

CASE REPORT

ADVANCED

CLINICAL CASE

Remission of a Perimyocardial Melanoma Metastasis With Pembrolizumab Treatment



Frederik Uttenthal Larsen, MD,^a Johannes Katate Wilhelm, MD,^b Eric Steen Nielsen, MD^b

ABSTRACT

Malignant melanoma demonstrates the highest rate of cardiac metastases. The incidence of melanoma is rising. The prognosis of people with advanced melanoma is generally poor. This case report emphasizes the potential need for early detection of cardiac involvement in advanced melanoma in view of promising advances in treatment with immune checkpoint inhibitors. (**Level of Difficulty: Advanced.**) (J Am Coll Cardiol Case Rep 2019;1:5-8)
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Although primary tumors of the heart are rare and most often have an intracavitary location, metastatic heart tumors are far more common (by more than 100 times) (1). Given its prevailing hematogenous spread, malignant melanoma demonstrates the highest rate of cardiac metastases, with an old autopsy study indicating cardiac metastases in >50% of all cases of advanced disease (2). The incidences of in situ and invasive melanoma are rapidly rising in many European countries and represent a significant health concern (3). The prognosis of people with advanced melanoma is generally poor.

In the past few years the progress of immune checkpoint inhibitors as an effective and tolerable therapy for metastatic melanoma has revolutionized the management of patients and improved longevity (4). Here we report an unusual case of a solitary perimyocardial melanoma metastasis of unknown origin infiltrating the myocardium and having a major response to pembrolizumab.

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HISTORY OF PRESENTATION

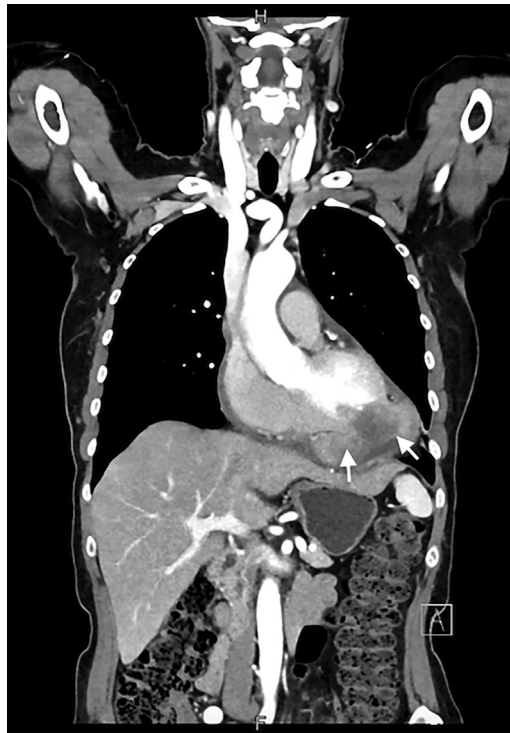
A 68-year-old woman was admitted to the emergency department of a local hospital following 2 weeks of persistent fever, cough, night sweats, and fatigue. Physical examination of her heart and lungs was unremarkable. The electrocardiogram showed sinus tachycardia with a pulse rate of 120 beats/min and inverted T waves in V₃ to V₆. Initial laboratory results were a C-reactive protein level of 155 mg/l (reference range <8 mg/l), elevated total white blood cell count of $12.2 \times 10^9/l$ (3.50 to $10.0 \times 10^9/l$), D-dimer 8.0 mg/l (<0.7 mg/l), and erythrocyte sedimentation rate

LEARNING OBJECTIVES

- To be able to recognize the high proportion of cardiac dissemination in advanced malignant melanoma.
- To be able to acknowledge the potential need for early detection of cardiac involvement in advanced melanoma considering promising advances in treatment with immune checkpoint inhibitors.

From the ^aDepartment of Cardiology, Aalborg University Hospital, Aalborg, Denmark; and the ^bDepartment of Cardiology, Viborg Regional Hospital, Viborg, Denmark. All authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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FIGURE 1 Thoracic CT at Diagnosis

A baseline computed tomography (CT) coronal plane cut shows a massive pericardial tumor ($60 \times 80 \times 40$ mm) infiltrating the myocardium (**arrows**) in the apical and inferolateral segments of the left ventricle. There is an insignificant pericardial effusion. The differential diagnoses were mesothelioma, sarcoma, or lymphoma, but a needle biopsy surprisingly revealed a metastasis of an unknown melanoma. There were no sign of other metastatic tumor lesions and no lymph node enlargement. Also see [Videos 1](#) and [2](#).

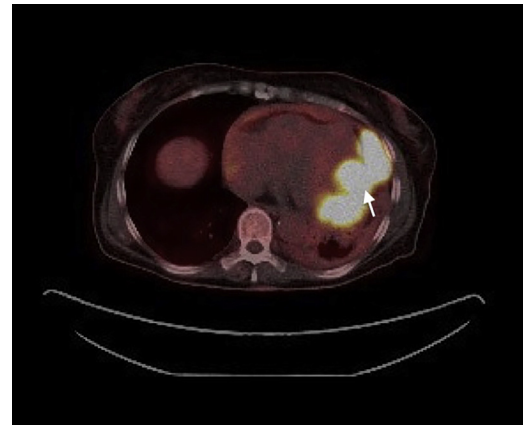
of 94 mm/h (<30 mm/h), with normal values of high-sensitivity cardiac troponin T (8 ng/l), procalcitonin (0.1 $\mu\text{g/l}$), and lactate dehydrogenase (161 U/l). On the basis of the symptoms and preliminary diagnostic findings, pneumonia was suspected, and antibiotic treatment (cefuroxime) was commenced on admission.

PAST MEDICAL HISTORY

Her medical record included hypertension only and no history of smoking or drug abuse.

INVESTIGATIONS

Transthoracic echocardiography had showed a mild degree of left ventricular lateral hypokinesia and revealed a large vascularized mass in the chest wall

FIGURE 2 Thoracic FDG PET-CT at Diagnosis

An axial plane cut from positron emission tomography-computed tomography (PET-CT) at baseline shows abnormal fluorodeoxyglucose (FDG) activity in the pericardial tumor (**arrow**) and pericardium. The main purpose of this investigation was to assess other potential metastatic sites. No myocardial physiological uptake suppression diet was used, but the patient underwent a standard fasting period of 6 h. The European Association of Nuclear Medicine recommends a low-carbohydrate diet for 24 h before fluorodeoxyglucose positron emission tomography-computed tomography when evaluating tumor lesions in close proximity to the myocardium or in the heart ([5](#)).

with perimyocardial infiltration to the inferolateral segments of the left ventricle and insignificant pericardial and pleural effusion ([Videos 1](#) and [2](#)). The patient underwent thoracocentesis, but pleural fluid cytological analyzes were negative. Magnetic resonance imaging was performed to assess local tumor invasion, whereas computed tomography (CT) of the thorax, abdomen, and pelvis with contrast ([Figure 1](#)) and follow-up fluorodeoxyglucose positron emission tomography combined with CT ([Figure 2](#)) were completed to evaluate dissemination pattern and for the purpose of tumor staging. These imaging studies confirmed the findings of transthoracic echocardiography and uncovered a solitary infiltrating extracardiac tumor ($60 \times 80 \times 40$ mm), with abnormal fluorodeoxyglucose activity in the tumor and pericardium but no lymph node enlargement.

DIFFERENTIAL DIAGNOSES

The differential diagnoses were mesothelioma, sarcoma, or lymphoma, but histopathological examination of a transthoracic needle biopsy sample revealed metastasis of an unknown melanoma.

FIGURE 3 Thoracic CT After 4 Series of Pembrolizumab



A computed tomography (CT) coronal plane cut after 4 cycles of pembrolizumab treatment compared with baseline computed tomography (Figure 1) shows almost complete remission of the melanoma metastasis. There is a persistent minor pericardial effusion (arrow). Also see Video 3.

MANAGEMENT

The tumor samples showed programmed cell death protein 1-ligand 1 (PD-L1) expression. PD-L1 is frequently up-regulated on tumor cells from diverse human cancers (6). The patient was started on pembrolizumab (2 mg/kg) given once every 3 weeks. Pembrolizumab is a selective monoclonal antibody against the programmed cell death protein-1 (PD-1) receptor expressed on particularly activated T cells. Normally, the antitumor immune response is suppressed when PD-1 is engaged by its ligands on tumor cells, including PD-L1 (6). Cardiac transplantation was not discussed.

DISCUSSION

Malignant melanoma is generally recognized as the neoplasm with the greatest tendency to cardiac involvement despite the overall decline in autopsy numbers, the absence of clinical manifestations in estimated 90% of cases, and inadequate sensitivity of basic cardiac and thoracic examinations (7). The cardiac dissemination pattern can be localized, but metastases are usually diffuse, with multiple small intramyocardial tumor lesions, which in any case represent far advanced malignant melanoma (8). The incidence of melanoma is rapidly rising and may be accompanied by an increasing incidence of silent cardiac metastases. Patients with malignant melanoma are not currently referred to systematic screening for cardiac involvement.

FOLLOW-UP

The results in this patient have been remarkable. After 3 series of treatments, her heart function was fully restored (Video 3), with no signs of myocardial tumor infiltration or fenestration of the left ventricular wall. A new CT scan was performed after 4 series of treatments (Figure 3) and showed almost complete tumor regression.

CONCLUSIONS

To our knowledge this is the first case of a solitary pericardial melanoma metastasis infiltrating the heart and impairing left ventricular function with almost complete tumor regression and recovery of left ventricular ejection fraction after treatment with pembrolizumab. This case supports the encouraging results of recent breakthroughs in the treatment of advanced melanoma with immune checkpoint inhibitors.

ADDRESS FOR CORRESPONDENCE: Dr. Frederik Uttenthal Larsen, Department of Cardiology, Aalborg University Hospital, Hobrovej 18-22, 9000 Aalborg, Denmark. E-mail: uttenthal@gmail.com. Twitter: [@fred_utla](https://twitter.com/fred_utla).

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KEY WORDS cardio-oncology, cardiovascular imaging, cardiac metastases, immune checkpoint inhibitors

APPENDIX For supplemental videos, please see the online version of this paper.