

Metastatic Colon Cancer Involving the Right Atrium

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Colorectal cancer rarely metastasizes to the heart. In the world medical literature, we identified only 7 cases of well-documented colorectal cancer metastasis to the right atrium. Herein, we describe the case of a 72-year-old man in whom metastatic mucinous adenocarcinoma of the colon involved the right atrium and caused superior vena cava syndrome. To our knowledge, this is the first case report of sudden cardiac death due to embolization of metastatic colon cancer from the right atrium. We also present the first comprehensive case series review of this rare entity.

Given improvements in diagnostic and therapeutic methods that have increased the longevity of many cancer patients, the detection of cardiac metastases is likely to increase in frequency. Accordingly, we recommend that previously asymptomatic cancer patients with a history of colorectal cancer who develop cardiac symptoms undergo prompt investigation for possible cardiac metastasis. (Tex Heart Inst J 2012;39(1):79-83)

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Tumors involving the heart are more commonly metastatic than primary, and the prognosis for patients with metastatic cardiac tumors is typically poor.¹ Although clinical recognition of cardiac metastasis from colorectal cancer is rare and continues to present a diagnostic and therapeutic challenge, this neoplasm should be considered among the broad differential of cardiac intracavitary masses. Herein, we report a rare case of mucinous adenocarcinoma of the colon that metastasized to the right atrium (RA) and resulted in superior vena cava syndrome. We also present a comprehensive review of this rare entity, including pertinent diagnostic methods.

Case Report

In 2007, a 72-year-old man was transferred to our hospital for surgical treatment of a newly identified RA mass. In 2004, he had undergone hemicolectomy of a T4b N2b M0 mucinous adenocarcinoma of the colon. His medical history included myocardial infarctions, treated with coronary artery bypass grafting; ischemic cardiomyopathy, treated with a prophylactic implantable cardioverter-defibrillator (ICD); lower-extremity peripheral arterial disease, treated with bypass surgery; and type 2 diabetes mellitus, hypertension, hyperlipidemia, and chronic anemia. The patient was admitted to another hospital for evaluation and treatment of a nonhealing right-foot ulcer. During hospitalization, he had mild shortness of breath and facial swelling; however, he had no fever, chest pain, or rash. Transthoracic echocardiography (TTE) revealed an RA mass that prolapsed through the tricuspid valve into the right ventricle. Transesophageal echocardiography (TEE) confirmed the presence of a heterogeneous, lobulated mass attached to the RA by a pedicle (Fig. 1). The mass bore little resemblance to a thrombus, and no other mass, vegetation, or cardiac shunt was detected. Upon transfer to our hospital, the patient remained dyspneic. Infectious process was excluded with serial negative blood, urine, and wound cultures. Duplex Doppler ultrasonography of the lower extremities revealed no deep vein thrombosis. Chest computed tomography (CT) showed multiple bilateral pulmonary nodules of up to 1 cm in size, raising the suspicion of metastasis. Surgical resection of the RA mass was scheduled.

On the evening before the planned excision of the mass, the patient was found on the bathroom floor, minimally responsive and pulseless, with ventricular tachycardia on telemetry. Advanced cardiac life support was initiated. His ICD fired 3 times. Subsequently, he developed electromechanical dissociation and was pronounced dead. Gross autopsy findings included a friable mass, composed of tan mucinous tissue admixed with blood; the mass was attached to the endocardial surface of the RA free wall by a fine stalk and extended into the superior vena cava. Microscopic pathologic

examination of this mass confirmed metastatic mucinous adenocarcinoma that resembled the histologic appearance of his primary adenocarcinoma of the colon (Fig. 2). Multiple tumor emboli recovered from the bilateral pulmonary arteries were the proximate cause of the patient's sudden cardiac death.

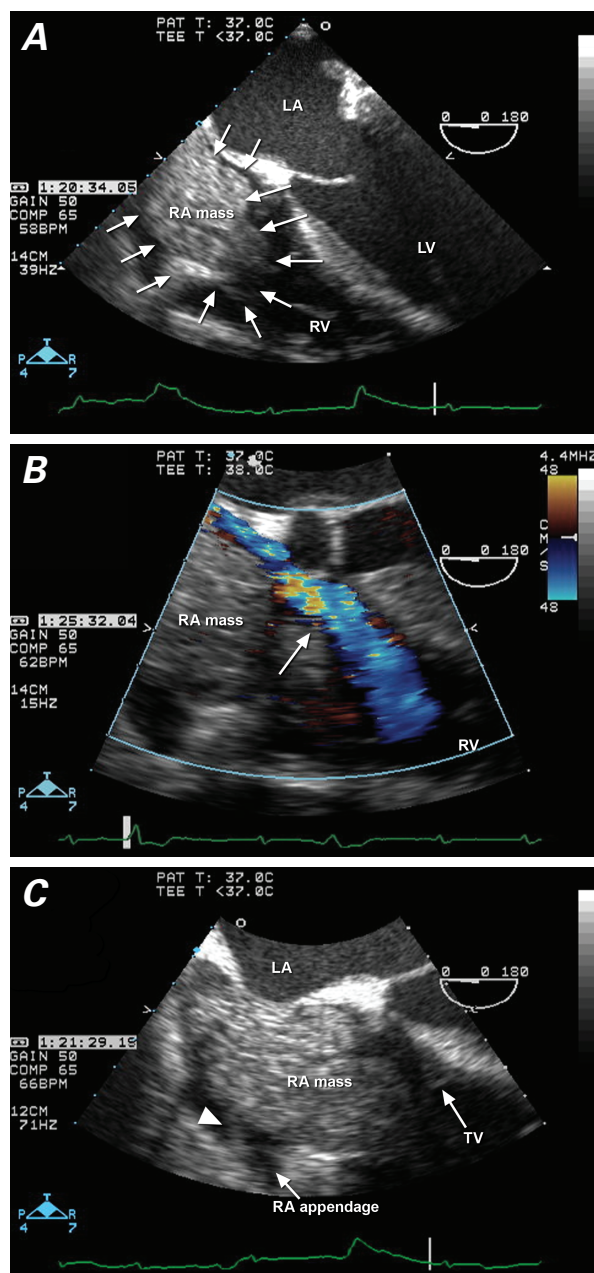


Fig. 1 Transesophageal echocardiography in a patient with superior vena cava syndrome shows **A**) a mass filling the entire right atrium (RA) and protruding through the tricuspid valve (4-chamber view); **B**) restricted venous return (arrow) around the RA mass into the right ventricle (RV) (color-flow Doppler), and **C**) attachment by pedicle (arrowhead) of the RA mass to the RA free wall.

LA = left atrium; LV = left ventricle; TV = tricuspid valve

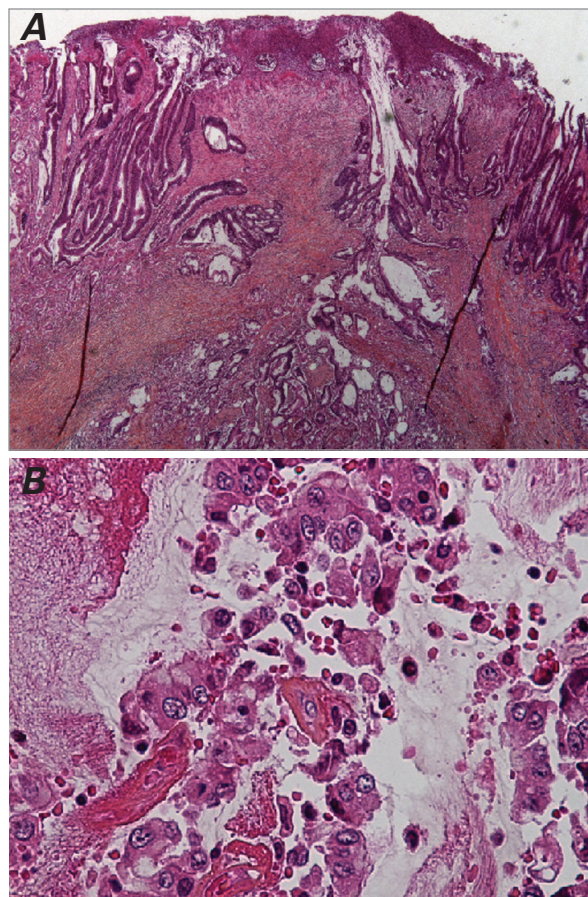


Fig. 2 Photomicrographs (H & E) show **A**) an infiltrating, moderately to poorly differentiated primary colonic adenocarcinoma, with desmoplastic response in the bowel wall (orig. $\times 2$); and **B**) a metastatic tumor thrombus in the right atrium, with scattered, preserved tumor cells floating in mucin and fibrin (orig. $\times 20$).

Discussion

We found only 7 cases of well-documented metastatic colorectal cancer that had involved the RA (Table I).²⁻⁸ To our knowledge, ours is the first reported case of sudden cardiac death due to embolization of metastatic colon cancer from the RA.

Metastatic Cardiac Tumors

In autopsy series of cancer patients, metastatic cardiac tumors have a prevalence of 1.5% to 20%.¹ The most common cancers with cardiac metastatic potential are melanoma, lymphoma, carcinomas of the lung, breast, and esophagus, and leukemia.^{1,9} The metastatic pathway of the primary tumor can be by the lymphatic system,^{10,11} bloodstream, transvenous extension, or direct contiguous extension.¹¹ In decreasing order of frequency, metastatic cardiac tumors involve the pericardium, myocardium, epicardium, endocardium, and intracavitary regions.¹¹ Right-sided cardiac involvement, mainly ventricular, is

more common than left-sided involvement.^{10,12} Metastases to the valvular endocardium, known as marantic endocarditis, are rare and are associated with adenocarcinomas and hypercoagulable states.^{13,14} The clinical manifestations of cardiac metastases are protean and depend on the location and size of the metastatic tumor; however, extensive involvement may occur with few or no symptoms¹¹—and more than 90% of metastatic cardiac tumors are clinically silent.¹

The lymph nodes, liver, and lungs are the most common sites of metastases from colorectal cancer. Colorectal cancer rarely metastasizes to the heart (in autopsy series, the prevalence is 1.4%–2% vs 23%–31% for bronchogenic carcinomas) and most commonly involves the pericardium.⁵

Review of Reported Cases

From the world medical literature, we identified only 7 cases of well-documented metastatic colorectal cancer

that involved the RA.^{2–8} Similar to our case, metastatic involvement of the RA from colorectal cancer was found predominantly in men aged 65 to 72 years. The mass in the RA was diagnosed as early as 8 months² and up to 5 years⁴ after treatment of the primary tumor. Choi and colleagues⁷ reported a case in which primary colon cancer and RA involvement were diagnosed concurrently. In most of these reported cases, the metastatic adenocarcinomas were of moderately differentiated histology. The primary tumor in 3 cases,^{3,4,8} as in ours, was mucinous adenocarcinoma; characterization was not specified in the other reports. Of note, in about half of the cases, isolated RA involvement was the only clinical evidence of metastasis.^{2,3,6,7}

The clinical manifestations of RA involvement from metastatic colorectal cancer are nonspecific and include symptoms of right-sided heart failure,⁴ shortness of breath, arrhythmias, pulmonary thromboembolism, and—as in our patient—superior vena cava syndrome.²

TABLE I. Cases Reported of Metastatic Colorectal Cancer Involving the Right Atrium in the World Medical Literature

Author	Sex, Age (yr)	Primary Tumor Location	Primary Tumor and Tumor Stage	Method of Diagnosis of Cardiac Metastasis	Tumor Size (cm)	Treatment of Metastatic Mass	Outcome
Nishida H, et al. ² (1991)	M, 69	Colon	Moderately differentiated adenocarcinoma; NA	TTE and MRI	10 × 8 × 3	Resection	Died 2 wk postoperatively
Zipoli A, et al. ³ (1994)	F, 41	Colon	Mucinous adenocarcinoma; NA	TTE	4.1 × 3.7	Resection	Died 6 mo after resection of tumor
Teixeira H, et al. ⁴ (1997)	M, 81	Colon	Mucinous adenocarcinoma; Duke B2	TTE and CT	NA	Chemotherapy	Died shortly after diagnosis of RA tumor
Choufani EB, et al. ⁵ (2001)	M, 59	Colon	Moderately differentiated adenocarcinoma; T3 N1 MX (stage III)	TTE	5 × 3	Chemotherapy	Alive 10 mo after chemotherapy
Koizumi J, et al. ⁶ (2003)	M, 65	Rectum	Well-differentiated adenocarcinoma; Duke C	TTE	6 × 5	Resection	Lived for 11 mo after resection and without chemotherapy
Choi PW, et al. ⁷ (2009)	F, 70	Colon	Moderately differentiated adenocarcinoma; T4 N2	TTE	5.5 × 5 × 3	Resection	Died within 3 d postoperatively due to recurrent cardiac bleeding
Makhija Z, et al. ⁸ (2009)	M, 70	Rectum	Poorly differentiated mucinous adenocarcinoma; T3 N2 M1	TTE	5.6 at greatest diameter	Debulking due to invasion of tumor in RA wall	Alive at 56 mo from time of diagnosis of rectal cancer
Current	M, 72	Colon	Moderately differentiated mucinous adenocarcinoma; T4b N2b M0	TTE and TEE	8.5 × 5 × 4	None	Sudden cardiac death due to pulmonary embolism from tumor

CT = computed tomography; F = female; M = male; MRI = magnetic resonance imaging; NA = not available; RA = right atrial; TEE = transesophageal echocardiography; TTE = transthoracic echocardiography

Differential diagnosis is broad and includes thrombus, vegetation, or primary tumors such as myxoma. As a tumor marker, the carcinoembryonic antigen assay (CEA) can be helpful in detecting recurrence of primary or metastatic disease; however, this test is nonspecific for the diagnosis of cardiac metastatic disease.⁵ In our patient, the CEA values were within normal range during serial follow-up after hemicolectomy, including the time of diagnosis of the RA mass. This can be explained by the mucinous nature of adenocarcinoma, which yields relatively low amounts of the tumor marker. The CEA levels were not specified in the other reports of mucinous adenocarcinoma.^{3,4,8}

In all of the reported cases,²⁻⁸ the primary tumor was surgically treated at the time of diagnosis; however, only 3 patients underwent postoperative adjuvant chemotherapy.^{5,6,8} In 2 of those patients, the RA mass was found at 6 months⁶ and 16 months⁵ after the discontinuation of chemotherapy; in the 3rd instance,⁸ the RA mass was detected while the patient was undergoing chemotherapy. Our patient had refused further chemotherapy after 3 cycles due to intolerable side effects, and the mass was discovered within 3 years after his hemicolectomy.

Chemotherapy treatment of the RA mass was attempted in 2 patients^{4,5}; in the younger patient, a favorable response was evidenced by the resolution of the mass.⁵ In the other instance, chemotherapy was discontinued due to disease progression, and the patient died shortly thereafter.⁴ Surgical resection was attempted in 4 cases of isolated solitary RA mass, and debulking was successful in a circumstance of RA wall invasion by the tumor.⁸ The tumor was successfully excised in 2 patients.^{3,6} A 3rd patient could not be weaned from mechanical ventilation and died postoperatively as a result of presumed pulmonary embolization of the tumor,² and a 4th patient died due to postoperative recurrent cardiac bleeding.⁷ Of note, we learned that the patient who underwent debulking⁸ was still alive with the aid of chemotherapy 56 months after the diagnosis of the RA mass. We had advised our patient to undergo surgical removal of the large RA mass, to alleviate superior vena cava syndrome and prevent impending massive pulmonary embolism.

Diagnostic Imaging Methods

On TTE, the characteristics of RA masses are variable and may be homogeneous^{2,4} or heterogeneous^{3,7} with variable mobility and echogenicity. Contrast-enhanced echocardiography with microbubble agents has been found to be useful in differentiating malignant tumor from benign tumor or avascular thrombus.¹⁵ Typically, the increased vascularity of malignant tumor enhances preferentially more than does the surrounding myocardium. More recently, 3-dimensional TTE has become the diagnostic method of choice for the characterization

of cardiac metastases.¹⁶ Of note, the use of TEE was not described in any of the other reports.

Transesophageal echocardiography can distinguish among solid, liquid, and hemorrhagic lesions, and can be useful in confirming metastatic disease. In our patient, TEE revealed a lobulated, multicystic mass with a clearly delineated pedicle that was attached to the RA free wall (Fig. 1C). In light of the negative serial blood cultures and chest CT description of bilateral pulmonary nodular masses, the TEE findings suggested metastatic disease. Compared with echocardiography, contrast-enhanced CT or cardiovascular magnetic resonance (CMR) will provide a broader field of view for the evaluation of cardiothoracic disease, and the contrast resolution of CMR enables the clear distinction of a tumor from myocardium.¹⁶ Both are useful to diagnose a mass noninvasively on the basis of enhancement and tissue density.^{2,4,16} Enhancement of the RA mass after the injection of intravenous contrast agents distinguishes a tumor from a thrombus: nonnecrotic tumors typically enhance, whereas thrombus does not.

Conclusion

Metastatic involvement of the RA from colorectal cancer is rarely reported. Because improved diagnostic and therapeutic methods have extended the lives of many cancer patients, the detection of cardiac metastases is likely to increase in the future. Any patient with a history of colorectal cancer who presents with cardiopulmonary symptoms should undergo prompt evaluation for possible cardiac metastasis. A multidisciplinary approach involving cardiologists, oncologists, and cardiothoracic surgeons is crucial for deciding the best therapeutic regimen for such patients. We believe that an isolated RA mass in the absence of other metastases has important therapeutic implications for adjunctive surgical treatment. On the basis of the current incidence and prevalence of colorectal cancer, we postulate that a multicenter registry would provide more conclusive recommendations for the best diagnostic and treatment approaches in this unusual subgroup of patients.

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