

An unusual cause of respiratory failure in a colon cancer patient

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Received February 4, 2015; Accepted April 22, 2015

DOI: 10.3892/mco.2015.608

Abstract. Permanent central venous catheters (CVC), such as Port-a-Cath®, Hickmann® or PICC®, are widely used in oncology patients for cancer treatment. Thrombosis is a frequent complication that should be ruled out, as it is associated with potentially severe infection and hemodynamic consequences. This is the case report of a male patient who was undergoing chemotherapy for colon cancer. The patient presented with an atrial mass secondary to a CVC-related organized thrombus located inside the atrial cavity. The mass was inducing a massive right-to-left intracardial shunt due to a persistent foramen ovale and signs of respiratory failure that required surgical intervention to remove the intracardial mass.

Introduction

Cancer and its treatment are frequently complicated by pulmonary disorders, mainly thromboembolic disease, although infections and drug toxicity may also develop. Diagnosis is usually based on clinical and radiological manifestations.

Permanent central venous catheters (CVC), such as Port-a-Cath® and Hickmann®, are widely used in oncology patients for cancer treatment. The most commonly reported complications of CVCs are infections and thrombosis. The incidence of CVC-related thrombosis was reported to be ~30% in adults (1). The clinical manifestations sometimes are obvious, with congestion of the collateral veins of the shoulder and chest wall on the affected side; however, thrombosis of the deep veins may occasionally be asymptomatic or present with mild symptoms. Rarely, CVC may be associated with the development of an atrial mass as a consequence of a CVC-related organized thrombus located inside the atrial cavity (1).

Herein, we report the case of a patient with colon cancer and a CVC who developed severe hemodynamic complications associated with an atrial thrombotic mass.

Case report

A 43-year-old man was admitted to the hospital due to severe and progressive shortness of breath and platypnea. The patient was on chemotherapy for colon cancer and a liver metastasis had been resected 1 month earlier. The patient was receiving FOLFOX as a perioperative regimen and had received the sixth course of chemotherapy several days prior to his admission. The patient's medical record included dyslipidemia and first-degree relatives with cancer (mother, colon and breast cancer; and father, bladder cancer).

A few days after his fifth course of chemotherapy, the patient developed rapidly progressive dyspnea on exertion. The dyspnea improved in the supine position (platypnea); the oxygen saturation while breathing room air was 75% and it also improved in the supine position (orthodeoxia).

An arterial blood gas analysis while breathing room air revealed a pH of 7.54, PaCO₂ of 19 mmHg and PaO₂ of 45 mmHg. The patient was admitted to the emergency room due to worsening of the respiratory symptoms and was transferred to the intensive care unit due to severe respiratory distress and very low oxygen saturation. The laboratory analysis did not show relevant data, apart from elevated levels of D-dimers. On electrocardiography, there was sinus rhythm with no abnormalities. The chest X-ray was normal and a chest computed tomography (CT) excluded pulmonary embolism and revealed no airway or parenchymal pathological findings, thus excluding infection and drug toxicity. The tip of the CVC was inside the right atrial cavity, in close proximity to the tricuspid valve. A transthoracic echocardiogram revealed a mild interventricular septal hypertrophy and normal biventricular systolic function. The patient was treated with high fraction of inspired oxygen and low-molecular weight heparin and exhibited progressive improvement. On discharge, the patient had an oxygen saturation of 93% while breathing room air in the supine position, which was reduced to 88% while sitting (orthodeoxia). In addition to the hypoxemia, the blood gas analysis revealed a respiratory alkalosis (pH=7.49, PaCO₂=28, PaCO₂=65 and HCO₃=24). The abdominal CT revealed post-hepatectomy and -hemicolecotomy surgical alterations. No portal hypertension was detected. Due to the suspicion of a right-to-left intracardiac shunt, a transcranial Doppler ultrasound of the left medial cerebral artery was performed with the infusion of an agitated saline solution through the right arm, which revealed a 'shower-curtain effect', suggesting a massive intracardiac

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Key words: central venous catheter, atrial thrombosis, shunt

shunt. A transesophageal echocardiography confirmed a right-to-left shunt through a patent foramen ovale (PFO) and detected a fixed mass in the right atrium in close proximity to the mouth of the superior cava, causing an obstruction of the entry flow, which was directed towards the foramen ovale. The distal end of the CVC was seen inside the right atrium, but the mass did not appear to be attached to it. Magnetic resonance imaging (MRI) of the heart and a new CT revealed a mass inside the right atrium (Figs. 1 and 2). Considering all these findings, the patient continued to receive low-molecular weight heparin and was referred for cardiac surgery.

The right atrium was opened and a large mass (6x5 cm) was identified, which filled the entire atrium. The mass was intimately attached to the free atrial wall and obstructed the tricuspid valve. The entire free wall of the right atrium was resected along with the mass and the atrium was reconstructed with autologous pericardium. The PFO was closed and the CVC was moved in place. Several hours after surgery, the patient suffered a pericardial tamponade requiring a pericardial window.

The pathological examination revealed a section of resected cardiac wall with a fibrous pericardium and a mass composed of fibrin and thrombotic hyaline, with isolated lymphocyte aggregates. No neoplastic cells were identified. Following surgery, the patient exhibited a significant improvement of the dyspnea, whereas the oxygen saturation while breathing room air increased to 95-98%. The patient is currently on chemotherapy with FOLFOX, with acceptable tolerance, apart from progressive cumulative peripheral neuropathy secondary to oxaliplatin.

Discussion

We herein described a rare complication in colon cancer: A right-to-left shunt with moderate-to-severe hypoxemia associated with a right atrial mass. Several differential diagnoses are possible when a right atrial mass is detected in a cancer patient. Myxomas are the most common atrial tumors and are classically described as arising on the left side, although a significant proportion of these tumors occur on the right side. Cardiac metastases from primary colorectal carcinomas are extremely rare (2). However, metastatic involvement of the heart is relatively common in melanoma, lung cancer, breast cancer and renal cell carcinoma. Klatt and Heitz (2) examined a total of 1,029 autopsies from patients diagnosed with malignancies and found cardiac involvement in 10.4% of all cases, 36.4% of which originated from adenocarcinomas of the lung, gastrointestinal tract, female genitourinary tract, breast or pancreas.

CVC-related thrombosis is another cause of atrial masses and it may be a complication and frequent cause of death in cancer patients (3). The incidence of CVC-related thrombosis has changed over the last few decades, being reported by more recent studies as ~14-18% in asymptomatic and 5% in symptomatic patients (4). Several authors have suggested that, when the tip of the catheter is located in the right atrium, the risk of thrombosis is higher (5). Several mechanisms may underlie this complication, mainly direct endocardial injury by the tip of the catheter, although antitumor drugs and their action on endothelial cells may also be involved. Maney *et al* (6)

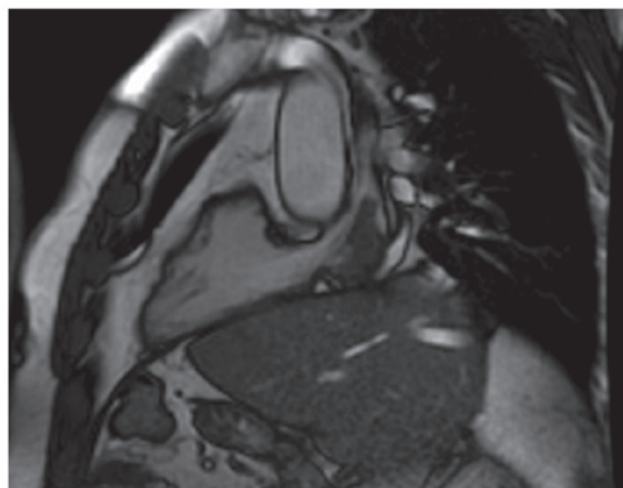


Figure 1. Magnetic resonance imaging of the heart (sagittal plane). A mass is seen in the right atrium, next to superior vena cava outlet.

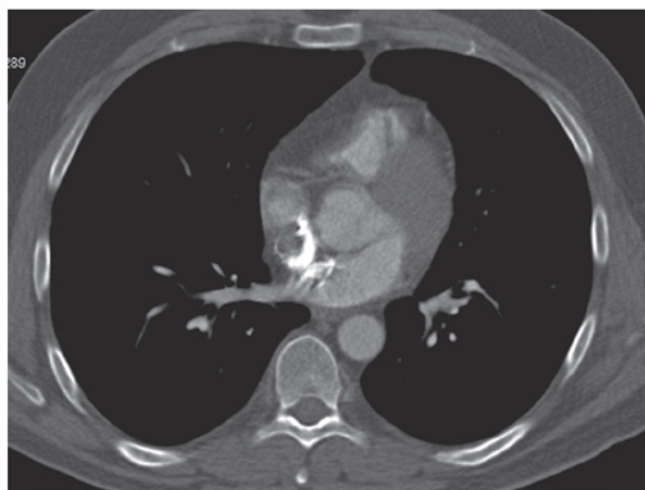


Figure 2. Computed tomography scan, showing a mass inside the right atrium.

reported that certain antitumor agents may induce apoptosis of endocardial endothelial cells when these cells are directly exposed to the chemotherapeutic agents.

As we have previously mentioned, the differential diagnoses of intracardiac masses include vegetations, thrombi or tumors. Echocardiography has become the gold standard for the diagnosis of intracardiac masses and the transesophageal approach has improved the overall accuracy (7). MRI may be suitable for tissue characterization, identifying the amount of fat with a high degree of specificity and may be used to diagnose cardiac lipomas and cardiac thrombi, which usually exhibit delayed enhancement. Cardiac MRI may also reveal in detail the location, insertion site and size of the mass, facilitating surgical resection. However, although all these tests are very useful, they are frequently unable to distinguish with certainty between a solid organized thrombus and a tumor.

Systemic thrombolysis may be suitable for pulmonary thromboembolism or free-floating emboli in the right atrium (type A thrombi) (5). Giant thrombi (type B) (5), which develop within the heart chambers, are usually fixed, well-organized and fibrotic, intimately associated with the atrial wall and very

unlikely to respond to thrombolytic therapy; in fact, in such cases, thrombolytic therapy is often ineffective and unsafe. The few cases of giant atrial thrombi reported in the literature suggest open surgical removal as the procedure of choice (8).

Gas exchange impairment with normal thoracic radiology and pulmonary function tests should suggest a right-to-left shunt, either intrapulmonary or intracardiac; both are typically associated with platypnea and orthodeoxia. In addition to PFO, which is as frequent as 27% in some autopsy series (9-14), other causes have been described, such as other interatrial defects, pericardial effusion, constrictive pericarditis and non-cardiac disorders, including emphysema, amiodarone-related pulmonary toxicity and cirrhosis (15,16). In cancer patients, conditions such as pneumonectomy and primary benign and malignant cardiac tumors may be associated with a PFO (17). Latif *et al* (18) described a patient with a right-to-left shunt secondary to intracardiac metastasis from a nasopharyngeal epidermoid carcinoma diagnosed 2 years earlier. We hypothesized that, in our patient, the right atrial mass redirected the flow from the superior vena cava to the interatrial septum, opening a PFO that had caused no hemodynamic consequences up to that point.

One possible explanation for the development of an organized thrombus inside the right atrium may be that the tip of the catheter was moved inside the atrial cavity, coming into direct contact with the endocardium, initiating a fibrotic reaction and inducing the release of several prothrombotic proteins, leading to the formation of an atrial thrombotic mass and the subsequent complications.

Although several examinations (ultrasound and MRI) did not reveal that the chemotherapy infusion directly over the endocardium induced a reaction leading to the development of an organized thrombus, Maney *et al* (6) reported that certain antitumor agents may induce apoptosis of endocardial endothelial cells when these cells are directly exposed to the chemotherapeutic agents.

The need for an etiological diagnosis of the atrial mass and the increased risk of embolization using a percutaneous procedure made a surgical approach mandatory. In addition, our patient exhibited symptoms and signs of valvular obstruction. Surgery is the procedure of choice in cases of valvular obstruction, since it may resolve the obstruction and prolong life expectancy in such patients. Several authors have reported cases of obstructive cardiac metastasis that have been successfully treated with surgery (18,19). The majority of authors consider that organized thrombi require a surgical approach, as conservative treatment with low-molecular weight heparin or dicumarins cannot resolve the thrombus or reverse its hemodynamic consequences. Although there is not enough evidence to establish the optimal treatment approach to intracardiac thrombosis, surgery is preferred in the majority of the cases (19,20). Another reason for surgery in such patients is the closure of the atrial septal defect (20).

In conclusion, although gas exchange impairment in oncology patients is most frequently due to pulmonary emboli secondary to thrombosis unrelated to CVC, pulmonary infections or pulmonary drug toxicity, other infrequent causes should be considered, including an intracardiac shunt, particularly if

the radiological findings are normal. CVC-related thrombosis is a frequent complication that should be ruled out due to the potentially severe hemodynamic consequences, particularly if the tip of the catheter is located inside the atrium.

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