency of intradialytic hypotensive episode between before and after a trial of midodrine when ultrafiltration volume was below 3kg. The frequencies of ultrafiltration volume under 3kg were 7 and 11 of each 14 sessions before and after midodrine therapy. Intradialytic hypotensive episodes occurred in 6 of 7 sessions before midodrine therapy and 4 of 11 sessions after midodrine therapy, respectively ($p=0.04$). Also, the degree of intradialytic hypotension was changed. Intradialytic hypotension, before midodrine therapy, had fallen to 50 mmHg of systolic pressures, but the systolic pressures had fallen only to 80 mmHg after midodrine therapy.

In conclusion, NOMI should be included in differential diagnosis when patients on maintenance dialysis present abdominal pain after intradialytic hypotension. Also, we suggest that midodrine be considered for the treatment of intradialytic hypotension of unknown origin or unresponsiveness to other trials.

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