[CASE REPORT]

Stent Placement for Malignant Inferior Vena Cava Syndrome in a Patient with Recurrent Colon Cancer

Shinichi Morita¹, Shunsuke Sugawara², Takeshi Suda¹, Didik Prasetyo¹, Yuka Kobayashi³,
Takahiro Hoshi¹, Satoshi Abe¹, Kazuyoshi Yagi¹ and Shuji Terai⁴

Abstract:

A 70-year-old man was admitted to our hospital with gait disturbance due to marked edema of the lower limbs for more than 6 months. He had been receiving systemic chemotherapy over two years for multiple recurrence after sigmoid colon cancer resection. Contrast-enhanced computed tomography demonstrated severe inferior vena cava (IVC) stenosis due to compression by lymph node metastases, i.e. IVC syndrome. As increased doses of diuretic agents failed to improve the edema, IVC stent placement was performed. This led to significant improvement of the edema and complete gait normalization. This case demonstrates the efficacy of IVC stent placement for IVC syndrome.

Key words: inferior vena cava syndrome, IVC stent, stent placement, colon cancer, quality of life

(Intern Med 59: 2885-2890, 2020)

(DOI: 10.2169/internalmedicine.5033-20)

Introduction

Vena cava syndrome is a complication of malignant tumor progression (1-3). Enlarged tumors disturb the venous return by compressing the vena cava, causing various symptoms. Lung or mediastinal tumors may cause superior vena cava (SVC) stenosis; this results in SVC syndrome, with edema of the chest, upper limbs, head, and neck, followed by respiratory and central nervous symptoms, which can sometimes be fatal and therefore require immediate treatment (2, 4-6). Liver and retroperitoneal tumors, by contrast, can cause inferior vena cava (IVC) stenosis and IVC syndrome, with lower limb edema and intractable ascites (7-9). This causes lower limb pain, abdominal bloating, and gait disturbance. However, IVC syndrome is only rarely fatal, and many patients are followed up with conservative treatment with only minimal improvement of symptoms. As a result, the quality of life (QOL) is significantly impaired.

In recent years, several reports have indicated that percutaneous stent placement in the stenotic area can achieve a rapid and effective therapeutic effect for vena cava syn-

drome (10-14). We herein report a case of IVC syndrome caused by lymph node metastases from recurrent colon cancer. The patient had been suffering from severe lower limb edema for more than six months, but the symptoms were significantly improved by IVC stent placement.

Case Report

A 70-year-old Japanese man was referred to our hospital with a complaint of marked lower limb edema and gait disturbance. He had undergone laparoscopic partial resection for sigmoid colon cancer at a referral hospital three years earlier. Utilizing the Union for International Cancer Control TNM classification (8th edition) (15), the tumor of the sigmoid colon was classified as pT3N0M0, Stage IIA. A year later, multiple recurrences of liver and para-aortic lymph node metastases were noted, necessitating continuation of systemic chemotherapy. Lower limb edema had appeared six months earlier. Despite diuretic therapy, his lower limb edema had worsened, and his body weight had increased by more than 10 kg. He had difficulty walking due to edema in both legs, and urination had become difficult due to marked

¹Department of Gastroenterology and Hepatology, Uonuma Institute of Community Medicine Niigata University Hospital, Japan, ²Department of Diagnostic Radiology, National Cancer Center Hospital, Japan, ³Department of Gastroenterology and Hepatology, Nagaoka Central General Hospital, Japan and ⁴Division of Gastroenterology and Hepatology, Graduate School of Medical and Dental Sciences, Niigata University, Japan

Received: April 6, 2020; Accepted: June 11, 2020; Advance Publication by J-STAGE: July 28, 2020

Correspondence to Dr. Shinichi Morita, m0riz0u@extra.ocn.ne.jp

Figure 1. (a) Photograph before IVC stent placement showing severe hydrocele testis and bilateral leg edema. (b) Axial abdominal contrast-enhanced CT image showing the IVC surrounded by lymph node metastases (arrow), causing stenosis (arrowheads). (c) CT reconstruction venography showing severe stenosis of the IVC about 3 cm cranial from the confluence of the left and right common iliac veins (arrowheads).

Table 1. Laboratory Data on Admission.

Hematologic test		Coagulation		BUN	
White blood cells	5,100 / μ L	PT-INR	0.92	Creatinine	1.1 mg/dL
Neutrophils	82.9 %	APTT	27.9 s	Sodium	142 mmol/L
Lymphocytes	9.9 %	D-dimer	0.8 μ g/mL	Potassium	3.8 mmol/L
Monocytes	6.4 %	Chemistry		Chloride	105 mmol/L
Eosinophils	0.6 %			CRP	0.54 mg/dL
Basophils	0.2 %			BNP	16.5 pg/mL
Red blood cells	295 $\times$ 10 ⁴ / μ L			CEA	53.6 ng/mL
Hemoglobin	10.0 g/dL	AST	25 IU/L	CA19-9	16.0 U/mL
Platelet count	26.6 $\times$ 10 ⁴ / μ L	ALT	27 IU/L	Urine test	
		ALP	397 IU/L		
		γ -GTP	121 IU/L		
		T.Bil	0.9 mg/dL		
		D.Bil	0.1 mg/dL	Occult blood	negative
		LDH	158 IU/L	Glycosuria	negative
				Proteinuria	negative

PT: prothrombin time activity, APTT: activated partial thromboplastin time, AST: aspartate aminotransferase, ALT: alanine aminotransferase, ALP: alkaline phosphatase, γ -GTP: γ -glutamyl transpeptidase, T.Bil: total bilirubin, D.Bil: direct bilirubin, LDH: lactate dehydrogenase, BUN: blood urea nitrogen, CRP: C-reactive protein, BNP: brain natriuretic peptide, CEA: carcinoembryonic antigen, CA19-9: carbohydrate antigen 19-9

scrotal edema (Fig. 1a). Based on these symptoms, the patient's Eastern Cooperative Oncology Group Performance Status Grade had decreased from one to three, so systemic chemotherapy had been discontinued.

On presentation, the patient's body weight was 64 kg, and marked pitting edema was evident in the lower limbs, but not the upper limbs. Biochemical tests revealed no abnormalities of the liver or renal function, and the serum albumin level was not decreased. His blood coagulation remained within normal limits, and a urinalysis was negative

for proteinuria (Table 1). Electrocardiography and chest X-ray revealed no abnormalities. Contrast-enhanced computed tomography (CT) demonstrated para-aortic lymph node metastases around the IVC, with compression and stenosis (Fig. 1b). The IVC was stenotic about 3 cm cranially from the confluence of the left and right common iliac veins (Fig. 1c). However, the stenosis did not reach the hepatic portion of the IVC. The right renal vein joined normally with the IVC, while the left renal vein was obstructed by the tumor. No thrombus was found in the IVC distal from

the stenotic site. IVC syndrome was diagnosed, and IVC stent placement was recommended.

With informed consent from the patient, IVC venography was performed via the right femoral vein approach. A 3-cm-long stenosis was found with the retrograde visualization of collateral veins, such as the ascending lumbar, azygos and hemiazygos veins (Fig. 2a). A guidewire was passed through the stenosis, and a stent delivery system was inserted beyond the site. A self-expandable metallic bare stent, 18 mm in diameter and 60 mm in length (Spiral relief stent; COS-

MOTEC, Tokyo, Japan), was placed across the stenotic site. Venography was then performed to confirm the improvement of flow in the IVC and disappearance of the collateral veins (Fig. 2b). No adverse events were observed during the procedure. A direct oral anticoagulant (edoxaban tosylate hydrate 5 mg/day) was provided from the next day to prevent thrombus formation in the stent. After stent placement, the urine output increased, and the thigh edema began to lessen. One week after the treatment, the bilateral leg edema was markedly reduced, and the average circumference of both the thighs and calves was reduced from 51.6 to 42.5 cm and 40.4 to 33.5 cm, respectively (Fig. 3). The patient's body weight decreased by 14 kg, along with disappearance of the scrotal edema. Furthermore, a normal gait returned without any issues. One month later, systemic chemotherapy was resumed. Seven months after stent placement, there were no stent-related complications, the edema had not recurred, and chemotherapy was able to be continued.

Discussion

Edema is a symptom that reduces the QOL of cancer patients but does not significantly affect the disease prognosis. However, patients suffer gait disturbance and discomfort in the areas affected by edema. There are various causes and conditions responsible for edema, and their understanding is clinically useful (16, 17). Edema can be either systemic or local, with the former arising due to systemic conditions, such as renal dysfunction, congestive heart failure, liver cirrhosis, hypothyroidism, malnutrition and the side effects of anticancer drugs, such as docetaxel (17-22), while the latter is classified as venous, due to deep vein thrombosis or return obstruction; lymphatic, lymph node swelling, or obstruction of lymphatic vessels; inflammatory due to cellu-

Figure 2. (a) Digital subtraction venography showing severe stenosis of the IVC (arrowheads) and retrograde visualization of collateral veins, such as the ascending lumbar, azygos and hemiazygos veins (arrows). (b) Digital subtraction venography after stent placement (arrowheads) demonstrating improvement of flow in the IVC and disappearance of collateral veins.

Figure 3. Changes in the body weight and the circumference of the thigh and calf after placement of the IVC stent. BW: body weight, IVC: inferior vena cava

Table 2. Summary of Stent Placement for Malignant IVC Syndrome.

No.	Reference	Study design	No. of patients	Tumor type or primary disease	Technical success	Clinical success	Major adverse events	Patency	Anti-coagulation therapy	Survival time
1	(10)	Case report	1	Colon cancer with multiple liver metastases	Yes	Yes	No	19.5 months	Yes	19.5 months
2	(30)	Retrospective study	8	Five different tumor types	100%	60%	Stent breakage 1	N/A	N/A	3.0 months (median)
3	(31)	Retrospective study	50	Primary liver tumor 9, Metastatic liver tumor 41	100%	86.4%	Stent migration 2	92% at 3 months 59% at 18 months	No	75 days (median)
4	(9)	Retrospective study	19	Primary liver tumor 3, Metastatic liver tumor 15, Adrenal cancer invasion for IVC 1	100%	79%	Stent compression 2, Stent migration 1	52.6% until death	Yes	N/A
5	(34)	Retrospective study	62 (contain 46 cases of benign disease)	Cancer associated IVC compression 16, Others 46	98%	90%	Stent occlusion 13, Stent stenosis 10	57% at 24 months	Yes	N/A
6	(14)	RCT, prospective study	44 (contain 25 cases of SVC syndrome)	Lung cancer 21, Colorectal cancer 9, Breast cancer 2, Others 12	97.7 %	QOL score significantly improved compared to control group	Pulmonary thromboembolism 2, Dyspnea 1, Hypotension 1	N/A	N/A	67 days (median)
7	Our case	Case report	1	Colon cancer with abdominal lymph node metastases	Yes	Yes	No	7 months (patent)	Yes	7 months (alive)

IVC: inferior vena cava, SVC: superior vena cava, RCT: randomized controlled trial, QOL: quality of life, N/A: information not available

tis; and angioneurotic, occurring in an area paralyzed due to cerebral infarction.

In the case of lower body edema, it is important to distinguish between the lymphatic and venous forms (17, 23). Lymphedema can develop gradually after gynecological, rectal and prostate cancer surgery. Lymphedema is appeared non-pitting edema with no pain. Venous edema, by contrast, is a rapidly developing congestive condition causing distention (17). Due to the large amount of water stored in the interstitium, pitting edema appears.

Malignant vena cava syndrome is associated with the progression of tumors that compress or infiltrate the vessel, impairing blood flow and causing venous edema (1-3). IVC syndrome is caused by liver and retroperitoneal tumors and results in lower limb edema and intractable ascites (7-9). Consequently, the patient experiences lower limb pain, abdominal bloating, renal dysfunction, dysuria and other problems that significantly reduce the QOL. However, the symptoms of IVC syndrome are not necessarily life-threatening, and-unlike SVC syndrome-the condition is often followed with conservative treatment (2, 4-6).

Treatment of IVC syndrome essentially focuses on chemotherapy for the tumor and irradiation for the primary disease (24). This approach is particularly suited as a first-line

treatment for highly sensitive tumors, such as malignant lymphoma and germ cell tumors. However, most patients must maintain an extended course of treatment if the cancers are refractory to chemotherapy, which can lead to a significant reduction in the performance status. Therefore, pharmacotherapy, such as diuretics and albumin preparations (16, 17, 25), is generally complemented by physical therapy, such as massage and the use of compression stockings (26, 27). Collateral venous circulation may develop during follow-up of IVC syndrome, resulting in spontaneous relief of symptoms. In most cases, however, the symptoms do not improve despite long-term conventional treatment.

Vascular bypass is mainly used for vena cava syndrome resulting from a benign disease, but it is also performed for tumor resection in cases of venous invasion (28, 29). However, its degree of invasiveness for malignant vena cava syndrome caused by unresectable cancer is extremely high. The placement of a metal stent for vena cava syndrome has also been used for patients with malignant tumors, resulting in symptom improvement in 60-100% of cases (4, 7, 9, 10, 14, 30-33). Furthermore, stent placement has a low degree of physical invasiveness while achieving rapid and sustained symptom relief. Thus far, two case reports and five clinical studies, including our own, on malignant IVC syndrome

treated with stent placement have been described, and their details are summarized in Table 2 (9, 10, 14, 30, 31, 34). The adverse events of IVC stent placement were reported to include a fever, pain, stent migration and sepsis. Pulmonary embolism was rare but life-threatening (14). The use of pre-operative imaging to confirm the presence of thrombus in the vena cava was considered significant.

Symptom relapse due to stent occlusion has been reported (9, 33). The venous blood flow may become slow and stagnant; coagulation abnormalities resulting from malignant tumors tend to cause thrombotic stent blockage. Although it is desirable to perform anticoagulation therapy after stent placement (31-35), there is little evidence for its effectiveness. Furthermore, tumor invasion within the stent can result in occlusion due to ingrowth and thrombus attachment. Continuation of chemotherapy after stent placement may reduce tumor ingrowth, thus extending the period of stent patency. In the present case, direct oral anticoagulants were started after stent placement. In addition, the improvement in the patient's QOL with the IVC stent placement allowed chemotherapy to be resumed. No stent occlusion was evident during the first seven months of follow-up. Stent placement might improve the prognosis of cases with IVC syndrome.

Although further studies are necessary, the present case suggests that stent placement is feasible and effective for managing IVC syndrome and is not inferior to other treatments.

This case report was approved by the institutional Human Investigation Committee of Uonuma Institute of Community Medicine Niigata University Hospital. Written informed consent was obtained from the patient in accordance with the Helsinki declaration for publication of this case report.

The authors state that they have no Conflict of Interest (COI).

References

- Charnsangavej C, Carrasco CH, Wallace S, et al. Stenosis of the vena cava: preliminary assessment of treatment with expandable metallic stents. *Radiology* **161**: 295-298, 1986.
- Kishi K, Sonomura T, Mitsuzane K, et al. Self-expandable metallic stent therapy for superior vena cava syndrome: clinical observations. *Radiology* **189**: 531-535, 1993.
- Fletcher WS, Lakin PC, Pommier RF, Wilmarth T. Results of treatment of inferior vena cava syndrome with expandable metallic stents. *Arch Surg* **133**: 935-938, 1998.
- Tanigawa N, Sawada S, Mishima K, et al. Clinical outcome of stenting in superior vena cava syndrome associated with malignant tumors. Comparison with conventional treatment. *Acta Radiol* **39**: 669-674, 1998.
- Rowell NP, Gleeson FV. Steroids, radiotherapy, chemotherapy and stents for superior vena caval obstruction in carcinoma of the bronchus: a systematic review. *Clin Oncol* **14**: 338-351, 2002.
- Straka C, Ying J, Kong FM, Willey CD, Kaminski J, Kim DW. Review of evolving etiologies, implications and treatment strategies for the superior vena cava syndrome. *Springerplus* **5**: 229, 2016.
- Brountzos EN, Binkert CA, Panagiotou IE, Petersen BD, Timmermans H, Lakin PC. Clinical outcome after intrahepatic venous stent placement for malignant inferior vena cava syndrome. *Cardiovasc Intervent Radiol* **27**: 129-136, 2004.
- Kudo H, Yata Y, Orihara T, Kageyama M, Takahara T, Sugiyama T. Malignant inferior vena cava syndrome. *Intern Med* **45**: 219-220, 2006.
- Kuettling D, Thomas D, Wilhelm K, Pieper CC, Schild HH, Meyer C. Endovascular management of malignant inferior vena cava syndromes. *Cardiovasc Intervent Radiol* **40**: 1873-1881, 2017.
- Sato Y, Inaba Y, Yamaura H, Takaki H, Arai Y. Malignant inferior vena cava syndrome and congestive hepatic failure treated by venous stent placement. *J Vasc Intervent Radiol* **23**: 1377-1380, 2012.
- Fagedet D, Thony F, Timsit JF, et al. Endovascular treatment of malignant superior vena cava syndrome: results and predictive factors of clinical efficacy. *Cardiovasc Intervent Radiol* **36**: 140-149, 2013.
- Steinberger J, Schenning R. Endovascular reconstruction of malignant IVC and SVC obstruction. *Int Oncol* **111**-113, 2015.
- Marmagkiolis K, Lendel V, Cilengiroglu M. Endovascular management of IVC syndrome after IVC filter placement. *Rev Port Cardiol* **34**: 555.e551-e554, 2015.
- Takeuchi Y, Arai Y, Sone M, et al. Evaluation of stent placement for vena cava syndrome: phase II trial and phase III randomized controlled trial. *Support Care Cancer* **27**: 1081-1088, 2019.
- Gospodarowicz CW. TMN Classification of Malignant Tumors (UICC). 8th ed. Wiley-Blackwell, New York, 2017.
- O'Brien JG, Chennubhotla SA, Chennubhotla RV. Treatment of edema. *Am Fam Physician* **71**: 2111-2117, 2005.
- Trayes KP, Studdiford JS, Pickle S, Tully AS. Edema: diagnosis and management. *Am Fam Physician* **88**: 102-110, 2013.
- Siddall EC, Radhakrishnan J. The pathophysiology of edema formation in the nephrotic syndrome. *Kidney Int* **82**: 635-642, 2012.
- Navas JP, Martinez-Maldonado M. Pathophysiology of edema in congestive heart failure. *Heart Dis Stroke* **2**: 325-329, 1993.
- Sakaide I. Tolvaptan for the treatment of liver cirrhosis oedema. *Expert Rev Gastroenterol Hepatol* **8**: 461-470, 2014.
- Chaker L, Bianco AC, Jonklaas J, Peeters RP. Hypothyroidism. *Lancet* **390**: 1550-1562, 2017.
- Baker J, Ajani J, Scotte F, et al. Docetaxel-related side effects and their management. *Eur J Oncol Nurs* **13**: 49-59, 2009.
- Grada AA, Phillips TJ. Lymphedema: diagnostic workup and management. *J Am Acad Dermatol* **77**: 995-1006, 2017.
- Lepper PM, Ott SR, Hoppe H, et al. Superior vena cava syndrome in thoracic malignancies. *Respir Care* **56**: 653-666, 2011.
- Brater DC. Diuretic therapy. *New Engl J Med* **339**: 387-395, 1998.
- Partsch H, Flour M, Smith PC. Indications for compression therapy in venous and lymphatic disease consensus based on experimental data and scientific evidence. Under the auspices of the IUP. *Int Angiol* **27**: 193-219, 2008.
- Rabe E, Partsch H, Hafner J, et al. Indications for medical compression stockings in venous and lymphatic disorders: an evidence-based consensus statement. *Phlebology* **33**: 163-184, 2018.
- Alghulayqah A, Alghasab N, Amin T, Alkahtani N, Farhat R, Alzahrani AS. Long-term recurrence-free survival of adrenocortical cancer extending into the inferior vena cava and right atrium: case report and literature review. *Medicine* **96**: e6751, 2017.
- Kalra M, Sen I, Gloviczki P. Endovenous and operative treatment of superior vena cava syndrome. *Surg Clin North Am* **98**: 321-335, 2018.
- Oudkerk M, Heystraten FM, Stoter G. Stenting in malignant vena caval obstruction. *Cancer* **71**: 142-146, 1993.
- Brountzos EN, Binkert CA, Panagiotou IE, Petersen BD,

- Timmermans H, Lakin PC. Clinical outcome after intrahepatic venous stent placement for malignant inferior vena cava syndrome. *Cardiovasc Intervent Radiol* **27**: 129-136, 2004.
32. Okamoto D, Takeuchi Y, Arai Y, et al. Bridging stent placement through the superior vena cava to the inferior vena cava in a patient with malignant superior vena cava syndrome and an iodinated contrast material allergy. *Jpn J Radiol* **32**: 496-499, 2014.
33. Bjarnason H. Tips and tricks for stenting the inferior vena cava. *Semin Vasc Surg* **26**: 29-34, 2013.
34. Sebastian T, Dopheide JF, Engelberger RP, Spirk D, Kucher N. Outcomes of endovascular reconstruction of the inferior vena cava with self-expanding nitinol stents. *J Vasc Surg Venous Lymphat Disord* **6**: 312-320, 2018.
35. Sauter A, Triller J, Schmidt F, Kickuth R. Treatment of superior vena cava (SVC) syndrome and inferior vena cava (IVC) thrombosis in a patient with colorectal cancer: combination of SVC stenting and IVC filter placement to palliate symptoms and pave the way for port implantation. *Cardiovasc Intervent Radiol* **31**: S144-S148, 2008.

The Internal Medicine is an Open Access journal distributed under the Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License. To view the details of this license, please visit (<https://creativecommons.org/licenses/by-nc-nd/4.0/>).