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WJCC mainly publishes articles reporting research results and findings obtained in the field of clinical medicine and covering a wide range of topics, including case control studies, retrospective cohort studies, retrospective studies, clinical trials studies, observational studies, prospective studies, randomized controlled trials, randomized clinical trials, systematic reviews, meta-analysis, and case reports.

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Isolated synchronous Virchow lymph node metastasis of sigmoid cancer: A case report

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Abstract

BACKGROUND

Colorectal cancer (CRC) is one of the most common malignant tumors of the digestive tract. Lymphatic metastases of this tumor are mostly confined to the

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regional lymph nodes, and distant supraclavicular lymph node metastases are very rare.

CASE SUMMARY

In this report, we describe a patient with sigmoid carcinoma and isolated synchronous supraclavicular lymph node metastases. A 56-year-old male presented with a left cervical mass that was confirmed as a lymph node metastasis from sigmoid cancer by several auxiliary examinations. After 6 cycles of chemotherapy with the 5-fluorouracil, leucovorin and oxaliplatin + cetuximab regimen, the sigmoid colon tumor and Virchow's lymph node metastasis were significantly smaller than before treatment, and no new metastatic sites were observed. Considering the effects of chemotherapy on quality of life, resection of the primary tumor was performed followed by 4 cycles of chemotherapy with the original chemotherapy regimen. Virchow's lymph node dissection was selected by mutual consultation between the patient and us. After the second surgery, the patient received capecitabine and cetuximab chemotherapy and did not experience recurrence or metastasis during follow-up.

CONCLUSION

In conclusion, supraclavicular lymph node metastasis without any other solid organ metastasis is a potential metastatic pathway for CRC. In addition, after resection of the primary lesion, postoperative chemotherapy combined with supraclavicular lymph node dissection is feasible for the treatment of patients with CRC and isolated synchronous Virchow's lymph node metastases.

Key Words: Virchow's lymph node; Metastasis; Colorectal cancer; Case report

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Core Tip: A 56-year-old male presented with Virchow lymph node metastasis of sigmoid cancer. We treated the primary tumor and metastatic lymph nodes with chemotherapy combined with surgery. No recurrence or metastasis occurred during the follow-up period. According to our findings, supraclavicular lymph node metastasis without any other solid organ metastasis may be a potential metastatic pathway for colorectal cancer (CRC). In addition, after resection of the primary lesion, postoperative chemotherapy combined with supraclavicular lymph node dissection is feasible in the treatment of patients with CRC and isolated synchronous Virchow lymph node metastases.

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INTRODUCTION

Colorectal cancer (CRC) is one of the most common malignant tumors of the digestive tract[1]. CRC frequently metastasizes to the regional lymph nodes, liver, lung, and peritoneum[2]. CRC with distant lymph node site metastasis is rare, and synchronous distant lymph node metastasis from CRC without any other solid organ metastasis is extremely rare. Therefore, we report the case of a patient with sigmoid colon cancer who presented with isolated simultaneous Virchow's lymph node metastasis.

CASE PRESENTATION

Chief complaints

A 56-year-old male presented with a left cervical mass that had been present for one month.

History of present illness

The patient's left cervical mass was incidentally discovered and no other clinical manifestations.

History of past illness

The patient was previously diagnosed with diabetes and took oral hypoglycemic drugs for control of blood glucose level.

Personal and family history

The patient lived in Jinan, China. He did not smoke and was not addicted to alcohol. No relevant family history was reported.

Physical examination

Physical examination revealed a solid small peanut-sized mass in the left supraclavicular region.

Laboratory examinations

The laboratory assessment revealed that carcinoembryonic antigen (CEA), CA199, and CA724 serum levels were moderately elevated.

Imaging examinations

Ultrasonography of the cervical mass showed that multiple hypoechoic masses were present in the left supraclavicular fossa, and the larger mass measuring 0.9 cm × 0.5 cm had a clear border and unclear internal structure. This mass was mildly enhanced on contrast-enhanced computed tomography (CT) (Figure 1). Positron emission tomography/CT (PET/CT) scan demonstrated that no significant fluorodeoxyglucose (FDG) uptake was observed in the left supraclavicular region (Figure 2). To determine the nature of the enlarged lymph nodes, lymph node biopsy was performed, and histopathological examination revealed metastatic adenocarcinoma (Figure 3). In the immunohistochemical analysis, the biopsied tissue was positive for SP-B, CK8/18, CK20, CDX-2 and P504S expression with a Ki-67 index of 80%; the tissue was negative for CK5/6, CgA, P40, P63, CK7, TTF-1, Napsin A, SPA and Syn expression. The laboratory assessment revealed that CEA, CA199, and CA724 serum levels were elevated. To further clarify the diagnosis, the patient underwent gastroenteroscopy, and the results revealed one pedunculated polyp with mucosal erosion in the sigmoid colon, measuring 2.0 cm in diameter (Figure 4). Histological examination with hematoxylin-eosin staining revealed adenocarcinoma was in the intramucosal tissue (Figure 5). Immunohistochemical analysis revealed that the polyp was positive for CDX-2 and CK20 expression, negative for CgA, Syn and CD56 expression, and the Ki-67 index was 70%. In addition, high-throughput gene sequencing showed wild type K-Ras.

FINAL DIAGNOSIS

According to the results of the auxiliary examination, this patient was diagnosed with late-stage sigmoid colon cancer with distant lymph node metastasis.

TREATMENT

The patient received chemotherapy with the 5-fluorouracil, leucovorin and oxaliplatin (FOLFOX) + cetuximab regimen. After 6 cycles of chemotherapy, the patient was reexamined with CT and ultrasonography, and the results showed that the sigmoid colon tumor and Virchow's lymph node were significantly smaller than before treatment and no new metastatic sites were found. Considering the effects of chemotherapy on quality of life, the patient and his family members strongly

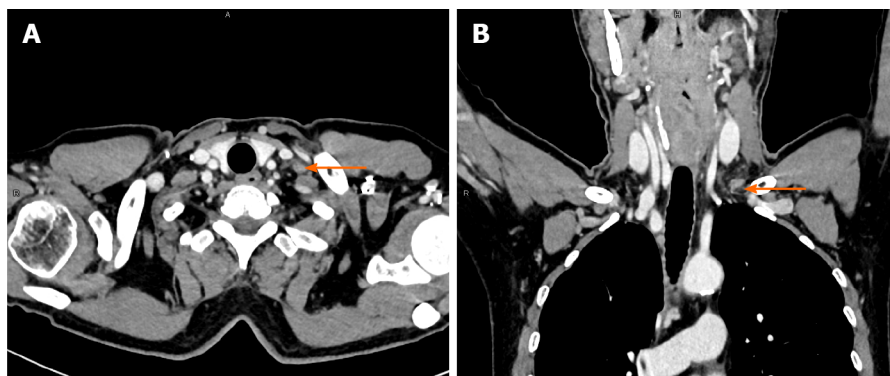


Figure 1 Contrast-enhanced computed tomography: The mass appeared to be mild enhancement. A: Axial view; B: Coronal view.

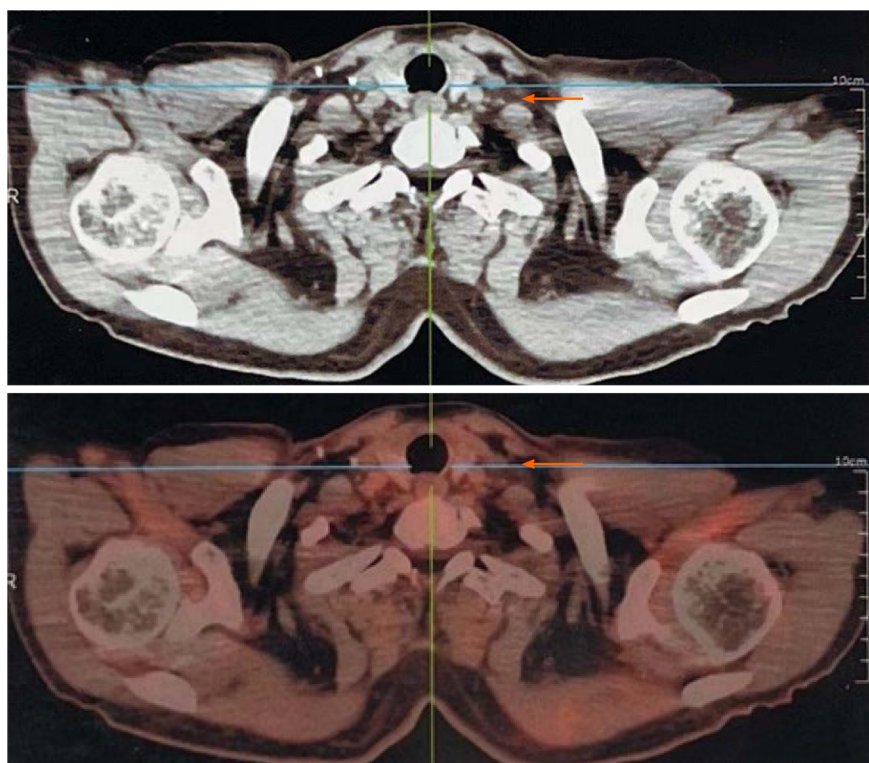


Figure 2 Positron emission tomography-computed tomography: No significant fluorodeoxyglucose uptake was observed in left supraclavicular region.

requested surgery after receiving education on the risks and benefits of surgery and other therapeutic regimens. Therefore, sigmoid carcinoma resection and mesenteric lymph node dissection were performed. Histological examination (**Figure 6**) showed moderately differentiated adenocarcinoma localized in the mucosa, and one of five paracolic lymph nodes contained metastatic carcinoma (pT1N1M1). Immunohistochemically, the excised tissues were positive for CK20, MSH2 and SATB2 and negative for CK7 (**Figure 7**). After surgery, the patient received the same chemotherapy regimen as before. After undergoing 4 cycles of chemotherapy, Virchow's lymph node dissection was selected by mutual consultation between the patient and us. We removed the lymph nodes in the triangle bounded by the lower abdomen of the omohyoid, the posterior margin of the sternocleidomastoid and the superior clavicle (the level IV and VB lymph nodes of the neck). Histological examination revealed that five of the eight dissected cervical lymph nodes contained metastatic carcinoma. Immunohistochemically, these lymph nodes were positive for CDX2, SATB2, CK20, KIAA1429 and RBM15 and negative for IC3H13, CK7, TTF1 and P40. Histopathologic examination and immunohistochemistry staining again confirmed sigmoid metastasis. During the dissection of the enlarged left supraclavicular lymph node, there was clear fluid outflow from the left venous angle, which suggested lymphatic leakage. We

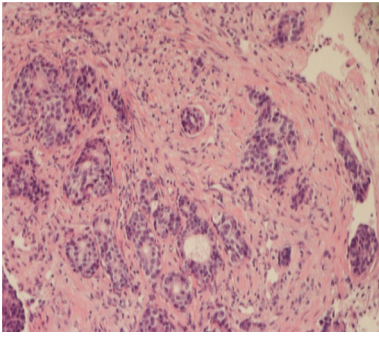


Figure 3 The left supraclavicular lymph node biopsy exhibited typical morphological findings of adenocarcinoma (hematoxylin & eosin staining $\times 200$).

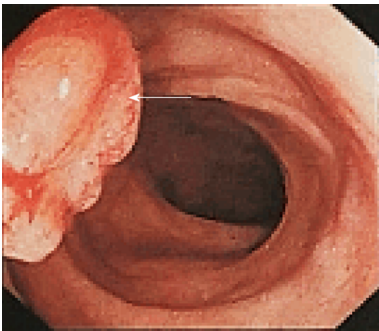


Figure 4 Colonoscopy examination: A pedunculated polyp measuring 2.0 cm in diameter was observed in sigmoid colon.

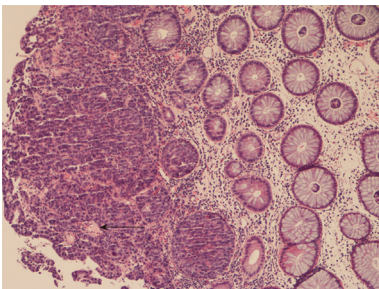


Figure 5 Pathological finding of the endoscopic biopsy (hematoxylin & eosin staining $\times 100$): Carcinoma tissue invades the muscularis mucosa.

immediately sutured the site with silk thread and pressed it with a gelatin sponge; subsequently, the fluid outflow stopped. On the second day after surgery, the left cervical drainage tube drained approximately 2000 mL milky white fluid. After the diagnosis of postoperative lymphatic leakage, the patient was treated with diet restriction, total parenteral nutrition, local wound compression, and somatostatin pumping. From the 4th to 7th day after surgery, approximately 500-100 mL of clear liquid was drained from the left cervical drainage tube per day. On the 10th day after surgery, 2 mL *Pseudomonas aeruginosa* (1.8×10^9 /mL, Beijing Wanteer Biopharmaceutical Co. Ltd) was injected near the left venous corner under the guidance of ultrasonography, and the drainage tube was clamped. Thirty minutes after the injection, the patient developed chills and high fever, with the highest body temperature recorded at 39 °C. After a large amount of fluid infusion, anti-inflammatory and other symptomatic treatments, the patient's symptoms gradually improved, and no further lymphatic fluid drainage was observed. Considering the patient has reached the predetermined number of cycles of chemotherapy after sigmoid tumor resection, the patient received a maintenance chemotherapy regimen with capecitabine and cetuximab after the second surgery.

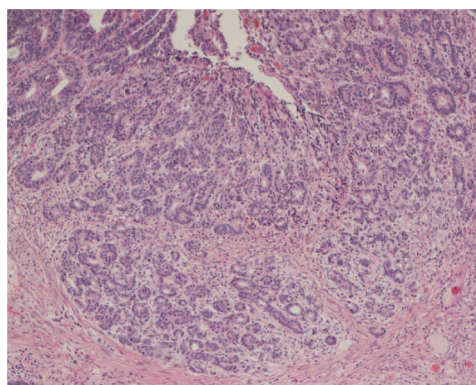


Figure 6 Pathological findings of sigmoid tumor (hematoxylin & eosin staining × 100): Moderately differentiated adenocarcinomas limited to mucous membranes.

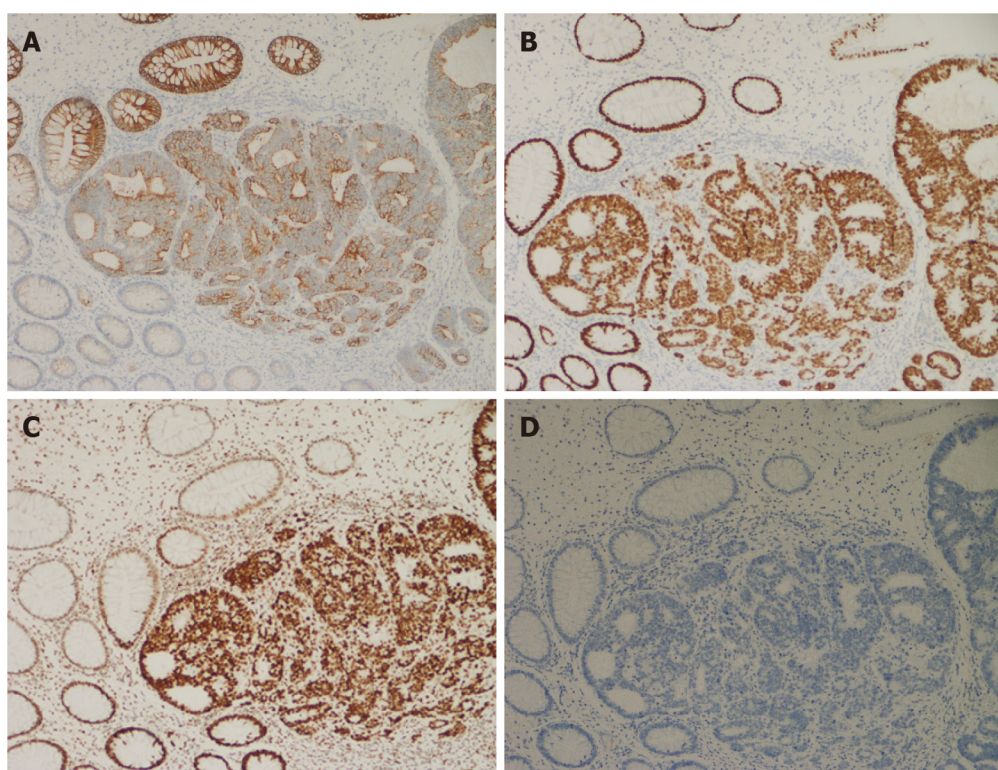


Figure 7 Immunohistochemical examination of sigmoid tumor (hematoxylin & eosin staining × 100). A: CK20 is positive; B: MSH2 is positive; C: SATB2 is positive; D: CK7 is negative.

OUTCOME AND FOLLOW-UP

At half of a year after the surgery, the patient was asymptomatic, and there were no signs of tumor recurrence or progression.

DISCUSSION

CRC can spread by lymphatic, hematogenous, and transperitoneal dissemination as well as direct extension. Regional lymph nodes (52%), liver (78%), lung (20%), and peritoneum (29%) are frequently observed metastatic sites of CRC[2]. CRC with distant lymph node metastasis is very rare. Although a few cases[3-6] of synchronous supraclavicular lymph node metastases from colorectal carcinoma have been reported (Table 1), most were complicated with multiple metastases or treated exclusively with chemotherapy. To the best of our knowledge, this is the first case of lymph node

Table 1 Long-term survival of cases with synchronous Virchow lymph node metastasis of colorectal cancer

No.	Ref.	Year	Age/gender	Primary location	Metastasis of another organ	Resection of Virchow LN	Postoperative chemotherapy	Disease free survival time	Overall survival time
1	Watanabe <i>et al</i> [3]	2009	73/Male	Cecum	Paraortic lymph nodes; Lung	-	5-fluorouracil, Leucovorin, FOLFOX, FOLFIRI	-	3 yr
2	Hirose <i>et al</i> [4]	2010	57/Male	Rectum	-	-	FOLFOX, FOLFIRI	-	3 yr
3	Ando <i>et al</i> [5]	2013	63/Male	Sigmoid colon	-	-	FOLFOX, FOLFIRI	-	5 yr
4	Suliman <i>et al</i> [6]	2019	54/Male	Transverse colon	-	+	FOLFOX, FOLFIRI	-	-
5	Our case	2020	56/Male	Sigmoid colon	-	+	FOLFOX, capecitabine, cetuximab	So far	So far

FOLFOX: Fluorouracil, leucovorin and oxaliplatin; FOLFIRI: Fluorouracil, leucovorin and irinotecan; LN: Lymph node.

dissection combined with chemotherapy to treat isolated synchronous Virchow's lymph node metastasis from sigmoid cancer (Table 2).

An enlarged Virchow's lymph node located near the junction of the thoracic duct and the left subclavian vein is often considered a sign of gastric and esophageal cancer metastasis[7]. The specific mechanism of distant lymph node metastasis from CRC, such as metastasis to the Virchow lymph node, has not been reported. One possible metastatic mechanism is that this patient developed intraperitoneal micrometastases prior to systemic chemotherapy. Lymph from intraperitoneal metastatic lymph nodes enters the thoracic duct through lymphatic drainage, resulting in left supraclavicular lymph node enlargement[8].

The surgical indications for colorectal tumors with distant lymph node metastases remain controversial[9]. Traditionally, supraclavicular lymph node metastasis is considered a relative contraindication to surgery. CRC with supraclavicular lymph node metastasis is typically diagnosed as stage IV and indicates poor prognosis[10-12]. However, some CRC patients with supraclavicular lymph node metastasis achieve a good response and better prognosis after chemotherapy[3-6]. Therefore, preoperative chemotherapy combined with surgical resection has been reconsidered for this indication given the development of increasingly effective chemotherapy regimens [13]. In our case, because genetic sequencing of the patient's sigmoid tumor revealed at wild type K-Ras gene, the patient was administered six cycles of chemotherapy with the FOLFOX + cetuximab regimen. Due to the timely intervention with an appropriate systemic chemotherapy regimen, the patient did not develop systemic organ metastasis, and the primary tumor and metastatic lymph nodes showed a good response. This notion was further confirmed by postoperative pathology showing a retraction of sigmoid tumor invasion and fewer paracolic lymph node metastases. After resection of the primary site and 4 cycles of postoperative chemotherapy with the original regimen, this patient underwent left supraclavicular region lymph node dissection followed by chemotherapy with capecitabine + cetuximab. During the follow-up period, no signs of tumor recurrence or progression were observed. Therefore, we suggest that preoperative chemotherapy combined with surgical resection may be used to extend the survival interval of patients with CRC, especially patients who respond well to chemotherapy and have a strong desire to undergo surgery.

Previous literature has reported that PET/CT offers value in predicting distant tumor metastases[14]. In our case, however, no significant FDG uptake was observed in the patients' left supraclavicular lymph nodes on PET/CT. The false negative PET/CT results of this patient may be related to the smaller diameter of the supraclavicular lymph nodes. The standard uptake value (SUV) of the lesion is generally proportional to its size, so the SUV of smaller metastatic lymph nodes is often low and more difficult to detect by PET/CT[15]. In other words, PET/CT has lower sensitivity and higher specificity for distant metastatic lymph nodes than contrast-enhanced CT.

Pseudomonas aeruginosa injection is performed using attenuated *Pseudomonas aeruginosa*. Previous studies have confirmed that injection of *Pseudomonas aeruginosa* has a significant effect on improving postoperative lymphatic leakage of

Table 2 Information from this case report organized into a timeline

Time lane	Events
June 3, 2020	The male presented with a left cervical mass for one month
June 9, 2020	Lymph node biopsy was performed and histopathological examination revealed that the metastatic adenocarcinoma was found in the tissue
June 18, 2020	The patient underwent gastroenteroscopy and the results revealed that one pedunculated polyp with mucosal erosion was observed in sigmoid colon, and histological examination revealed that adenocarcinoma was found in the intramucosal tissue
June 30, 2020 to September 30, 2020	Undergoing 6 cycles of chemotherapy with FOLFOX + cetuximab regimen
October 22, 2020	The resection of sigmoid carcinoma and mesenteric lymph node dissection were performed. Histological examination showed moderately differentiated adenocarcinoma localized in the mucosa, and one of five paracolic lymph nodes contained metastatic carcinoma (ypT1N1M1)
November 30, 2020 to January 30, 2021	Undergoing 4 cycles of chemotherapy with FOLFOX + capecitabine regimen
February 24, 2021	Virchow lymph node dissection was selected by mutual consultation between the patient and us
February 25, 2021 to March 5, 2021	Postoperative lymphatic leakage
March 24, 2021-So far	The patient received chemotherapy with capecitabine and cetuximab. At nearly half of a year following the surgery, the patient was asymptomatic, and there were no signs of tumor recurrence or progression

FOLFOX: Fluorouracil, leucovorin and oxaliplatin.

thyroid cancer[16]. The possible mechanism is as follows: *Pseudomonas aeruginosa* can penetrate into the subcutaneous space and produce aseptic inflammation, which promotes the closure of lymphatic vessels and reduces lymphatic leakage. In our case, the patient developed a lymphatic fistula after supraclavicular lymph node dissection. After the failure of a series of conservative treatments, we attempted to inject *Pseudomonas aeruginosa* from the left venous angle to reduce lymphatic leakage and achieved good results.

CONCLUSION

In summary, isolated Virchow's lymph node metastasis is a potential metastatic route of CRC. In addition, when supraclavicular lymph node metastases are controlled by chemotherapeutic drugs, radical resection of both the primary site and the metastatic lesion is feasible. However, there is a need for further research to determine the optimum duration of preoperative chemotherapy and to further perfect surgical interventions.

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