

Virchow Lymph Node Metastatic Recurrence of Sigmoid Colon Cancer with Severe Lymph Node Metastases Successfully Treated Using Systemic Chemotherapy Combined with Radiotherapy

TAKAFUMI OHCHI¹, YOSHITO AKAGI¹, TETSUSHI KINUGASA¹, YOSHIKI ISHIBASHI¹, NATSUKI TANAKA¹, SHINYA FUJINO¹, SHIRO KIBE¹, KOTARO YUGE¹, TERUO SASATOMI¹, TOMOAKI MIZOBE¹, YOSUKE OKA¹, KAWANG DAE HONG² and KAZUO SHIROUZU¹

¹Department of Surgery, Faculty of Medicine, Kurume University, Fukuoka, Japan;

²Department of Surgery, Faculty of Medicine, Korea University Hospital, Guro-gu, Seoul, Republic of Korea

Abstract. *Metastatic recurrence of colon cancer in the left supraclavicular lymph node (Virchow lymph node) is rare, and to date there are no reports on radiotherapy as treatment. We report on a case of metastatic recurrence of sigmoid colon cancer in the Virchow lymph node with severe lymph node metastases successfully treated with a combined modality therapy of systemic chemotherapy and radiotherapy. The case is of a 58-year-old man, who underwent sigmoid excision and lymph node excision, and subsequently received systemic chemotherapy. After left supraclavicular lymph node recurrence appeared he later received radiotherapy. Complete response was achieved, and there has been no further recurrence, to date, 10 months after the radiotherapy. Radiotherapy was effective as a local treatment, and local control of distant metastasis of colonic cancer may lead to a good prognosis.*

Chemoradiotherapy is widely used in Europe and America for rectal cancer before and after surgery. For any metastases from colonic cancer, systemic chemotherapy is often added in combination with surgery. Here we report on a case of combined systemic chemotherapy and radiotherapy for metastatic recurrence in the left supraclavicular (Virchow) lymph node.

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Correspondence to: Dr. Takafumi Ohchi, Department of Surgery, Faculty of Medicine, Kurume University, 67 Asahi-machi, Kurume, Fukuoka 830-0011, Japan. Tel: +81 942353311, Ext. 3505, Fax: +81 942340709, e-mail: ohchi_takafumi@med.kurume-u.ac.jp

Key Words: Colon cancer, Virchow lymph node metastasis, combination therapy.

Case Report

The case is of a 58-year-old man who presented with the main complaint of defecation trouble, diarrhea and stool pillar narrowness. On physical examination, the performance status (PS) was 0, there was no abdominal pain, and an elastic hard mass was palpable in the left lower quadrant of the abdomen. Colonoscopy showed type 2 advanced colonic cancer in the sigmoidal colon. A barium enema study showed irregular stenosis of approximately 3 cm from the sigmoidal colon (Figure 1). Computed tomography (CT) showed hypertrophy in the sigmoidal wall with a heterogeneous contrast effect and fluffing in the surrounding adipose tissue. The border with the small intestine was indistinct, and permeation was suspected. A small nodular shadow was suspected as being lymph node metastases in the adipose tissue around the tumor. Swelling in the para-aortic lymph nodes in the area of the superior mesenteric artery bifurcation suggested lymph node metastases (Figure 2). No metastasis was seen in the liver and lungs. The preoperative carcinoembryonic antigen level was 0.8 ng/ml. The preoperative diagnosis was sigmoidal colonic cancer, cSI, cN3, cH0, cP0, cM1 (para-aortic lymph node) cStageIV in the Japanese Classification of Colorectal Carcinoma (JCCC) (1).

Treatment strategy. To treat the passage disorder, we resected the primary tumor with palliative intent, and resected the para-aortic lymph node for histological examination. R2 surgery was achieved (para-aortic lymph node remained). We administered bevacizumab at 7.5 mg/kg and oxaliplatin at 130 mg/m² on day 1 plus capecitabine at 1000 mg/m² twice daily on days 1-14, every three weeks from postoperative day 21 as systemic chemotherapy.

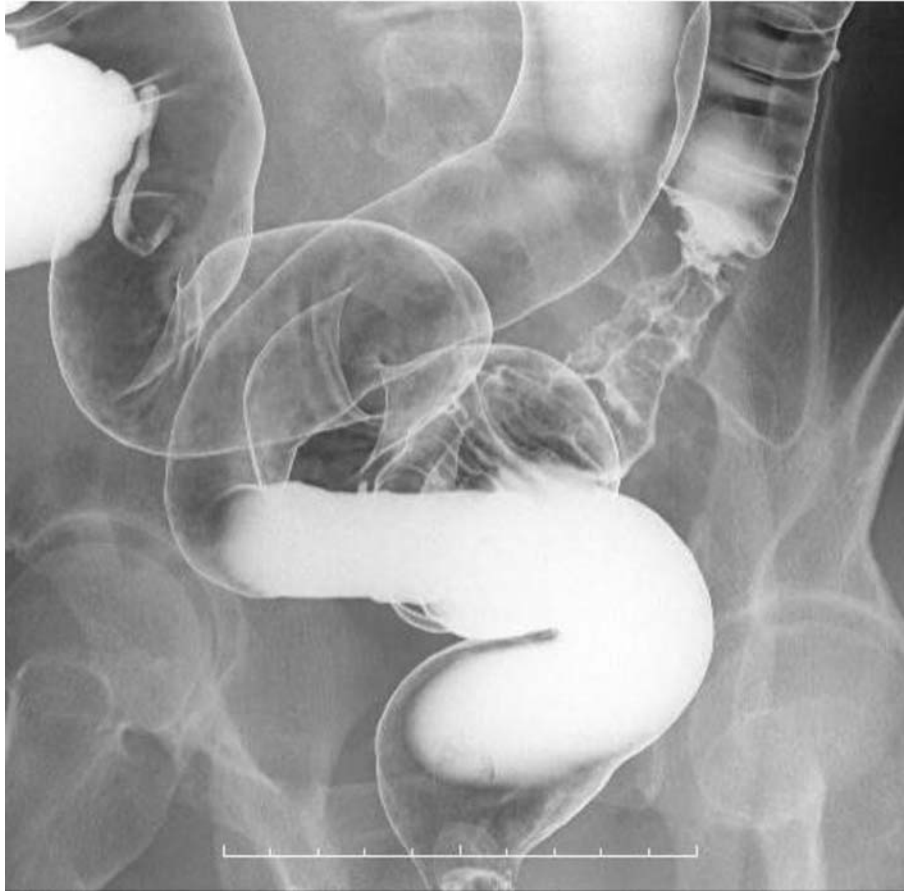


Figure 1. The barium enema study showed an irregular stenosis image of approximately 3 cm from the sigmoidal colon.

Pathological findings. The pathology results were poorly-differentiated adenocarcinoma, ly2, v2, lymph node metastasis: 3/17 (positive total), para aortic lymph node: 3/17 (positive total), pSS, pN1, cH0, pP0, pM1 (para aortic lymph node) fStage IV by JCCC (1) (Figure 2). Staining for epidermal growth factor receptor (EGFR) was positive on immunohistochemistry. V-Ki-ras2 Kirsten rat sarcoma viral oncogene homolog (KRAS) was wild type.

Episode of care. The patient received 11 cycles of capecitabine, oxaliplatin and bevacizumab therapy for para-aortic lymph node metastases. The best overall response was a partial response, and we then changed to FOLFIRI plus bevacizumab (bevacizumab at 5 mg/kg, irinotecan at 180 mg/m², folinic acid at 400 mg/m², fluorouracil (5-FU) bolus at 400 mg/m² on day 1 and 5-FU continuous intravenous infusion at 1200 mg/m² on days 1-2, every two weeks) due to onset of peripheral neuropathy grade 3. Peripheral neuropathy was improved by the four-cycle dosage of FOLFIRI plus bevacizumab to grade 1, and then we changed therapy to modified FOLFOX6 plus bevacizumab (bevacizumab at 5 mg/kg, oxaliplatin at 85 mg/m², intravenous infusion folinic

acid at 400 mg/m², bolus 5-FU at 400 mg/m² on day 1 and continuous intravenous infusion of 5-FU at 1200 mg/m² on days 1-2, every two weeks) and FOLFIRI plus bevacizumab every four cycles (2). At 20 months postoperatively, metastasis in the left supraclavicular lymph node was detected on CT (Figure 4), on fluorodeoxyglucose positron-emission tomography (PET) (Figure 5), and on ultrasonography after 24 cycles in total. The abdominal para-aortic lymph node metastasis had disappeared. We started modified FOLFOX6 plus cetuximab [(250 mg/m²) on day 1, every week]. For the metastasis to the left supraclavicular lymph node, stable-disease status was achieved, and for other metastases, complete response (CR) was achieved. However, we switched to tegafur, gimeracil, oteracil potassium (TS1) at 80 mg/day (two weeks administration, one week discontinuation) plus cetuximab at 250 mg/m² (weekly) because we noticed protraction in peripheral neuropathy grade 2 and fatigue grade 1. The side-effect was relieved, and compliance was improved. After eight cycles, the metastasis to the left supraclavicular lymph node had increased to approximately 5 cm, with tenderness macroscopically. Surgical treatment was difficult anatomically, and so radiotherapy was performed. At 22

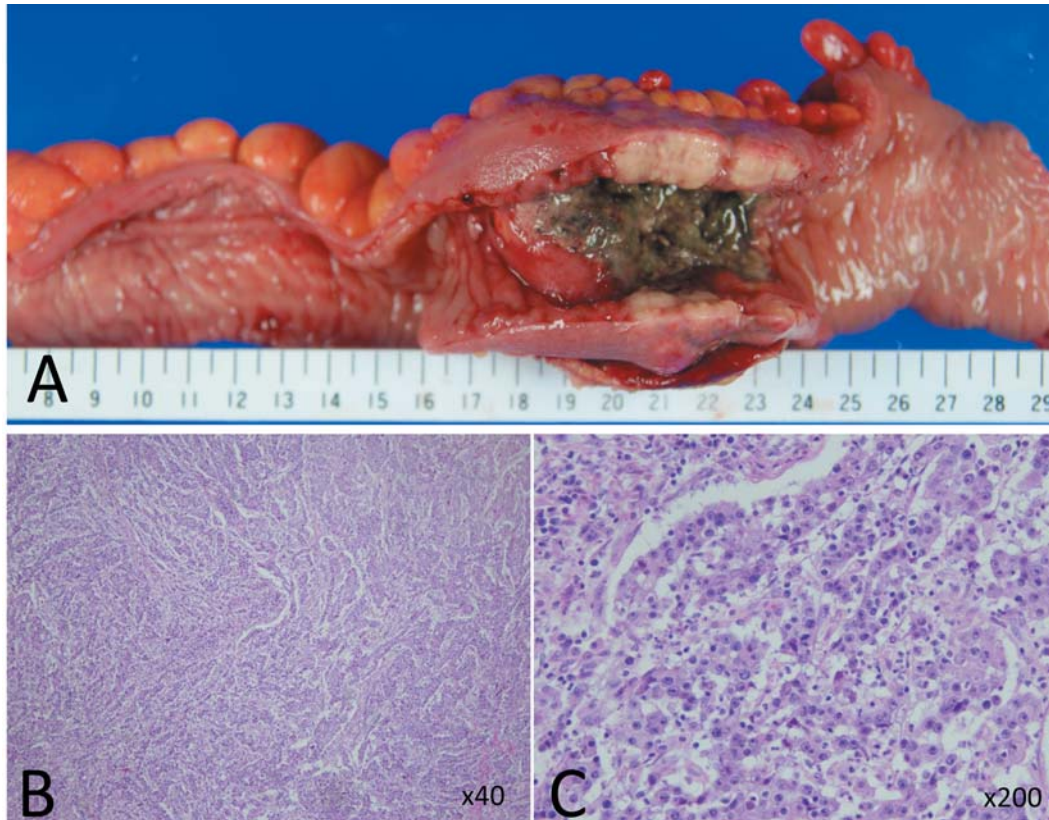


Figure 2. Pathological findings: Macroscopic findings (A) and microscopic findings of poorly differentiated adenocarcinoma (B, $\times 40$; C, $\times 200$).

months postoperatively, this site was irradiated with 15 times of 3 Gy a total 45 Gy. Other sites of metastasis were controlled, and systemic chemotherapy was resumed. The symptoms were relieved immediately after radiotherapy, and there was reduction in tumor size. The tumor was gradually reduced and had disappeared macroscopically by day 48 after radiotherapy. We continued TS1 plus cetuximab, and the metastasis of the left supraclavicular lymph node disappeared on CT (Figure 4). No other metastasis was seen. There was no accumulation on PET (Figure 5). CR was maintained by 12 cycles of TS1+cetuximab administration in total. Because dermatopathy, paronychia, fatigue and diarrhea grade 1 appeared, we switched to TS1 alone. However, he was not able to receive it because diarrhea continued. We are following-up with no treatment, and CR has continued for more than 10 months. Figure 6 shows the clinical course.

Discussion

For lymph node recurrence from colonic cancer, we remove the lymph nodes surgically if resectable, and if it is hard to resect, in the Japanese guidelines it is recommended that a case with PS 0-2 is given systemic chemotherapy and local

treatment (3). Radiotherapy as the treatment for distant metastasis of colonic cancer is not often used for metastases other than to the brain or bone, because the site of the main distant metastasis is usually the liver. However, improvement in radiation exposure technology can suppress injury to normal tissue, and allows irradiation to a local site, so that a good effect from local treatment can be expected (4-7). We conducted irradiation for the purpose of pain relief in our case, but irradiation remarkably reduced the tumor, which subsequently disappeared on imaging. Other metastases were controlled by systemic chemotherapy, and CR was achieved generally. Radiotherapy is thought to be suitable as the local treatment instead of surgery in some cases.

As a third line of therapy, after failure of standard chemotherapy, a randomised study revealed a highly significant increase in median overall survival (OS) with cetuximab compared with best supportive care, from 4.8 months to 9.5 months, in patients with a KRAS wild-type tumor (8, 9). Administration of an antibody to EGFR for KRAS wild-type cancer is a novel made-to-order treatment, and no other markers are yet available. Research into such markers as amphiregulin is currently conducted (10). Thus, the development of an effective predictor marker of the outcome from radiotherapy is expected.

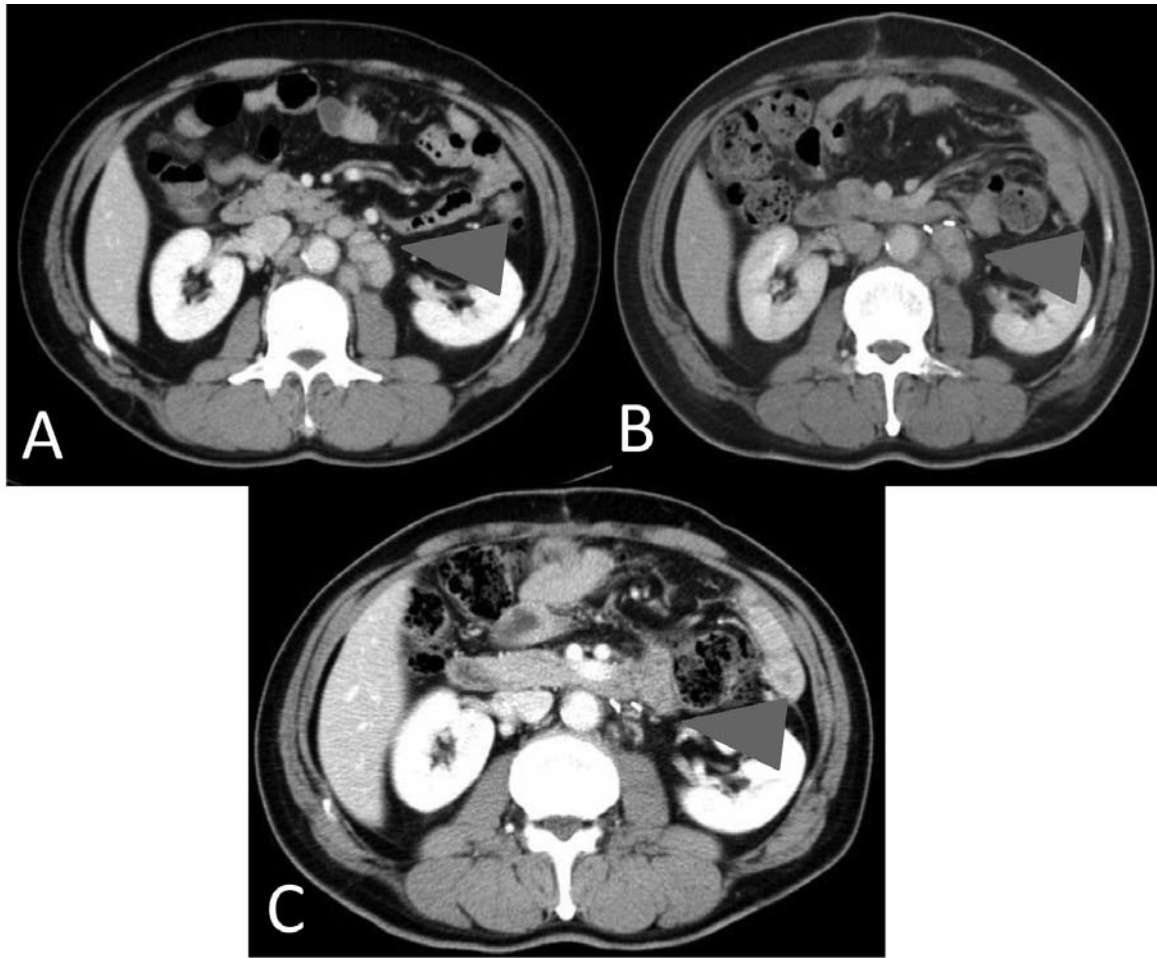


Figure 3. *Computed tomographic findings of para aortic lymph node metastasis: prior to surgery (A), chemotherapy (B), and radiation therapy (C).*

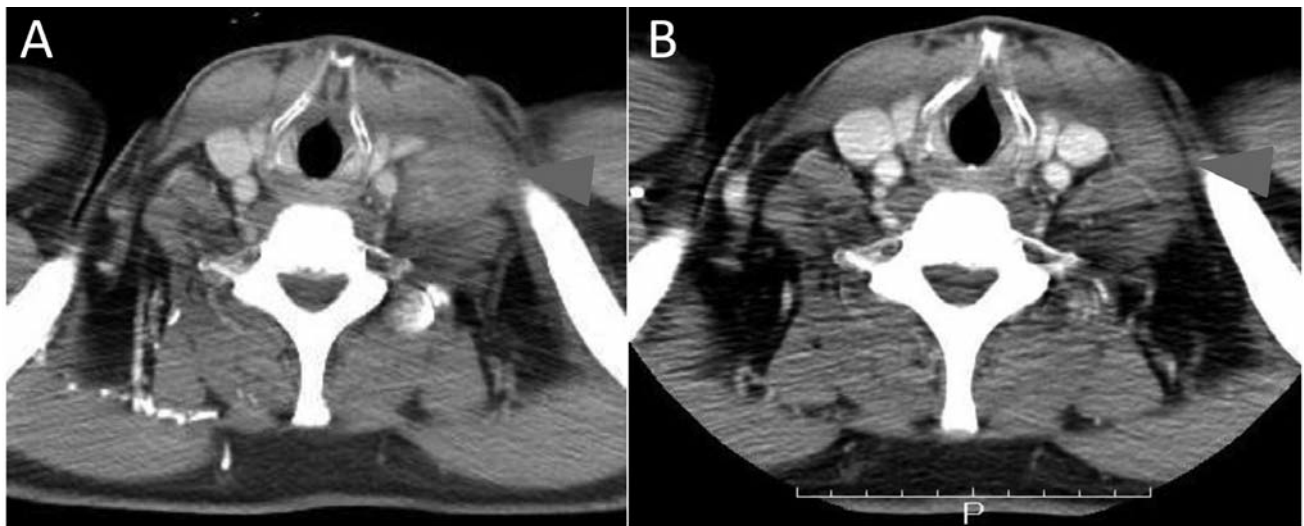


Figure 4. *Computed tomographic findings of the metastasis to the Virchow lymph node : before radiation (A) and after radiation (B).*

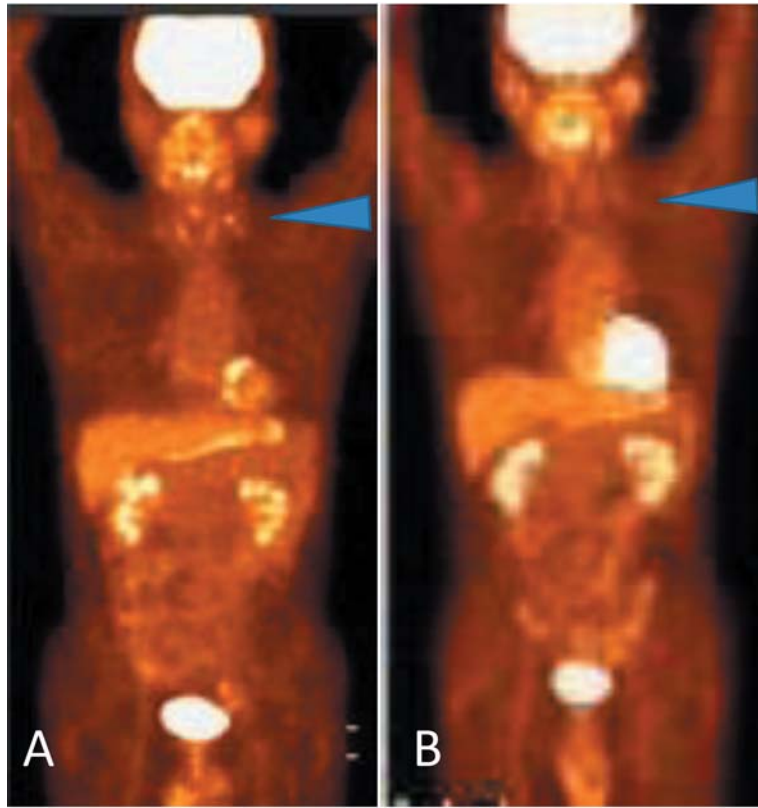


Figure 5. Fluorodeoxyglucose positron-emission tomographic findings. A: The left supraclavicular lymph node shows accumulation. B: There is no abnormal accumulation.

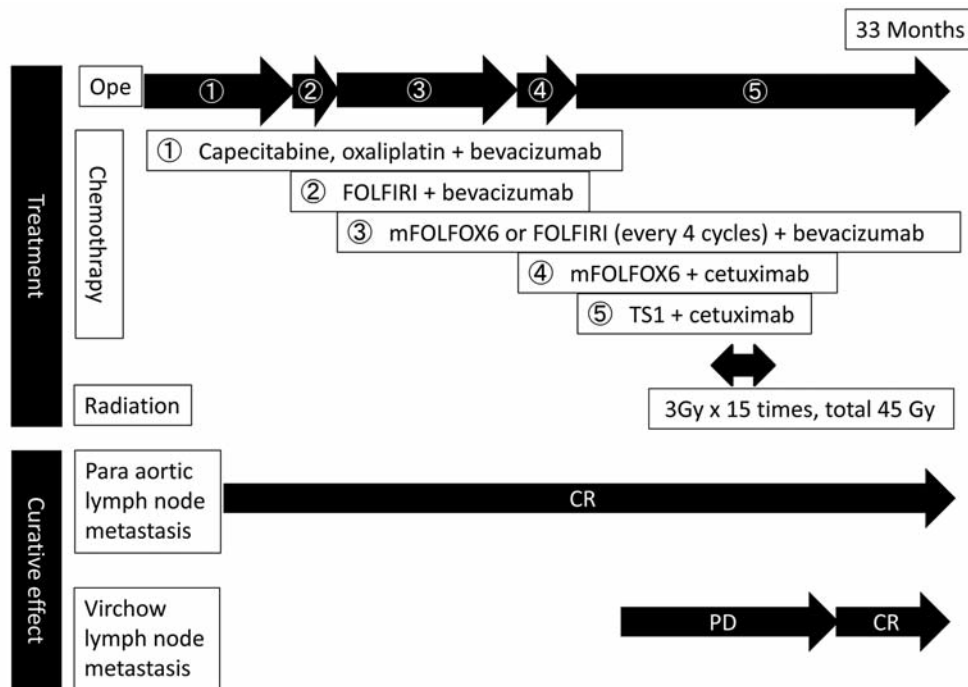


Figure 6. Treatment course. Tegafur, gimeracil, oteracil potassium (TS1).

The lymphatic vessels including the thoracic duct arrives at the Virchow lymph node, and this is recognized as being the end node of lymph nodes (11). The prognosis of patients with stage IV colorectal carcinoma remains poor, with a median survival of just 9-10.3 months (12-15). The 5-year survival rate of patients with distant node-positive colonic cancer involving the para-aortic lymph node is approximately 3% (16). In the present case, the findings suggested that the number of metastatic organs was limited to only the one Virchow para-aortic lymph node. Treatment for colonic cancer usually involves the curative resection of the colonic tumor together with any metastasis in the lungs or peritoneum, to achieve a good prognosis and extend survival (17-20). If there is only one organ of metastasis, then survival can be extended in cases of colonic cancer using a combination of local treatment and systemic chemotherapy.

In the present case, radiotherapy was administered to metastasis in the Virchow lymph node, no other such report has been found in the literature. Radiotherapy can be considered as a strategic local treatment after using 5-FU, oxaliplatin, and irinotecan. For metastatic recurrence of sigmoidal colonic cancer to the Virchow lymph node with severe lymph node metastases, we report our successful experience in one patient using combined systemic chemotherapy and radiotherapy. Radiotherapy was an effective local treatment, and the local control of distant metastasis of colonic cancer may lead to good prognosis.

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