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An unusual case of colorectal adenocarcinoma presenting as an anterior mediastinal mass

Joshua L. Rodríguez-López, M.D.¹, Alia M. Toro-Bahamonde, M.T., Ph.D.², Roberto J. Santiago-Méndez, M.D., DABR³, Iván F. González-Cancel, M.D.⁴, and Héctor A. Vélez-Cortés, M.D.⁵

¹Transitional Year Program, University of Puerto Rico-Medical Sciences Campus, San Juan, P.R. 00921

²Ad-Vance Medical Research, Ponce, P.R. 00717

³Department of Radiation Oncology, Auxilio Mutuo Hospital, San Juan, P.R. 00919

⁴Department of Cardiothoracic Surgery, Centro Cardiovascular de Puerto Rico y del Caribe, San Juan, P.R., 00921

⁵Ponce Hematology Oncology, Ponce, P.R. 00717

Keywords

carcinoma; distant metastasis; Hispanic; mediastinum; unknown primary

Introduction

Colorectal cancer is the second leading cause of cancer-related death in the United States when both sexes are combined (1), but in Puerto Rico is the leading cause of cancer-related death (2). Puerto Rican men and women ages 40 years to 59 years have a greater risk of incidence and mortality than their United States Hispanics counterpart (3). Most commonly, colorectal cancer spreads to the regional lymph nodes (52%), liver (78%), lung (20%), and peritoneum (29%) (4). However, solitary metastases without evidence of a primary lesion are extremely rare, and the mediastinum as initial site of presentation has only being described a few times in the medical literature. We present a case of 45-year-old Hispanic male, with a diagnosis of stage IV (T0 N0 M1 G3) colorectal adenocarcinoma, which was referred to the clinic due to an anterior mediastinal mass and no other primary lesion. The patient provided written consent to publish this data.

Case description

This is a case of a 45-year-old Hispanic male, with no family history of cancer and no significant medical history other than essential hypertension and gastroesophageal reflux disease, who was evaluated because of a three month history of chest pain and facial

swelling. The initial physical exam was unremarkable. A chest computer tomography (CT) imaging was ordered to determine cause of pain and showed an anterior superior mediastinal mass (Figure 1). A percutaneous core biopsy was performed and the preliminary pathology report suggested a malignant mediastinal neoplasm suspected to be of germ cell tumor origin. Abdominal and pelvic CT images were unremarkable. Alpha-fetoprotein, lactase dehydrogenase, and beta human chorionic gonadotropin values were within normal limits 4.24 ng/mL (0–40 ng/mL), 149.00 IU/L (105–333 IU/L), 0.14 μ IU/mL (<5 IU/L), respectively. However, the final pathology result came back positive for Villin, CK20, CDX2, CK8/18, and CAM 5.2 (Figure 2), which correlated with an adenocarcinoma, favoring a colorectal primary. Carcinoembryonic antigen (CEA) was 1.75 ng/mL (0–3 ng/mL).

Due to the unexpected result, Positron emission tomography (PET)/CT was ordered to determine disease extent, and results showed a large hypermetabolic anterior/superior mediastinal soft tissue density of 8.4 SUV and a low-level hypermetabolic activity within the large bowel, most prominent at proximal rectum of 3.4 SUV (Figure 3). Thus, the patient underwent a colonoscopy, but no masses or lesions were noticed (Figure 4), and blind biopsies were negative for malignancy. In view that the disease was only confined to the mediastinum, a video-assisted thoracoscopic surgery (VATS) was attempted. However, it was suspended due to tumor close proximity to major blood vessels, but a bigger tumor sample was taken for molecular and genetic studies. Several genetic mutations were identified (ALK, ERBB2, ROS1, and TP53). Mismatch repair proteins were also analyzed by immunohistochemistry (IHC). There was expression of MLH-1, MSH-2, MSH-6, and PMS-2, which correlated with stable to low microsatellite instability (MSS/MSI-L).

Although, the disease was considered to be a primary colorectal adenocarcinoma of the mediastinum. It was decided to treat him as an unresectable/metastatic colorectal adenocarcinoma. Patient was started on FOLFOX-6 + bevacizumab therapy. After five cycles of chemotherapy, the patient decided to undergo debulking surgery with another cardiothoracic surgeon. Chest CT was repeated and the mass measured $6.5 \times 5.0 \times 4.0$ cm, which was relatively stable when compared with first CT. Bevacizumab was suspended 28 days before surgery. Complete surgical resection was not possible. Margins were grossly positive for adenocarcinoma. Patient did not have any complications during or after the surgery, and patient's wound healed properly. Adjuvant therapy was recommended. Chemotherapy was reinitiated one month after surgery. 11 cycles of FOLFOX-6 + bevacizumab were given for a total of 16, and followed by 6,000 cGy in 30 fractions. RT was started with his last cycle of chemotherapy.

PET/CT scan was repeated three months after finishing treatment. A partial response was achieved, the anterior mediastinal mass had a SUV of 3.9 and measured 1.6 cm AP, no other abnormalities were seen. Patient was asymptomatic and CEA level was 1.53 ng/mL (0–3). It was decided to observe him closely. Unfortunately, after three months, he started complaining of constant sternal chest pain. Chest CT was done which showed the mass measuring $5.3 \times 3.5 \times 2.8$ cm, and this finding was concerning for disease progression. Another PET/CT was done, and the mass SUV increased to 5.1 and measured 2.5 cm AP $\times$ 2.1 cm transverse $\times$ 3.5 cm CC, also new small hypermetabolic bilateral paratracheal

lymphadenopathy with a SUV of 3.5 and right upper lobe parenchymal densities with a SUV of 4.0 were seen. Palliative systemic therapy was offered, but the patient did not return to subsequent visits.

Discussion

This case shows an unusual presentation for a colorectal adenocarcinoma. Differential diagnosis for anterior mediastinal mass include: teratoma, thymoma, lymphoma, and thyroid disease. For this reason, tumor markers for these specific etiologies were done. IHC analysis showed no signal on the following markers: CD20, CK7, TTF1, and C-Kit, eliminating the possibility of lymphoma, lung adenocarcinoma, or germ cell type origin. However, positive results on the following markers were observed: CK20, CDX2, CK8/18, and CAM 5.2, confirming the unexpected result of metastatic adenocarcinoma, favoring a primary colorectal tumor. Yet, there was no evidence of a primary lesion.

The 5-year survival rate for colorectal cancer is 90%, 70%, and 13% for patients diagnosed with localized, regional, and distant stage disease, respectively (1). Colorectal cancer metastasis to mediastinal lymph nodes has been previously described. Most mediastinal metastases occur after completing treatment for a colorectal primary lesion or re-metastasis from previous sites (5–13). However, other cases have been described to show synchronous mediastinal metastases with a primary colonic lesion (14,15). Interestingly, colon cancer metastasis to the mediastinal lymph nodes without evidence of other organ involvement has been reported (9,11,15), but these cases had a previous history of colon cancer or a synchronous primary lesion was found. Still, little is known about the presentation of distant metastasis, like the mediastinum, favoring primary colorectal carcinoma without evidence of a primary colonic lesion as shown in this current case.

Several therapeutic approaches for metastatic colorectal carcinoma to the mediastinum have been reported in the literature. There are cases where solitary lesions have been surgically removed (6,8,10,11), and others have been treated with chemotherapy only (9,15). One particular case was reported to receive adjuvant chemotherapy after resection of recurrent solitary mediastinal lymph node metastasis (11). The patient was still alive after six years of completing his treatment (11).

Advances in metastatic colon cancer management have demonstrated that metastases confined to the liver or lung can be surgically removed (16). Neoadjuvant chemotherapy can be administered for tumor shrinkage and improve surgical outcomes in patients with extensive hepatic disease (17). On the other hand, fluorouracil-based chemotherapy in combination with bevacizumab improves progression-free survival, median survival and response rate in metastatic colorectal cancer (18). The role of RT in colon cancer is unclear, whereas for rectal cancer, the addition of postoperative RT improves local control (19).

In our patient, due to the extensive infiltration of the mediastinal mass to surrounding tissue, surgery was not recommended initially. For this reason, he was started on chemotherapy with FOLFOX-6 + bevacizumab. After 5 cycles of chemotherapy, surgery was performed, due to patient's preferences. Unfortunately, complete removal of the tumor was not

amenable. Adjuvant chemoradiation was recommended to ensure local and distant disease control. Patient had a good response, unfortunately, the disease relapsed six months after finishing treatment. Due to the limited literature of metastatic colorectal adenocarcinoma to the mediastinum, prognosis is difficult to predict. Further case series, retrospective, or prospective data will be needed to address properly this type of unusual presentations.

Conclusion

In summary, this case came to our attention due to the unexpected diagnosis of metastatic colorectal adenocarcinoma in the mediastinum, without evidence of a primary lesion on the colon or any other site. The current case provides evidence that distal organ metastasis should not be excluded when initially screening an oncology patient. Early identification of disease extent, genetic alteration profiling, and targeted therapy might favor a better therapeutic approach.

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Clinical Practice Points

- Distant colorectal cancer metastasis to the mediastinum is extremely rare.
- Metastatic colorectal cancer usually invades regional lymph nodes, liver, lung, brain or peritoneum.
- The current case is an unusual presentation of a mediastinal mass favoring metastatic carcinoma of colorectal cancer with unknown primary.

Figure 1.
Chest computer tomography (CT) imaging shows an anterior superior mediastinal mass measuring 7×6×5cm.

Figure 2.
(A) H&E staining; IHC staining for (B) Villin, (C) CAM5.2, (D) CK20. A mediastinal mass CT-guided percutaneous biopsy was collected for diagnosis. Immunohistochemistry results showed positive Villin, CK20, CDX2, CK8/18, and CAM 5.2 suggestive of a metastatic adenocarcinoma, favoring primary colorectal carcinoma.

Figure 3. Positron emission tomography (PET)/CT shows large hypermetabolic anterior/superior mediastinal soft tissue density of 8.4 SUV and a low-level hypermetabolic activity within the large bowel most prominent at proximal rectum of 3.4 SUV.

Figure 4.
Colonoscopy showing no evidence of lesions or abnormalities.