Solitary anterior mediastinal lymph node metastasis with pericardial invasion from colon cancer: A case report

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Abstract. Colorectal cancer commonly metastasizes to the regional lymph nodes, liver, lungs and peritoneum. At present, mediastinal lymph node metastasis from colorectal cancer is uncommon and poorly understood. The present study reported a case of solitary anterior mediastinal lymph node metastasis with pericardial invasion from transverse colon cancer. An 82-year-old woman had a history of colectomy with regional lymph node dissection for transverse colon cancer (T1N1bM0 stage IIIA in the UICC classification). The patient had no symptoms, but follow-up contrast-enhanced computed tomography revealed an anterior mediastinal tumor compressing the heart 18 months after colectomy. The tumor showed fluorodeoxyglucose uptake on positron emission tomography. Resection of the anterior mediastinal tumor with pericardiectomy was performed. The tumor was 35x25 mm in size and was histopathologically characterized to be adenocarcinoma. These cells expressed cytokeratin (CK)20 and caudal-type homeobox protein 2 but not CK7 and thyroid transcription factor 1 on immunohistochemical analysis, confirming a diagnosis of metachronous mediastinal metastasis originating from colon cancer. The tumor cells invaded the adjacent pericardium and diaphragm pathologically. The patient has lived without recurrence 8 months after the surgery for mediastinal metastasis. In conclusion, clinicians should consider metastasis to the mediastinum during follow-up in patients with colorectal cancer. Surgery may be the most reliable treatment for solitary anterior mediastinal lymph node metastasis, preventing carcinomatous pericarditis through direct pericardial invasion.

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Abbreviations: CRC, colorectal cancer; CECT, contrast-enhanced computed tomography

Key words: colorectal cancer, recurrence, metastasis, mediastinum, surgery

Introduction

An estimated 19.3 million new cancer cases and 10 million cancer deaths occurred worldwide in 2020 (1). About 1.9 million new colorectal cancer (CRC) cases and 916,000 deaths were estimated to occur, representing about one in 10 cancer cases and deaths. CRC is the second most common cancer in women and the third in men and the second most common cause of cancer-related mortality worldwide (1). The primary prevalent metastatic organs are the regional lymph nodes, liver, lungs, and peritoneum (2). In CRC with regional lymph node metastasis, intestinal resection with lymph node dissection is recommended for curative treatment. On the other hand, in cases with distant (extraregional) lymph node metastasis, para-aorta lymph node metastasis predominantly occurs and the resection is performed in selected patients to have potential to achieve a cure and bring longer survival, although no prospective comparative clinical trials have a clear therapeutic effect (2). Mediastinal lymph node metastasis from CRC uncommonly occurs and is occasionally recognized with lung metastasis (3). There were few cases of mediastinal lymph node metastasis with liver or para-aorta lymph node metastasis (4-9). Moreover, solitary mediastinal lymph node metastasis from CRC without any other organ involvement is extremely rare, and the optimal treatment remains unclear. Here we report a case of solitary anterior mediastinal lymph node metastasis with pericardial invasion from transverse colon cancer and review the relevant literature.

Case report

An 82-year-old Japanese woman underwent laparoscopic right hemicolectomy with regional lymph node dissection for transverse colon cancer, which was a pathologically well-differentiated adenocarcinoma classified as T1N1bM0 stage IIIA in the UICC classification (Fig. 1A and B). The patient was followed up postoperatively without adjuvant chemotherapy. At 18 months post-colectomy, the patient had no symptoms, but follow-up contrast-enhanced computed tomography (CECT) revealed a mediastinal tumor that rapidly increased (Fig. 2A-D). The tumor was located at the anterior inferior mediastinum and compressed the heart (Fig. 2D). The results of the tumor marker test were within the normal range, with the carcinoembryonic antigen and carbohydrate antigen 19-9 levels of 2.7 ng/ml and 4.14 U/ml, respectively.

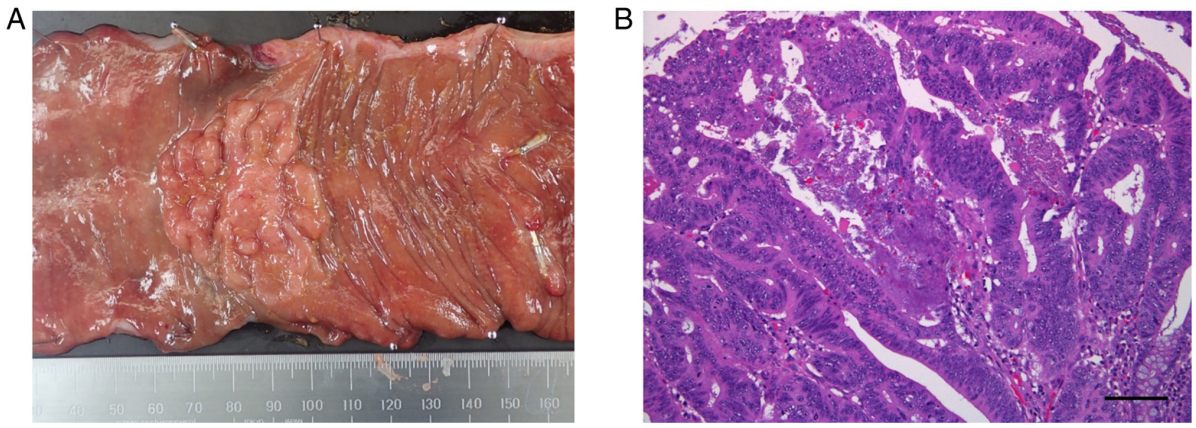

Figure 1. Macro- and microscopic examinations of the resected primary transverse colon cancer. (A) A 40-mm sized tumor in the transverse colon. (B) Histopathological findings of primary colon cancer revealed a well-differentiated adenocarcinoma which proliferated invasively with glandular formation. Hematoxylin and eosin staining. Scale bar, 100 μm.

Positron emission tomography revealed that the tumor showed fluorodeoxyglucose uptake with a standardized uptake value of 16.5 (Fig. 3). Further, the liver adjacent to the surgical site of the previous cholecystectomy showed fluorodeoxyglucose uptake but did not show any abnormal findings on CECT scan. Mediastinal lymph node metastasis from CRC was considered a preoperative diagnosis. Thus, surgical resection of the tumor would be an appropriate method as the rapidly growing tumor may cause fatal complications in the future.

The patient underwent resection of the anterior mediastinal tumor. Intraoperative findings suggested tumor invasion to the adjacent pericardium, and therefore, pericardiectomy and pericardial reconstruction were performed. The resected mediastinal tumor was 35x25 mm in size (Fig. 4A). Microscopic examination revealed that the tumor was an adenocarcinoma (Fig. 4B). Immunohistochemical analysis (refer to Supplementary data for method) revealed that the cells expressed CK20 (Fig. 4C) and CDX2 but not CK7 (Fig. 4D) and TTF-1. These pathological findings were consistent with the diagnosis of mediastinal metastasis originating from the previous transverse colon cancer. Additionally, the cancer was pathologically identified to have invaded the adjacent pericardium and diaphragm. However, no cancer cells were detected in the surrounding lymph node, thymus, and pericardial fluid. Furthermore, the molecular mutation status of the primary transverse colon cancer was examined retrospectively. The tumor expressed BRAF V600E mutations but did not express RAS mutations and microsatellite instability.

The patient was postoperatively treated with thoracic drainage for pleural effusion and was discharged on postoperative day 28. The patient refused additional chemotherapy. Follow-up CECT and gadolinium ethoxybenzyl diethylenetriamine pentaacetic acid-enhanced magnetic resonance imaging showed no recurrent metastases in any organ. The patient has been alive without recurrence 8 months after the surgery for mediastinal metastasis.

Discussion

Metachronous metastatic sites after curative resection of CRC are the liver, occurring in 7.1% of patients, lung in 5.5%, peritoneum in 2.0%, and local lesion in 2.0% of patients (2). Saito *et al* reported that 14% of patients who underwent lung resection for metastatic CRC had mediastinal or hilar lymph node metastasis (3). Some mediastinal lymph node metastases have been identified in patients with liver, para-aorta lymph node, or thyroid metastases (4-10). From these reports, mediastinal lymph node metastasis from CRC is considered re-metastasis from concurrent or previously metastasized organs. Conversely, solitary mediastinal lymph node metastasis from CRC without any other organ involvement is extremely rare, and to the best of our knowledge, only two patients, including our case, have been reported (11). In retrospect, the mediastinal tumor was not detected 12 months after colectomy; therefore, we should have taken more care when examining the mediastinum even in the cases where other organ metastases were absent during follow-up.

The mechanism of mediastinal lymph node metastasis depends on the presence or absence of intrathoracic lesions. Mediastinal metastasis can occur following lung metastasis through the lymphatic drainage system (3). In patients without intrathoracic lesions, mediastinal metastasis is presumed to be primarily caused by the thoracic duct (4,12,13). Most previous reports showed a middle or posterior mediastinal metastasis (5-9,11) as the anterior mediastinum does not directly communicate with the thoracic duct (12). In contrast, it is hypothesized that hematogenous metastasis via the paravertebral venous plexus exists in exceptional cases with ovarian metastasis (14). In our case, the mediastinal tumor had no lymph node structure pathologically. However, the metastasis was considered lymphogenous because primary colon cancer had regional lymph node metastasis and CECT showed an increase in mediastinal lymph node metastasis over time. The uniqueness of our case could be attributed to solitary metastases and its location in the anterior mediastinum. Vetto *et al* reported a metastatic form via lymphatic drainage from the liver to the anterior mediastinum through the right diaphragm, caval foramen, and esophageal hiatus (4). Therefore, the patient was followed up with careful attention to latent cancer metastasis, primarily the liver, after complete resection of anterior mediastinal metastasis. Notably, to the best of our knowledge, this is the first study that reported the molecular mutation

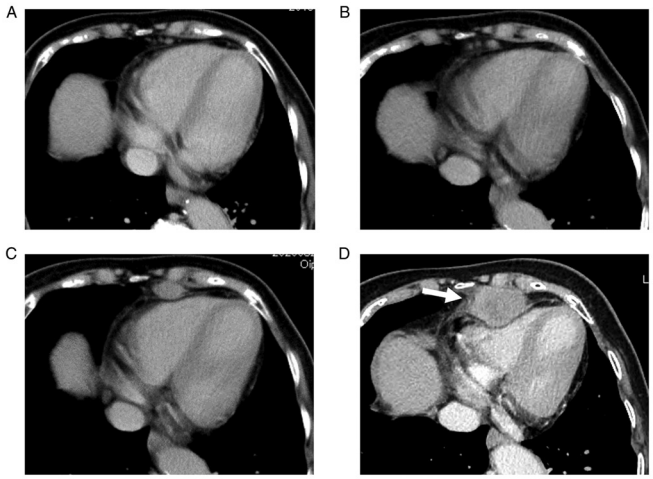

Figure 2. Computed tomography images. Axial images acquired using contrast-enhanced computed tomography (A) before colectomy, (B) six months after colectomy and (C) twelve months after colectomy. (D) Anterior mediastinal tumor compressing the heart 18 months after colectomy (indicated by arrow).

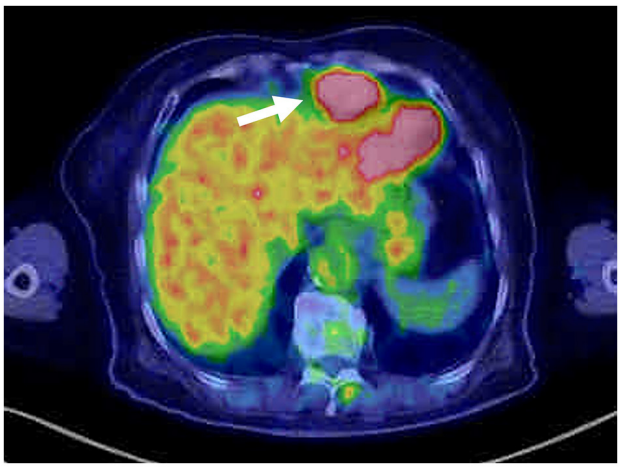

Figure 3. Positron emission tomography images. The tumor showed fluorodeoxyglucose uptake with a standardized uptake value of 16.5 (indicated by arrow).

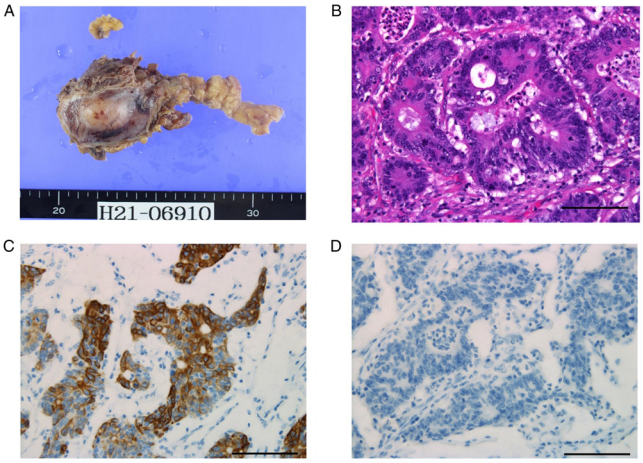

Figure 4. Histopathological examination of the resected mediastinal tumor. (A) A 35x25-mm sized mediastinal tumor. (B) Tumor was identified using hematoxylin and eosin staining as adenocarcinoma which proliferated invasively with glandular formation in microscopic examination. (C) Tumor cells expressed brown stain, which indicated CK20 immunohistochemistry. (D) Tumor cells presented a lack of brown stain, which indicated CK7 immunohistochemistry.Scale bars, 100 μm. CK, cytokeratin.

status expressing BRAF V600E mutations but not RAS mutations and microsatellite instability. BRAF mutant CRC is widely known to have a different pattern of metastatic spread compared with wild-type CRC (15). Distant lymph node and peritoneal metastases in BRAF mutant CRC are observed more frequently and lung metastases are observed less frequently than those in wild-type CRC (15). Additionally, it has been reported that the rate of distant lymph node metastases was not different between tumors expressing microsatellite instability and those with stable microsatellite (15). Thus, oncogenic mutations in BRAF might be involved in mediastinal lymph node metastasis from CRC and further studies are needed for a deeper understanding.

The borders of the anterior mediastinum are the sternum anteriorly, the pericardium posteriorly, the thoracic inlet superiorly, and the diaphragm inferiorly (16). Anatomically, the anterior mediastinal tumor can cause direct pericardial invasion, which may lead to carcinomatous pericarditis (17). Carcinomatous pericarditis can develop cardiac tamponade and has a poor prognosis with a median survival of 3-5 months (18-20). Our patient showed rapid tumor growth and pathological pericardial invasion, although no cancer cells were found in the pericardial fluid. Resection of the mediastinal metastasis was considered effective in preventing possible fatal complications.

CRC treatment progression has created more opportunities for even patients with metastasis to undergo surgeries, including hepatectomy and pneumonectomy. The prognosis after hepatectomy and pneumonectomy is favorable, with a 5-year survival rate of 35-58 and 30-68%, respectively (21-26). However, Saito *et al* reported that patients with lung and mediastinal lymph node metastases had a poor prognosis, and therefore, surgery might not be indicated (3). Conversely, the prognosis of patients with solitary mediastinal lymph node metastasis remains unknown because of its rarity and unclear optimal treatment. In the Japanese Society for Cancer of Colon and Rectum guidelines, surgical treatment is indicated when a recurrent tumor is observed in a single organ and when complete surgical resection is possible (2). Within the guideline, the resection of solitary mediastinal lymph node metastasis was performed, resulting in a satisfactory outcome without recurrence 8 months postoperatively. Our patient has undergone short-term postoperative follow-up every 1-2 months because early postoperative recurrence may occasionally occur (10).

In conclusion, a patient with a rare incidence of recurrent CRC was reported with a solitary anterior mediastinal lymph node metastasis, suggesting that clinicians should consider the metastasis to mediastinum during follow-up in patients with CRC. The anterior mediastinal lymph node metastasis from CRC can cause fatal complications because of the direct pericardial invasion. In the case of solitary anterior mediastinal metastasis, surgery may be the most reliable treatment. A large number of cases must be accumulated to establish optimal management.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

YW drafted the manuscript and provided original images. RS, MK and MH participated in treating the patient and revising the manuscript. All authors read and approved the final manuscript. YW and RS confirmed the authenticity of all the raw data.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

Written informed consent was obtained from the patient for publication of this article and any accompanying images.

Competing interests

The authors declare that they have no competing interests.

References

1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A and Bray F: Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 71: 209-249, 2021.
2. Hashiguchi Y, Muro K, Saito Y, Ito Y, Ajioka Y, Hamaguchi T, Hasegawa K, Hotta K, Ishida H, Ishiguro M, *et al*: Japanese society for cancer of the colon and rectum (JSCCR) guidelines 2019 for the treatment of colorectal cancer. Int J Clin Oncol 25: 1-42, 2020.
3. Saito Y, Omiya H, Kohno K, Kobayashi T, Itoi K, Teramachi M, Sasaki M, Suzuki H, Takao H and Nakade M: Pulmonary metastasectomy for 165 patients with colorectal carcinoma: A prognostic assessment. J Thorac Cardiovasc Surg 124: 1007-1013, 2002.
4. Vetto JT and Cohen AM: Isolated spread of hepatic metastatic disease to a mediastinal lymph node. Report of a case and review of pertinent anatomy and literature. Dis Colon Rectum 34: 1128-1130, 1991.
5. Sano A, Murakawa T, Morota T and Nakajima J: Resection of a posterior mediastinal metastasis of colon cancer. Ann Thorac Surg 92: 353-354, 2011.
6. Iwata T, Chung K, Hanada S, Toda M, Nakata K, Kato T and Miura T: Solitary bulky mediastinal lymph node metastasis from colon cancer. Ann Thorac Cardiovasc Surg 19: 313-315, 2013.
7. Nomura T, Katsumata K, Hara T, Sonoda I, Kasahara K, Kuwabara H, Shigoka M, Enomoto M, Ishizaki T, Sumi T and Tsuchida A: Long-Term survival of a patient with mediastinal lymph node metastasis treated with chemo-radiotherapy after surgery for cecal cancer. Gan To Kagaku Ryoho 44: 1698-1700, 2017 (In Japanese).
8. El-Halabi MM, Chaaban SA, Meouchy J, Page S and Salyers WJ Jr: Colon cancer metastasis to mediastinal lymph nodes without liver or lung involvement: A case report. Oncol Lett 8: 2221-2224, 2014.
9. Matsuda Y, Yano M, Miyoshi N, Noura S, Ohue M, Sugimura K, Motoori M, Kishi K, Fujiwara Y, Gotoh K, *et al*: Solitary mediastinal lymph node recurrence after curative resection of colon cancer. World J Gastrointest Surg 6: 164-168, 2014.
10. Yamamoto Y, Kodama K, Ide Y and Takeda M: Thymic and mediastinal lymph node metastasis of colon cancer. Ann Thorac Surg 103: e13-e15, 2017.
11. Musallam KM, Taher AT, Tawil AN, Chakhachiro ZI, Habbal MZ and Shamseddine AI: Solitary mediastinal lymph node metastasis in rectosigmoid carcinoma: A case report. Cases J 1: 69, 2008.
12. Baltaxe HA and Constable WC: Mediastinal lymph node visualization in the absence of intrathoracic disease. Radiology 90: 94-98, 1968.
13. McLoud TC, Kalisher L, Stark P and Greene R: Intrathoracic lymph node metastases from extrathoracic neoplasms. AJR Am J Roentgenol 131: 403-407, 1978.
14. Kuba H, Sato N, Uchiyama A, Nakafusa Y, Mibu R, Yoshida K, Kuroiwa K and Tanaka M: Mediastinal lymph node metastasis of colon cancer: Report of a case. Surg Today 29: 375-377, 1999.
15. Tran B, Kopetz S, Tie J, Gibbs P, Jiang ZQ, Lieu CH, Agarwal A, Maru DM, Sieber O and Desai J. Impact of BRAF mutation and microsatellite instability on the pattern of metastatic spread and prognosis in metastatic colorectal cancer. Cancer 117: 4623-4632, 2011.
16. Tecce PM, Fishman EK and Kuhlman JE: CT evaluation of the anterior mediastinum: spectrum of disease. Radiographics 14: 973-990, 1994.
17. Sawada H, Toyota K, Hakoda K, Kajiwara R, Hotta R, Inoue M, Ohmori I, Miyamoto K, Sadamoto S and Takahashi T: A case of stage II ascending colon cancer with cardiac tamponade due to pericardial metastasis. Am J Case Rep 22: e932239, 2021.
18. Dequanter D, Lothaire P, Berghmans T and Sculier JP: Severe pericardial effusion in patients with concurrent malignancy: A retrospective analysis of prognostic factors influencing survival. Ann Surg Oncol 15: 3268-3271, 2008.
19. Dosios T, Theakos N, Angouras D and Asimacopoulos P: Risk factors affecting the survival of patients with pericardial effusion submitted to subxiphoid pericardiostomy. Chest 124: 242-246, 2003.
20. Tsang TS, Seward JB, Barnes ME, Bailey KR, Sinak LJ, Urban LH and Hayes SN: Outcomes of primary and secondary treatment of pericardial effusion in patients with malignancy. Mayo Clin Proc 75: 248-253, 2000.
21. Martin LW and Warren RS: Current management of colorectal liver metastases. Surg Oncol Clin N Am 9: 853-876; discussion 877-8, 2000.
22. Abdalla EK, Vauthey JN, Ellis LM, Ellis V, Pollock R, Broglio KR, Hess K and Curley SA: Recurrence and outcomes following hepatic resection, radiofrequency ablation, and combined resection/ablation for colorectal liver metastases. Ann Surg 239: 818-825; discussion 825-7, 2004.
23. Nordlinger B, Sorbye H, Glimelius B, Poston GJ, Schlag PM, Rougier P, Bechstein WO, Primrose JN, Walpole ET, Finch-Jones M, *et al*: Perioperative FOLFOX4 chemotherapy and surgery versus surgery alone for resectable liver metastases from colorectal cancer (EORTC 40983): Long-term results of a randomised, controlled, phase 3 trial. Lancet Oncol 14: 1208-1215, 2013.
24. Watanabe K, Nagai K, Kobayashi A, Sugito M and Saito N: Factors influencing survival after complete resection of pulmonary metastases from colorectal cancer. Br J Surg 96: 1058-1065, 2009.
25. Iida T, Nomori H, Shiba M, Nakajima J, Okumura S, Horio H, Matsuguma H, Ikeda N, Yoshino I, Ozeki Y, *et al*: Prognostic factors after pulmonary metastasectomy for colorectal cancer and rationale for determining surgical indications: A retrospective analysis. Ann Surg 257: 1059-1064, 2013.
26. Kanemitsu Y, Kato T, Hirai T and Yasui K: Preoperative probability model for predicting overall survival after resection of pulmonary metastases from colorectal cancer. Br J Surg 91: 112-120, 2004.