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Case Report

Metastatic amelanotic melanoma with cardiac involvement: A case report

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ABSTRACT

Metastatic melanoma has a high rate of cardiac involvement and often presents with non-specific symptoms, including heart failure. We report a case of a 41-year-old woman with a remote history of resected flank melanoma, who presented with heart failure progressing to cardiogenic shock and death. Despite extensive workup including chest computed tomography, cardiac magnetic resonance imaging, and endomyocardial biopsy, the etiology of her heart failure was not diagnosed until autopsy revealed metastatic amelanotic melanoma. In patients with unexplained heart failure and a history of melanoma, imaging studies including fluorodeoxyglucose positron emission tomography should be included in the workup to guide early diagnosis and treatment.

<**Learning objective:** This case report highlights the importance of maintaining a high clinical suspicion for malignant melanoma in patients presenting with heart failure of uncertain etiology.>

Introduction

Melanoma has an annual incidence of 20.6 per 100,000, making it the fifth most common cancer to affect men and the sixth most common to affect women in the USA [1]. It has a high rate of metastatic spread, with cardiac involvement identified in up to 64% of cases [2]. Only 10–16% of those with cardiac metastases develop overt clinical manifestations [3], so ante-mortem diagnosis of cardiac involvement is rare. When present, cardiac manifestations are non-specific and can include heart failure and dysrhythmias [4]. Here, we report a case of a patient who presented with acute decompensated heart failure (ADHF) and was found to have cardiac metastasis from malignant amelanotic melanoma at autopsy.

Case report

A 41-year-old Caucasian woman with a history of recently diagnosed heart failure with reduced ejection fraction presented to an outside hospital with progressive heart failure symptoms. Other medical history included dysmenorrhea, for which she underwent total hysterectomy, and left flank melanoma status post excision approximately 2 years prior to presentation. Of note, lymph nodes were negative and she did not receive adjunctive therapy, although details of the melanoma resection were unavailable. Her symptoms began approximately 7 weeks prior to admission, when she presented to an outside hospital in atrial fibrillation with rapid ventricular response. She underwent transesophageal echocardiogram and successful direct current cardioversion. At that time, her left ventricular ejection fraction (LVEF) by echocardiogram was 65%. She had a nuclear stress test, which showed an area of possible ischemia and subsequently underwent coronary angiography without obstructive coronary atherosclerosis. She was discharged with an event monitor, which three weeks later captured nearly 30 s of symptomatic monomorphic ventricular tachycardia (VT). A transthoracic echocardiogram (TTE) at that time showed newly decreased LVEF to 40%. Two weeks later, she again experienced palpitations, dyspnea, dizziness, and chest tightness. Review of her event monitor was notable for premature ventricular beats, so she was readmitted to the outside hospital. Computed tomography (CT) with intravenous (IV) contrast was negative for pulmonary embolism, although it showed small pleural and pericardial effusions, pulmonary nodules, and

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splenomegaly. Cardiac magnetic resonance imaging (cMRI) demonstrated biventricular dilation with LVEF 23%, right ventricular ejection fraction 34%, left ventricular stroke volume 35 mL, and a small pericardial effusion, although further evaluation was limited due to motion artifact. She was discharged with a presumptive diagnosis of viral myocarditis on guideline-directed heart failure therapies. Over the course of the next 2 weeks, she developed worsening heart failure refractory to oral diuretics prompting hospital admission and transfer to our facility for consideration of endomyocardial biopsy.

On admission, she reported dyspnea with minimal exertion, orthopnea, abdominal bloating with a 6.8 kg weight gain despite poor appetite and a 2-week history of diarrhea. On clinical examination, she was noted to be in sinus tachycardia, otherwise hemodynamically stable, and saturating well on room air, although with diffuse rhonchi throughout the lung fields, jugular venous pressure to approximately 20 cm H_2O, and bilateral lower extremity pitting edema. Her laboratory data were notable for a microcytic anemia (hemoglobin 11.7 g/dL), elevated erythrocyte sedimentation rate (76 mm/h) and C-reactive protein (5.2 mg/dL), elevated *N*-terminal pro-B-type natriuretic peptide (33,904 pg/mL), mild troponin I elevation (0.11 ng/mL), hyponatremia (sodium 131 mmol/L), and otherwise normal renal and liver function with normal lactate. Her electrocardiogram was low voltage, in sinus tachycardia with left axis deviation, Q waves in V1–V3, and delayed R-wave progression. TTE showed LVEF 20–25% with moderate left ventricular dilation (Fig. 1). She responded well to IV diuresis and underwent right heart catheterization (RHC) with endomyocardial biopsy the following morning. RHC demonstrated elevated right and left heart filling pressures (mean right atrial pressure 16 mmHg, mean pulmonary capillary wedge pressure 28 mmHg), pulmonary hypertension (mean pulmonary artery pressure 36 mmHg), and low cardiac index (1.62 L/min/m^2). Her pulmonary artery saturation was 46.4% with a stroke index of 13.86 ml/m^2. Endomyocardial biopsy showed a focus of perivascular lymphocytes without myocyte damage and large collection of neutrophils on a single piece of tissue without overt evidence of myocardial inflammation, and was reported as borderline myocarditis.

She was continued on medical management of heart failure with a plan to repeat cMRI once she was better compensated, however, 24 h after her endomyocardial biopsy she went into a monomorphic VT, which rapidly deteriorated to ventricular fibrillation. She received cardiopulmonary resuscitation and was placed on peripheral veno-arterial extracorporeal membrane oxygenation (ECMO) by cardiac surgery at bedside. She required escalating vasopressors for hemodynamic support with ECMO flows remaining in the 1–2 L/min range. After discussion with her family, it was decided that there would be no further escalation of care and she expired. Autopsy was notable for an unexpected metastatic melanoma involving her heart, bilateral lungs, diaphragm, small bowel, meninges, and brain with lymphovascular invasion (Fig. 2). This tumor was positive for S100 and negative for AE1/3, CK7, CK20, melanA, MART-1, and HMB45 by immunohistochemistry. The lesions in the heart, lungs, and small bowel were amelanotic, while the brain lesions demonstrated rare melanin granules.

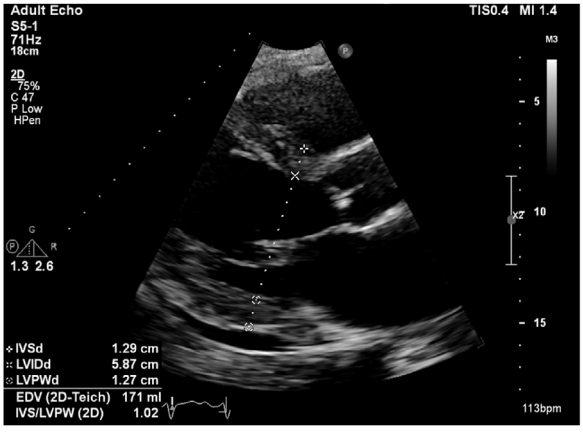

Fig. 1. Transthoracic echocardiogram, with parasternal long-axis view of the left ventricle. Left ventricular end-diastolic diameter is 5.9 cm with mild concentric left ventricular hypertrophy and a small pericardial effusion.

Discussion

New-onset cardiomyopathy can include a broad range of potential etiologies, but in patients who have a history of melanoma, consideration of metastatic cardiac involvement is warranted. Melanoma spreads to the heart via the hematogenous route and can present many years after diagnosis of the primary tumor [5]. The site and burden of metastatic involvement in the heart dictates symptom presentation. The myocardium and epicardium are most commonly involved, often resulting in heart failure and dysrhythmias.

Other case reports have been published on patients with heart failure secondary to metastatic melanoma. Schneider and Zienkiewicz report a similar case of a 58-year-old man who presented with ADHF secondary to metastatic cardiac involvement after thigh melanoma excision seven years prior [4]. Other case reports describe patients with pericardial effusions, supraventricular and

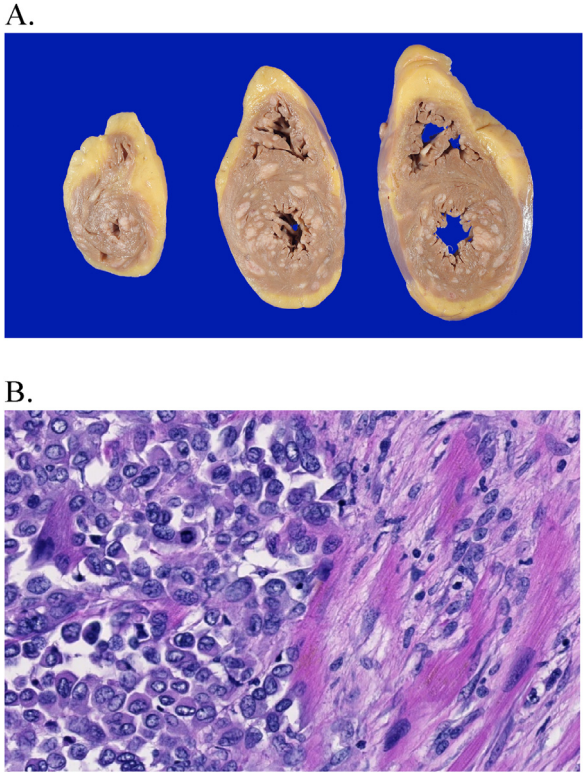

Fig. 2. Metastatic melanoma. (A) Gross pathology, cross-sections of right and left ventricles demonstrating multiple firm white nodules. (B) Hematoxylin and eosin stained sections of the myocardium demonstrating multiple nodules of metastatic melanoma composed of loosely cohesive and pleomorphic cells. An immunostain for S100 was positive in the nodules, consistent with the diagnosis of metastatic melanoma (200× magnification).

ventricular arrhythmias, and advanced atrioventricular nodal block [6].

Because echocardiography is widely available and non-invasive, it is typically the first imaging modality used in the evaluation of metastatic cardiac disease [5,7]. While echocardiography can often identify intra-cavitary or pericardial lesions, findings can be nonspecific due to the inherent difficulty in differentiating tumor from thrombus and defining the vascularity of lesions. Other imaging modalities include cardiac CT and cMRI, which offer improved spatial resolution when compared to echocardiography and provide information regarding metastatic tumor extension into extra-cardiac structures [7]. Cardiac CT has a sensitivity of 58% and specificity of 70% for metastatic melanoma, and sensitivity increases with the use of electrocardiogram-gating and IV contrast [8]. Importantly, cMRI detects melanin, a paramagnetic substance that results in a characteristic MRI pattern, however amelanotic melanoma requires special imaging techniques for detection and therefore a high index of suspicion is needed prior to testing to avoid false negative results [8]. Fluorine-18-fluorodeoxyglucose positron emission tomography (FDG-PET) is the imaging modality with the highest sensitivity and specificity for diagnosis (84% and 97%, respectively), and the ability to additionally diagnose extra-cardiac metastatic disease [9]. The definitive method for diagnosis is tissue histology from open or endomyocardial biopsy [10], however even this has limitations if the biopsy specimen fails to capture tumor. Our case highlights a particularly challenging diagnostic dilemma in which extensive diagnostic imaging, including echocardiography, CT with IV contrast, cMRI, and endomyocardial biopsy, failed to reveal a diagnosis of metastatic amelanotic melanoma.

In summary, a high degree of suspicion is needed in patients presenting with new heart failure or cardiac dysrhythmias and a history of melanoma. Early detection is important for timely implementation of treatment strategies. Diagnostic methods, including cMRI and endomyocardial biopsy, may not reveal evidence of metastatic disease and other imaging studies, such as FDG-PET, should be considered for prompt diagnosis and treatment planning.

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Conflict of interest

The authors declare that there are no reportable conflicts of interest.

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