

Cardiac Metastases of Recurrent Infiltrating Amelanotic Fusocellular Malignant Melanoma: Case Report

Alondra Nateras Quiroz*¹, Fernando Martínez Maldonado², Próspero Amín Ramírez Juárez³, Javier Iván Reyes Ramírez⁴, Tania Hernández Trejo⁵, Alejandro Godínez Montes de Oca⁶, Agustín Yáñez Serrano⁷, Elizabeth Armijo Yescas⁸, Ernesto Treviño Gómez⁹

^{1,2,3,4} Cardiology Residency, Instituto de Seguridad y Servicios Sociales de los Trabajadores del Estado, Hospital Regional de Alta Especialidad Bicentenario de la Independencia, Tultitlan, Estado de México, México

^{5,6,7,8,9} Department of Cardiology, Instituto de Seguridad y Servicios Sociales de los Trabajadores del Estado, Hospital Regional de Alta Especialidad Bicentenario de la Independencia, Tultitlan, Estado de México, México

ABSTRACT

Melanoma is one of the most aggressive types of skin cancer. The malignant amelanotic fusocellular melanoma subtype is an uncommon presentation, however, it has a high rate of cardiac involvement, it presents asymptomatic or with symptoms ranging from nonspecific to cardiac tamponade or heart failure. We present a case of a 48-year-old man with recurrent infiltrating amelanotic fusocellular malignant melanoma, with incidentally visualized biventricular lesion and right atrium, with cardiac tamponade with subsequent fluoroscopy-guided pericardiocentesis. Primary cardiac tumors have a prevalence of 1:2000 autopsies and secondary cardiac tumors of 1:100 autopsies, remaining as a secondary: primary ratio of 20:1. In patients with this type of melanoma, although cardiac metastases are common, the diagnosis of them is rare, when it occurs, the disease is very advanced and the treatment is usually palliative.

KEYWORDS: Melanoma, amelanotic fusocellular malignant melanoma, cardiac metastases, pericardial effusion, cardiac tamponade, pericardiocentesis.

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INTRODUCTION

The global incidence of melanoma is increasing, in 2021, in the United States, according to the American Cancer Society, an estimated 106,110 new cases of melanoma, with mortality reported of 7180 people. In the United States, the melanoma incidence is 1-3% of skin tumors and accounts for up to 60% of skin cancer-related deaths. It has a high rate of metastatic spread, with cardiac infiltration of up to 64%, but only 10-16% develop clinical manifestations, so most of the time it is diagnosed postmortem. Cardiac metastases of melanoma often affect the right side of the heart. Up to 98% have myocardial infiltration, 78% epicardial and 73% endocardial

(1, 2, 3). The clinical presentation is nonspecific, usually masked by other visceral metastases (4). Different imaging modalities for diagnosis include magnetic resonance imaging, echocardiogram and computed axial tomography (CT) and positron emission tomography (PET). Often the first or most easily accessible study is the echocardiogram where preliminary information is obtained from cardiac tumors, on the other hand, PET helps to identify metastases in general, regarding computed tomography and magnetic resonance imaging, both are useful for the characterization of cardiac tumors, particularly magnetic resonance imaging. (2,3)

TIMELINE

September 2016	Diagnosis of amelanotic fusocellular malignant melanoma infiltrating adipose tissue.
April 2019	Emergence of new axillary adenopathy.
December 2019	Recurrence of amelanotic fusocellular malignant melanoma infiltrating adipose tissue.

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March 2021	Disease-free, loses follow-up.
December 2022	Cardiac metastasis.
February 2023	Immunotherapy treatment
September 2023	Massive thrombosis, left pelvic limb thrombosis, placement of vena cava filter, phlebography and mechanical thrombectomy.

CASE REPORT

48-year-old male with a history in 2016 of amelanotic fusocellular malignant melanoma infiltrating adipose tissue at axillary level, immunohistochemistry with report of: MelanA positive, HMB-45 positive, Protein S-100 positive, KI67 positive in 30%. He completed chemotherapy with Paclitaxel and Carboplatin (6 cycles) and radiation therapy (25 sessions), being disease-free for 3 years. He presented recurrence in 2019, with ganglionic resection and treatment with chemotherapy with Paclitaxel and Carboplatin (6 cycles) with subsequent follow-up and surveillance. It loses follow-up in March 2021.

In December 2022 he was hospitalized in the emergency department for desaturation and dyspnea of rest and suspicion of COVID-19 infection, during his evaluation, thoracoabdominal CT was performed, showing a biventricular lesion of 6 cm and lesion in the right atrium of 5 cm, with global pericardial effusion (Figure I). Transthoracic echocardiogram is performed where left ventricular ejection fraction of 62% is obtained; it is seen in both ventricles from middle segment and up to the apex significant thickening of the ventricular walls (40mm X 60mm), suggestive of ventricular, infiltrated tumoring, irregular edges, limiting contractility; pericardial thickening with global effusion estimated in 2000 ml, which causes 40% right atrium collapse and diastolic right ventricle collapse, with variation with 40% transtricuspid input flow respiration. Fluoroscopy-guided thoracentesis with total drainage of 2500cc is performed (Figure II). During hospitalization, biopsies of pericardial, pericardial and endomyocardial fluid are taken that report neoplastic cells suggesting an epithelial appearance with highly suggestive accented moderate atypia of malignant neoplastic cells; immunohistochemistry confirms the diagnosis of cardiac metastases of infiltrating amelanotic fusocellular malignant melanoma (figure III). After hospital discharge, chemotherapy is initiated with Paclitaxel/Carboplatin, 3 cycles. 1 month later control transthoracic echocardiogram is performed showing systolic function of the left ventricle 52%, in both ventricles from the middle segment and to the apex with significant increase in ventricular walls (55mm X 60mm), suggestive of ventricular, infiltrated tumor, irregular edges, limiting contractility, type II diastolic dysfunction, normal-sized of right ventricle, with systolic dysfunction data by TAPSE 14mm, Tissue Doppler of the tricuspid ring 7cm/s, right ventricle shortening fraction of 30%. Global pericardial effusion, quantified in approximately 400ml, without haemodynamic impact (Figure IV). Patient without response to chemotherapy, with rapid growth progression of recurrent infiltrating amelanotic fusocellular malignant melanoma lesion. In February 2023, treatment with immunotherapy begins: Nivolumab and Ipilimumab to unacceptable toxicity or disease progression. However, in September 2023 he presented with massive thrombosis, left pelvic limb thrombosis, required placement of vena cava filter, diagnostic phlebography and mechanical thrombectomy.

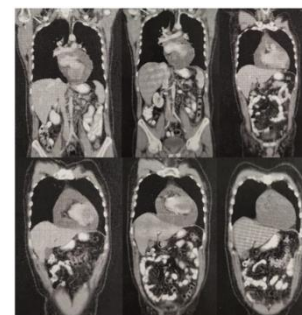


Figure I) Computed axial tomography with coronal cuts where visualized 6 cm biventricular lesion and 5 cm right atrium lesion, global pericardial effusion.

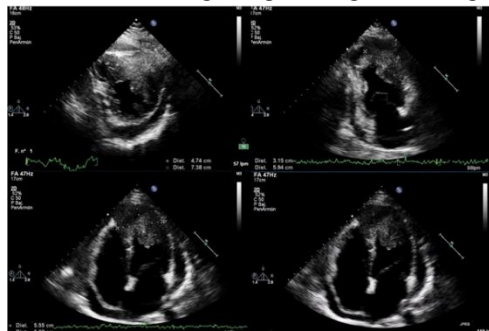
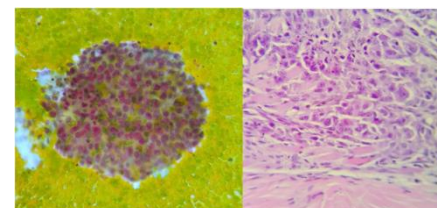


Figure IV) Transthoracic echocardiogram: LVEF 52%; cardiac metastasis with biventricular lesion (55mm X 60mm), global pericardial effusion without hemodynamic impact.]

Figure III) Left: Epithelioid pattern with moderate atypical cells, presence of some nucleoles. Right: Malignant cells with prominent nucleolus, an epithelioid pattern, are observed at the top. In the lower part, cells in fusocellular pattern are observed by elongated cells, moderate pleomorphism and with the presence of prominent nucleoles, consistent immunohistochemistry with metastasis confirmation of infiltrating fusocellular malignant melanoma.



DISCUSSION

Melanoma results from mutations in melanocytes. 20% of these occur in the neck and head, with these presentations being the worst prognostic (1). The diagnosis of this melanoma subtype is often a challenge due to its appearance anywhere on the body surface and often mimics amelanotic lesions, including inflammatory and scarring. In immunohistochemistry, markers of malignant melanoma of amelanotic fusiform cells are protein S-100, MelanA, tyrosine, c-kit, SOX-10, and HMB45 (1,5,6). In a study where

70 patients with autopsies were evaluated, with a history of metastatic melanoma, cardiac metastases were found in 64% of cases; however, of these only 16% had some cardiovascular symptom, so cardiac involvement without clinical evidence is frequent (7). The ante-mortem diagnosis of cardiac involvement is rare (3). Other retrospective cohort study conducted in outpatient care at the University of Michigan Health System from January 2009 to January 2022, 1254 patients with metastatic melanoma were evaluated, reporting cardiac metastasis to 23 of 1254 (1.8%) patients

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with metastatic melanoma. In this series of cases, right ventricular involvement was reported in 65%, left ventricle in 35% and right atrium in 35%. Among the most reported cardiac complications, arrhythmias are reported in 30%, heart failure in 22%, and pericardial effusion in 17%. The symptoms most reported by patients were fatigue in 35% and dyspnea in 30% of cases (8). In other series, the left ventricle was most frequently mentioned in 41.9%, subsequently the right atrium in 35.5% of cases (9). Major sites of metastasis to pericardium, myocardium and to a lesser extent endocardium have been mentioned in cardiac melanoma series (2). Clinical presentation is variable depending on the size, location, malignancy, relationship with underlying structures and propensity to embolize the tumor itself (10). The most common symptoms are dyspnea in 36.4% and physical examination tachycardia in 24% of cases (9). In addition to pericardial effusion, supraventricular arrhythmias and advanced AV node blockages (3). In these advanced stages of the disease, it is preferred to avoid surgical treatment, since its role is quite limited and is used as a palliative, in these cases the aim of this is the improvement of symptoms, especially in patients with symptoms of heart failure and obstruction of the left ventricular outflow tract. Recent immunotherapy treatments have been described that rely primarily on activation of cytotoxic T lymphocytes to induce an anti-tumor immune response (2). The main limitations of melanoma treatment are the manifestations derived from the toxicity of chemotherapy at the gastrointestinal, cutaneous, cardiac, among others; as well as the lack of specificity of tumor cells, they also have resistance to chemotherapy, targeted treatments, immunotherapies and intralesional therapies (4). Despite the different treatment strategies, adverse results have been reported where most are disease-free; however, if recurrences are reported per year of treatment and even deaths within the next 12 months of up to 36.4% (9). The average survival already with cardiac metastases is 12 to 24 months according to previously reported series (11). In conclusion, cardiac metastases secondary to metastatic malignant melanoma occur in less than 2%, which can occur in any cardiac structure and be associated with various cardiovascular complications, poor prognosis, as well as high mortality rates. Diagnosis is a challenge, it requires high suspicion especially in patients with cardiovascular symptoms, although most cardiac metastases go unnoticed. Comprehensive clinical evaluation with multimodal imaging studies is critical for differential diagnosis, however histopathological characterization is the gold standard study. This subtype of melanoma is rare, little bibliography mentions it, however since it is of the malignant subtype it has a high rate of metastasis, including at the heart. Usually cardiac metastases are diagnosed postmortem, however in the case of our patient it was of that minimum

percentage that was diagnosed before, although the prognosis is still bad and mortality is still high.

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