Internal Medicine
The Japanese Society of Internal Medicine
doi: 10.2169/internalmedicine.5033-20
Intern Med 59: 2885-2890, 2020
http://internmed.jp

【 CASE REPORT 】

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

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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 syndrome (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

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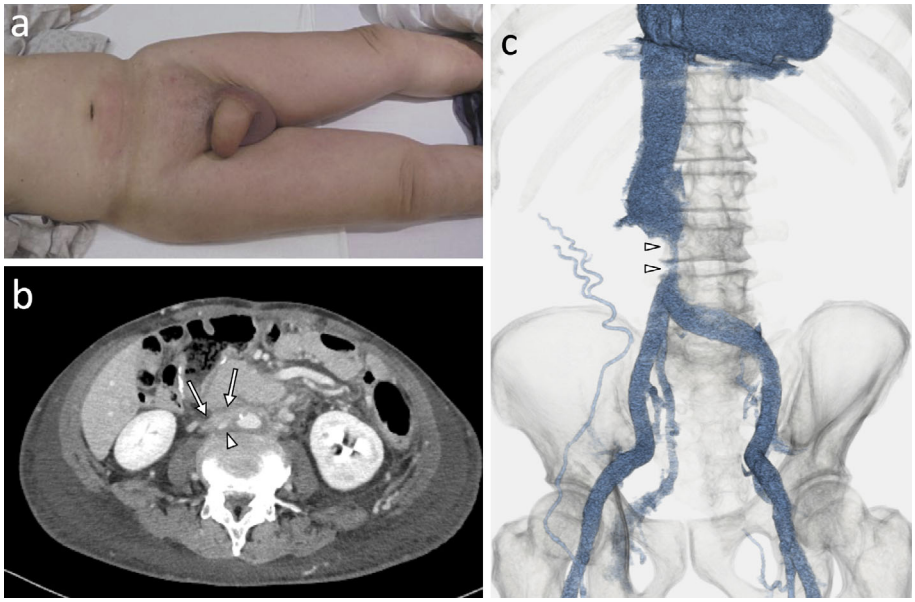

Figure 1. **(a) Photograph before IVC stent placement showing severe hydrocele testis and bilateral leg edema. (b) Axial abdominal contrast-enhanced CT image showing the IVC surrounded by lymph node metastases (arrow), causing stenosis (arrowheads). (c) CT reconstruction venography showing severe stenosis 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	16.1 mg/dL
White blood cells	5,100 /μL	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 μg/mL	Potassium	3.8 mmol/L
Monocytes	6.4 %			Chloride	105 mmol/L
Eosinophils	0.6 %	**Chemistry**		CRP	0.54 mg/dL
Basophils	0.2 %	Total protein	6.9 g/dL	BNP	16.5 pg/mL
Red blood cells	295×10^4 /μL	Albumin	3.9 g/dL	CEA	53.6 ng/mL
Hemoglobin	10.0 g/dL	AST	25 IU/L	CA19-9	16.0 U/mL
Platelet count	26.6×10^4 /μL	ALT	27 IU/L		
		ALP	397 IU/L	**Urine test**	
		γ-GTP	121 IU/L	Occult blood	negative
		T.Bil	0.9 mg/dL	Glycosuria	negative
		D.Bil	0.1 mg/dL	Proteinuria	negative
		LDH	158 IU/L		

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; COSMOTEC, 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 tosilate 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.

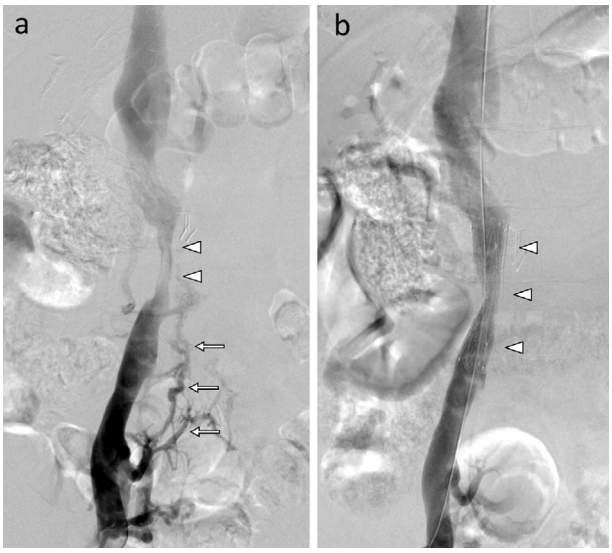

Figure 2. **(a) Digital subtraction venography showing severe stenosis of the IVC (arrowheads) and retrograde visualization of collateral veins, such as the ascending lumbar, azygos and hemiazygos veins (arrows). (b) Digital subtraction venography after stent placement (arrowheads) demonstrating improvement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

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 celluli-

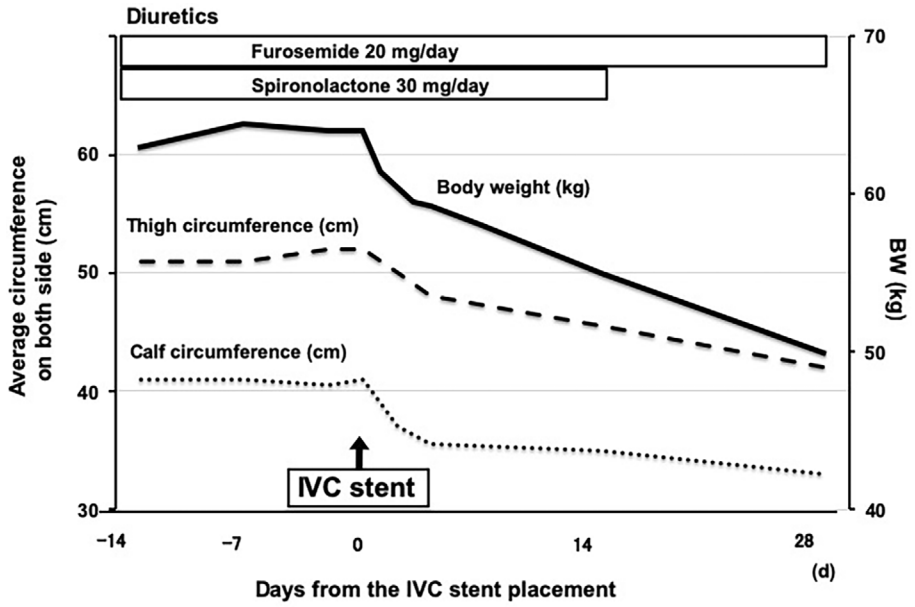

Figure 3. **Changes in the body weight and the circumference of the thigh and calf after placement of the IVC stent. BW: body weight, IVC: inferior vena cava**

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 preoperative 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).

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