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Incidental right atrial mass in a patient with secondary pancreatic cancer: A case report and literature review

Incidental right atrial mass

Agnese Maria Fioretti, Tiziana Leopizzi, Daniele La Forgia, Pietro Scicchitano, Donato Oreste, Annarita Fanizzi, Raffaella Massafra, Stefano Oliva

Abstract

BACKGROUND

The incidental detection of a right atrial mass during routine cardioncological workup is a rare condition. The correct differential diagnosis between cancer and thrombi is challenging. A biopsy may not be feasible and diagnostic techniques and tools may not be available.

CASE SUMMARY

We report the case of a 59-year-old female patient with a history of breast cancer and current secondary metastatic pancreatic cancer. She developed deep vein thrombosis and pulmonary embolism and was admitted to the Outpatient Clinic of our Cardio-Oncology Unit for follow-up. Transthoracic echocardiogram incidentally found a right atrial mass. Clinical management was difficult due to the abrupt worsening of the patient's clinical condition and the progressive severe thrombocytopenia. We suspected a thrombus, according to its echocardiographic appearance, the patient's cancer history and recent venous thromboembolism. The patient was unable to adhere to low molecular weight heparin treatment. Due to a worsening prognosis, palliative care was recommended. We also highlighted the distinguishing features between thrombi and tumors. We proposed a diagnostic flowchart to aid diagnostic decision making in the case of an atrial mass.

CONCLUSION

This case report highlights the importance of cardioncological surveillance during anticancer treatments to detect cardiac masses.

Key Words: Atrial mass; Cardiac tumor; Venous thromboembolism; Differential diagnosis; Case report

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Core Tip: Cardiac masses are rare occurrences. In this case report, the diagnosis of a right atrial mass during cardioncological follow-up of a patient with secondary metastatic pancreatic cancer and a recent diagnosis of cancer-associated thrombosis was challenging. Severe thrombocytopenia and an abrupt worsening of the patient's condition hindered a complete clinical workup. However, echocardiographic differentiation between thrombi and tumors lead to the diagnosis of a new venous thromboembolism event. We also proposed a diagnostic flowchart to aid diagnostic decision making in the case of an atrial mass.

INTRODUCTION

Cardiac masses are unique entities. Primary cardiac tumors are very uncommon, whereas metastases and "pseudotumors," such as intracardiac thrombi, are more frequent. They are typically discovered incidentally[1]. The differential diagnosis between cardiac tumors and cancer-associated thrombosis (CAT) is challenging because the symptoms are similar to other cardiac conditions[2]. Herein, we report the case of a 59-year-old Caucasian female with a history of breast cancer and secondary metastatic pancreatic cancer who was assessed by cardioncological follow-up, which revealed a large (2 cm × 3 cm) right atrial mass.

Currently, there is no standardized guideline for the differential diagnosis of cancer and thrombus. Accordingly, the clinical management of patients diagnosed with an incidental atrial mass is challenging, and the diagnosis is rarely recognized by physicians. Thus, a diagnostic algorithm was created as a guideline for a practical evidence-based decision-making approach for the differential diagnosis of cancer and thrombus.

CASE PRESENTATION

Chief complaints

A 59-year-old Caucasian female (height: 160 cm, weight: 60 kg) was referred to the Cardio-Oncology Unit for surveillance. She reported having shortness of breath at rest and after mild exercise in the prior 2 mo. She had experienced severe chest pain (without any anginal characteristic) in the prior 2 wk. The patient denied any history of syncope. Occasional cough and dizziness with no headache occurred.

History of present illness

The patient had jaundice due to choledochal obstruction from a pancreatic mass and underwent drainage *via* an endoprosthesis. Biopsy revealed stage IV pancreatic ductal adenocarcinoma of the head with liver metastases (Figures 1 and 2). After central line placement in the right subclavian vein, chemotherapy with nab-paclitaxel (125 mg/m^2) plus gemcitabine (1000 mg/m^2) was administered on days 1, 8 and 15 of a 28-d cycle. Due to cancer progression, a second-line treatment was started with 5-fluorouracil (2400 mg /m^2 continuous infusion for 44 h), folic acid (200 mg/m^2), oxaliplatin (85 mg/m^2) and irinotecan (150 mg/m^2). The patient was sensitive to this regimen because pretreatment pharmacogenomic evaluation of 5-fluorouracil degradation by DPYD and UGT1A1 yielded positive results.

History of past illness

The patient had undergone right mastectomy and lymphadenectomy for an infiltrating ductal carcinoma with axillary lymph node metastases 9 years prior. She had received adjuvant treatment with cyclophosphamide (600 mg/m^2), methotrexate (40 mg/m^2) and 5-fluorouracil (600 mg/m^2) for 12 cycles and hormone therapy with tamoxifen 20 mg/d for 5 years.

Personal and family history

The patient mentioned a positive family history for breast cancer (maternal aunt), whereas her personal and family history of cardiovascular disease was unremarkable. The patient was married without offspring. She complained of abdominal pain and social isolation due to the cancer diagnosis.

Physical examination

Upon physical examination, blood pressure was 110/80 mmHg at rest, while body temperature was 36.1 °C. Heart rate was 103 beats/min with a regular heart rhythm. Intensity of the first heart sound (S1) did not vary, and a regurgitant murmur was heard at the apex. The patient's physical examination revealed no other notable clinical findings. Electrocardiogram showed sinus tachycardia and biphasic T waves in the inferior leads (Figure 3). Once the patient's general clinical condition significantly declined, blood pressure was 95/70 mmHg and heart rate was 143 beats/min.

Laboratory examinations

Hemoglobin was 10.0 g/dL (normal range: 13.5-17.5 g/dL). The platelet count (PC) was 50 × 10^3/μL (normal range: 150-450 × 10^3/μL) and progressively declined to 40 × 10^3/μL and 20 × 10^3/μL.

Imaging examinations

Computed tomography (CT) identified enlargement of the hepatic metastases, partial occlusion of both branches of the pulmonary artery and deep vein thrombosis of the right external iliac vein and both common femoral veins (Figures 4 and 5). Furthermore, left pulmonary infarction and mild right pleural effusion were detected. After 3 mo of anticoagulant treatment, CT documented persistence of lower limb deep vein thrombosis and pulmonary embolism and a worsening of the liver metastases.

FINAL DIAGNOSIS

Due to the patient's worsening clinical condition, further investigations were suspended (despite the value of a complete diagnostic workup). Given the patient's history and the overall echocardiographic features, a new venous thromboembolism (VTE) event was suspected. In addition, the recent diagnosis of CAT strongly indicated the presence of a clot.

TREATMENT

After the diagnosis of deep vein thrombosis with pulmonary embolism, the patient refused hospitalization and was treated at home with anticoagulant therapy. Low molecular weight heparin treatment was started by her oncologist, consisting of enoxaparin sodium 100 IU and anti-Xa 1 mg/kg twice daily. However, it did not resolve the CAT. After a telephone interview with the patient's husband, we verified the patient's poor adherence due to difficulties with daily self-injections. Accordingly, due to lack of therapeutic efficacy and patient's preference for oral administration, we replaced the low molecular weight heparin with an oral anticoagulant (edoxaban 60 mg/d once daily)[3]. The patient's PC decreased to $60 \times 10^3/\mu L$, and we replaced edoxaban with enoxaparin sodium 100 IU and anti-Xa 1 mg/kg twice daily. The patient's PC continued to decrease ($40 \times 10^3/\mu L$). Therefore, we decreased the low molecular weight heparin dose by half. Anticoagulant therapy was completely discontinued when the patient's PC decreased to $20 \times 10^3/\mu L$[4].

OUTCOME AND FOLLOW-UP

The patient's disease continued to progress and worsen. While the patient was under our care, we surveyed her emotional well-being *via* questions on her perspectives on her clinical case history (Table 1). Afterwards, the patient's medical information was provided to us by her husband and her general practitioner. Chemotherapy treatment of carboplatin (250 mg/m^2) was started. However, after 3 mo the oncologist recommended discontinuation of any further anticancer treatment and suggested palliative care (Table 2).

DISCUSSION

Herein, we have described the very unusual finding of a large right atrial mass detected by TTE in a patient with a history of breast cancer and secondary metastatic pancreatic cancer who had developed CAT. Up to 12% of primary cardiac tumors are clinically silent and are detected during incidental cardiovascular workup or at autopsy[5]. For our patient, the suspicion for vegetations was quickly excluded due to clinical history, mass site, absence of vegetation-related presenting symptoms and absence of prosthetic valves. About 75% of infective endocarditis occurs in patients with underlying structural heart disease[6], which was absent in this patient.

The risk of VTE is up to 50-fold higher in patients with cancer than in those without[7]. Patients with advanced cancer have a higher risk of VTE than patients with localized cancers. Pancreatic and gastric and myeloma are associated with a higher risk of VTE as well[8]. VTE is associated with high morbidity and mortality rates[9]. CAT is the second leading cause of death in malignancy, with an incidence of 20%[10]. Cancer patients are also prone to bleeding[11] and renal failure, which typically leads to surgery and interventional procedures. Notably, cancer patients have a higher risk of both thrombosis relapse and bleeding while on anticoagulant therapy compared to patients without cancer[12]. In addition, the presence of indwelling lines increases the chance of developing a clot due to blood stasis around the port and the high viscosity of the drugs administered through the catheter[13].

According to the Khorana Risk Score the following parameters increase VTE risk: site of cancer (stomach, pancreas); PC $\geq 350 \times 10^3/\mu L$; hemoglobin level < 10 g/dL; leukocyte count > 11 $\times 10^3/\mu L$; and body mass index > 35 kg/m^2[14]. The recently established Protecht Risk Score determined that gemcitabine-based and platinum-based therapies increase the risk of VTE[15].

In 2015, the World Health Organization updated the classification of tumors of the heart and the pericardium[16]. Cardiac tumors are extremely rare diseases, with an incidence of approximately 0.02% in an autopsy series[17]. By contrast, cardiac thrombi are more common. Benign cardiac tumors lead to severe hemodynamic instability, leading to mechanical issues or the onset of embolic or arrhythmic events. Presenting symptoms include fever, weakness, fatigue and weight loss[18].

About 75% of all primary cardiac tumors are benign. The most frequent tumors in the adult population are myxomas (50%), papillary fibroelastomas (20%), lipomas (15%-20%) and hemangiomas (5%). The other 25% of primary cardiac tumors are malignant, with 95% of those being sarcomas and 5% being lymphomas. By far, metastases involving the heart and pericardium (secondary cardiac tumors) are 20-40 times more common than primary cardiac tumors and originate primarily from breast, esophageal or lung cancers, melanoma or renal cell carcinoma[19].

Malignant cancers metastasize to the heart through direct extension from mediastinal tumors, hematogenous spread, lymphatic spread or intracavitary extension arising from the inferior cava vein (renal cell carcinoma, adrenal carcinoma and hepatocellular carcinoma)[20] and rarely through the pulmonary vein. Particularly, the right atrium is a typical location for malignant cardiac tumors such as angiosarcoma, lymphoma and melanoma and for intracardiac metastases from renal cell carcinoma due to spread *via* the inferior cava vein. Chordoma commonly metastasizes to the right atrium[21]. Myxomas and lipomas are also typically localized to the atria, whereas rhabdomyosarcomas and lymphomas are commonly located in the ventricles and fibroelastomas are localized to the valves[22] (Figure 7).

Thrombi located in the right atrium are seldom visualized by echocardiography (ECO) and account for only 4% of cases. Atrial thrombi are more often located in the left atrium or appendage and are generally accompanied by structural heart disease[23]. They are usually highly mobile, serpiginous and without the typical myxoma features[24,25] such as the attachment *via* a stalk and the presence of intramass calcification[26].

The diagnostic pathway should be based on the tumor type epidemiology, imaging features and histopathological diagnosis. In this patient, the third component was missing due to her worsening prognosis. The non-invasive diagnostic armamentarium to discriminate thrombi from cancer includes ECO, CT, magnetic resonance imaging (MRI) and positron emission tomography (PET)[27].

ECO is the first-line modality to quantify the size, shape, location, attachment and mobility of the intracardiac and extracardiac mass. Its diagnostic sensitivity is 93% for TTE and 97% for transesophageal ECO[28]. Additionally, three-dimensional ECO (3DECO) offers notable advantages. The entire mass can be visualized compared to a thin slice obtained two-dimensional ECO. 3DECO can also evaluate the volume instead of just linear dimensions, making the measurement more accurate (Table 3). 3DECO can also identify clues, such as homogeneity, vascularity, calcification and necrosis, and outline the attachment point by the cropping technique. 3DECO sensitivity for identifying thrombi is > 90%, while specificity is > 85% compared to two-dimensional ECO[29]. Moreover, echocardiographic contrast perfusion is regarded as a mainstay to characterize the vascularity of cardiac masses. It typically detects differences among neovascularized malignant or highly vascular cardiac tumors, poorly vascularized stromal tumors, avascular thrombi and normal myocardium[30].

CT provides a precise delineation of the lesion margins, and it optimally evaluates calcified masses. Chest and lung tissue can also be evaluated and may exclude obstructive coronary artery disease or masses in the coronary arteries[31]. When the diagnosis by CT is uncertain and discrimination between benign and malignant lesions is challenging, ^{18}F-fludeoxyglucose (FDG)-PET/CT is an extremely powerful tool to elucidate substantial information regarding the nature of the mass. ^{18}F-FDG-PET is a molecular imaging method to visualize cell metabolism and to assess metabolic activity[32]. Although its availability is limited, ^{18}F-FDG-PET is an insightful tool to visualize the metabolic rate of glycolysis in tumors. Cardiac tumors typically exhibit a high ^{18}F-FDG uptake, while benign cardiac tumors exhibit a slight ^{18}F-FDG uptake[33].

The combination of ECO and MRI can be used for the diagnosis and monitoring of cardiac masses[34]. Compared to CT, MRI offers higher temporal resolution and additional tissue characterization. It also does not require ionizing radiation exposure[35]. Importantly, MRI may evaluate the age of a thrombus. Acute thrombi usually present intermediate signal intensity on both T1- and T2-weighted images, subacute thrombi have a lower T1-weighted signal intensity and increased T2-weighted signal intensity, and chronic organized thrombi have a lower signal intensity on both T1- and T2-weighted images. Unlike tumors, thrombi appear with an absence of contrast material uptake in early and late gadolinium enhancement due to their avascular nature[36]. Contrast MRI with first-pass perfusion and late gadolinium enhancement are particularly useful to define benign *vs* malignant tumors. All malignant tumors have first-pass perfusion due to their highly vascular nature and late gadolinium enhancement.

In contrast to current guidelines that regard ECO, CT, MRI and PET as equal diagnostic methods[27], our diagnostic algorithm proposes ECO as the only first-line tool due to its widespread availability and lack of radiation exposure. If ECO is inconclusive, equivocal or unreliable, CT, MRI and PET are second-line options to allow differential diagnosis between cancer and thrombi in a timely manner (Figure 8).

Our patient was at high risk for a prothrombotic burden due to metastatic pancreatic cancer, an indwelling line and gemcitabine and platinum therapy. Furthermore, the atrial mass did not appear to infiltrate other structures and was not vascularized. A cardiac tumor was excluded in our patient due to the lack of infiltrative growth, lobulated margins, pericardial effusion and large size. We recognize that the patient's workup was suboptimal, and the mass was in the right atrium, suggestive of a malignant tumor. However, the location of cardiac masses may be misleading. Due to the patient's age, mass localization, general clinical context (cancer site and stage, cancer treatment, recent extended CAT) and ultrasound features, the mass was likely a new VTE event.

CONCLUSION

We have reported herein the rare incidental finding of a notable intracardiac mass diagnosed as a VTE in a patient with secondary metastatic pancreatic cancer and CAT. Differential diagnosis of the mass was challenging due to the location of the mass. We suspected a new CAT event due to the patient's cancer history, echocardiographic characteristics of the mass and previously discovered CAT. Our patient was unable to adhere to injectable anticoagulant treatment of low molecular weight heparin. Due to worsening prognosis, palliative care was recommended.

Cardioncological surveillance is of utmost importance in patients with active cancer to detect incidental VTE, which may otherwise be missed and untreated. We presented a non-invasive evidence-based flow chart to guide the differential diagnosis of atrial masses to improve patient care and outcomes.

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