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MINI-FOCUS ISSUE ON CARDIAC MASSES

CLINICAL CASE

Tongue Squamous Cell Carcinoma With Cardiac Metastases

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ABSTRACT

A 60-year-old man with squamous cell carcinoma of the tongue had atypical chest pain and mild troponin elevation. No significant electrocardiogram changes or arrhythmias were noted. Cardiac magnetic resonance revealed several myocardial metastases with pericardial involvement, confirmed by positron emission tomography/computed tomography. Unsuitable for surgery, he was referred for palliative chemotherapy. (JACC Case Rep. 2025;30:102846)

A 60-year-old man with stage IVc metastatic squamous cell carcinoma (SCC) of the tongue was referred to our outpatient cardiology clinic because of episodes of atypical chest pain. The patient was taking retifanlimab (programmed cell death-1 inhibitor), incagn02385 (antilymphocyte activation gene 3), and incagn02390 (anti-T cell immunoglobulin and mucin domain-containing protein 3) for treatment of his malignancy.

LEARNING OBJECTIVES

- To appreciate the rarity of symptomatic cardiac involvement in oral squamous cell carcinoma and recognize the importance of using multimodality imaging, including cardiac PET, CT, and MRI, in assessing the extent of metastatic processes.
- To discern the significance of investigating solitary cardiac lesions in the context of accompanying distant metastases, emphasizing appropriate staging measures for accurate diagnosis and treatment planning.

The patient did not describe experiencing any heart failure symptoms or palpitations. The cardiovascular examination revealed no abnormal rhythm, murmur, jugular venous distention, or peripheral edema. The pain was not reproducible with palpation. The patient's vital signs were as follows: blood pressure 123/73 mm Hg, heart rate 74 beats/min, respiratory rate 14 breaths/min. He was afebrile, and his oxygen saturation was 100% while breathing ambient air.

He had a mild elevation in his high-sensitivity troponin I serum levels, which at their peak reached 96 ng/L (normal range, 3-17 ng/L). His 12-lead electrocardiogram (ECG) showed normal sinus rhythm with an isolated premature atrial beat, no acute ischemic changes, and nonspecific T-wave abnormalities. His hemoglobin level was 9.3 mg/dL, his platelet count was 335,000 μL (normal range, 150,000-450,000 μL), and his white blood cell count was 9.1 K/μL (normal range, 3.5-10.6 K/μL).

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ABBREVIATIONS AND ACRONYMS

anti-LAG-3 = anti-lymphocyte activation gene 3

anti-TIM-3 = anti-T-cell immunoglobulin and mucin domain-containing protein 3

CAD = coronary artery disease

CMR = cardiac magnetic resonance

ECG = electrocardiogram

EF = ejection fraction

EMB = endomyocardial biopsy

FDG = F-18 fluorodeoxyglucose

LV = left ventricle

LVEDP = left ventricular end-diastolic pressure

MRI = magnetic resonance imaging

pan-CT = whole-body computed tomography

PD-1 = programmed cell death-1

PET/CT = positron emission tomography/computed tomography

SCC = squamous cell carcinoma

PAST MEDICAL HISTORY

The patient had a past medical history of hyperlipidemia, anemia of chronic disease, and acquired hypothyroidism. He had no smoking history but consumed alcohol occasionally. The patient did not have any personal or family history of coronary artery disease (CAD).

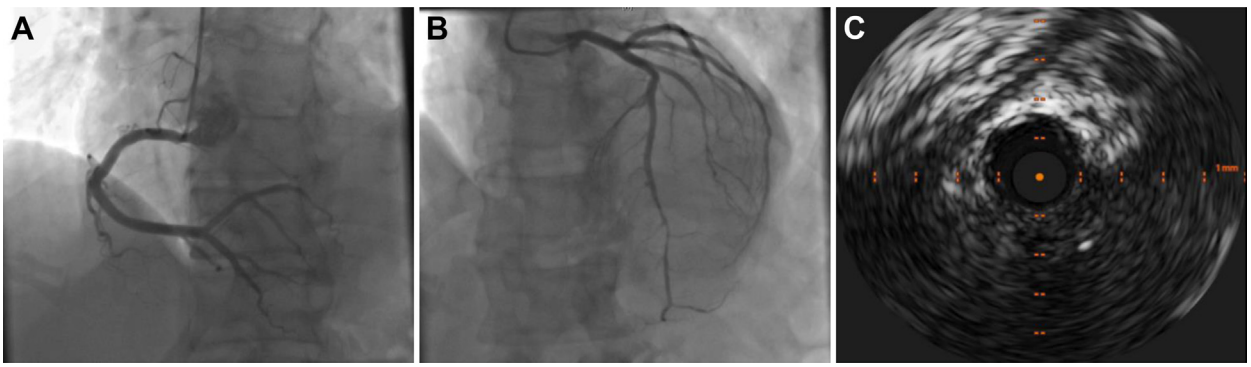
He had initially received a diagnosis of stage IVa (pT3pN2M0) SCC of the right lateral aspect of the tongue treated in 2012 with partial glossectomy and no adjuvant chemoradiation. He then underwent 2 additional partial glossectomies in February and June of 2022 because of local recurrence. Subsequently, he completed 6 weeks of adjuvant chemoradiation with intravenous cisplatin 40 mg/m^2 weekly. In August 2022, he underwent left lower lobe pulmonary nodule resection with negative margins because of a hypermetabolic isolated site of disease recurrence. His follow-up positron emission tomography/computed tomography (PET/CT) in December 2022 revealed new hypermetabolic left hilar lymph nodes and a new hypermetabolic nodule within the lingula, with no other metastatic foci. Treatment options were discussed, and the patient agreed to a clinical trial treatment with retifanlimab (programmed cell death-1 inhibitor), incagn02385 (anti-lymphocyte activation gene 3), and incagn02390 (anti-T-cell immunoglobulin and mucin domain-containing protein 3). Surveillance pan-CT (whole-body computed tomography) imaging in March 2023 showed multifocal lung metastases along with liver, chest wall, and kidney lesions. However, no cardiac involvement was noted on this scan at that time.

DIFFERENTIAL DIAGNOSIS

Given the patient's age and atherosclerotic risk factors along with mild troponin elevation, the differential diagnoses included obstructive CAD. which was ruled out by an invasive coronary angiogram. The patient had SCC with known metastatic disease and had been treated with chemotherapy and radiation; therefore, to rule out immune checkpoint inhibitor-induced myocarditis, cardiac magnetic resonance (CMR) was ordered. Possible cardiac or pericardial metastases were among the differential diagnoses. Of note, the patient's most recent PET/CT obtained just 3 months before the presentation did not demonstrate any invasive cardiac pathologic changes. Also important were the unremarkable ECG findings, which did not raise any red flags for a serious cardiac issue. Finally, as a cause of mild troponin elevation, infiltrative cardiomyopathies such as cardiac amyloidosis were thought of but were ruled out on the basis of the CMR findings.

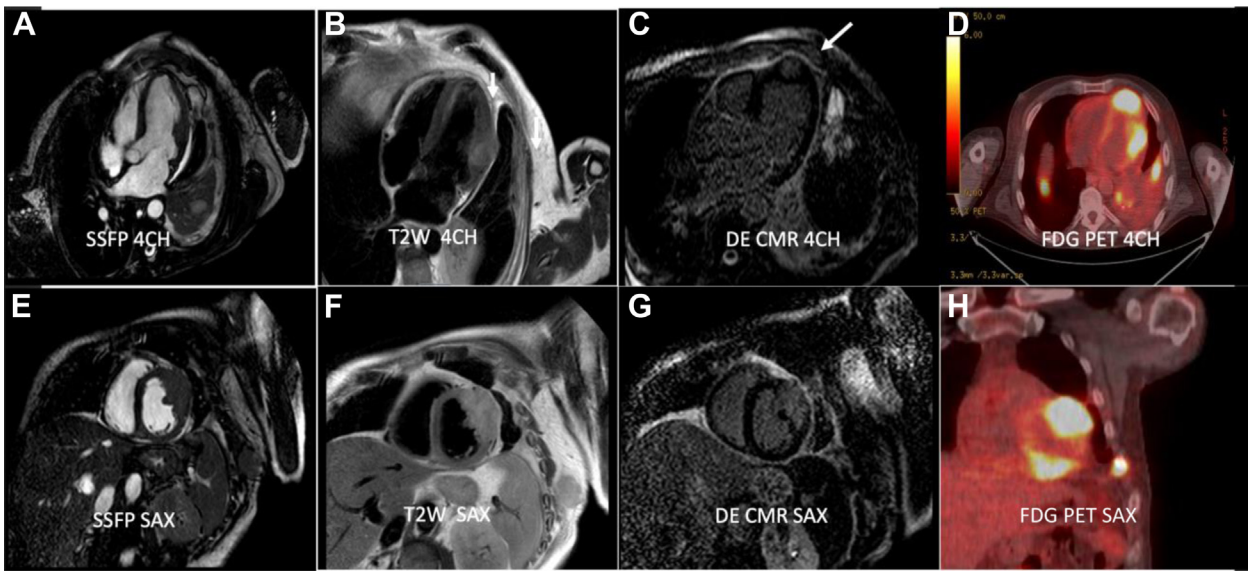
Despite consideration of other potential causes of atypical chest pain in light of the patient's malignancy and immunocompromised status, including musculoskeletal, gastrointestinal (esophagitis, gastritis), and pulmonary causes such as pulmonary embolism and pneumonia, further evaluation

FIGURE 1 Coronary Angiography



(A) Dominant right coronary circulation. (B) Left main coronary system. (C) Intravascular ultrasonography image of distal left anterior descending. No evidence of obstructive coronary artery disease.

FIGURE 2 **CMR and FDG-PET Images**



(A) SSFP 4-chamber view demonstrating distal septal and basal anterolateral mass. (B) Corresponding T2-weighted 4-chamber view with hyperintense signal in the lesions above. (C), DE 4-chamber image revealing areas of delayed hyperenhancement in the distal septal and basal anterolateral wall. (D) FDG-PET/CT showing avid FDG uptake in the lesions noted on CMR above. (E) SSFP SAX image revealing distal septal and basal antero-lateral lesions. (F) T2-weighted SAX image delineating the lesions. (G) DE SAX image. (H) FDG-PET/CT image of the distal septal and basal antero-lateral lesions. The findings are strongly suggestive of metastatic disease. CMR = cardiac magnetic resonance; DE = delayed enhancement; FDG = fluorodeoxyglucose; PET = positron emission tomography; SAX = short axis view; SSFP = steady state free precession sequence.

revealed that the nature of the pain, physical examination findings, and absence of hypoxia, fever, and leukocytosis effectively ruled out these alternative diagnoses.

INVESTIGATIONS

To rule out possible CAD (given chest pain and troponin elevation), the patient underwent a coronary angiogram with no evidence of obstructive CAD (**Figure 1**). The LV ejection fraction (EF) was 60%, with left ventricular end-diastolic pressure (LVEDP) of 22 mm Hg. In our case, we did not perform an echocardiogram and went directly to CMR because immune checkpoint inhibitor-induced myocarditis was high in the differential diagnosis list, given the patient's chemoradiation history.

CMR demonstrated normal size left ventricle (LV) along with normal global LV systolic function, multiple masses within the LV myocardium, and anterolateral pericardial invasion with a small amount of associated loculated pericardial effusion (**Figures 2A to 2C and 2E to 2G**). Follow-up PET/CT imaging showed several foci of increased myocardial metabolic activity that matched the CMR findings (**Figures 2D and 2H**), with multiple FDG-avid metastatic lesions in the cranial bones, liver, bilateral pleura, and lungs, but no recurrent tumor was found in the remnant tongue, oropharynx, or reconstructive flap.

MANAGEMENT

Before the CMR findings, the patient was treated with a 1-week tapering dose of steroids because of a concern for immune checkpoint inhibitor-induced myocarditis. When we discovered the presence of cardiac metastases, the patient received 3 weeks of palliative chemotherapy consisting of carboplatin, pembrolizumab, and paclitaxel, which were yet to be completed at the time of submission of this report.

DISCUSSION

Cardiac metastases are rare and are typically identified postmortem because of the lack of prominent symptoms necessitating cardiac investigations.[1-3] Sudden death frequently serves as the initial manifestation.[2] Malignancies with the highest cardiac metastases are outlined in **Table 1** according to an extensive postmortem analysis by Bussani et al,[4] revealing an overall incidence of cardiac metastases

TABLE 1 Incidence of Cardiac Metastases and Their Location by Type of Primary Neoplasm

Primary Malignancy	Incidence of Cardiac Metastases, %
Pleural mesothelioma	48.4
Melanoma	27.8
Lung adenocarcinoma	21
Undifferentiated carcinomas	19.5
Lung squamous cell carcinoma	18.2
Breast carcinoma	15.5
Leukemia/lymphoma	9.4
Oral cavity carcinoma	5.3

at 9.1%. Although oral cavity carcinoma can metastasize to multiple organs, the lungs being the primary site of metastases followed by bone and liver, cardiac metastases are highly unusual.[3,5]

When diagnosed ante mortem (as in our case), patients may experience nonspecific cardiac symptoms including chest pain, shortness of breath, or palpitations.[1,6] ECG findings may not effectively rule out even a significant cardiac involvement. The role of coronary angiography in this and other cases is rather supportive to rule out any significant epicardial CAD.[7] Several other diagnostic approaches, such as coronary computed tomography angiography (CTA), could have been considered to rule out CAD in our case. However, given the specifics of our clinical setting and the patient's ongoing chest pain with elevated troponin levels, we thought that the most effective, fast, and safe approach to rule out acute coronary syndrome was through an invasive coronary angiogram to exclude coronary occlusion.

In diagnosing cardiac metastases in patients for whom there is a high level of clinical suspicion, the best diagnostic approach is to proceed with advanced cardiac imaging applications.[1] In symptomatic patients or patients with ECG abnormalities, echocardiography can be performed as the initial diagnostic imaging because of its widespread availability and adequate sensitivity in detecting cardiac masses.[1,3,6] Cardiac CT and MRI offer a more thorough evaluation, providing better spatial resolution and enhanced details such as tissue characterization (lipid-rich vs vascular vs nonvascular tissue), assessment of the pericardium, and detection of extracardiac disease.[7] In patients with head and neck primary malignancies, PET/CT imaging holds value as a diagnostic tool reliably identifying metastatic involvement. Surprisingly, our patient's PET/CT 3 months before his referral to the cardiology office did not show any cardiac metastases. In our case, we did not perform an echocardiogram and went directly to CMR because immune checkpoint inhibitor-induced myocarditis was high in the differential diagnosis list, given his chemoradiation history. CMR successfully diagnosed extensive cardiac lesions and effectively ruled out immune checkpoint inhibitor-induced myocarditis or infiltrative cardiomyopathy.

The importance of endomyocardial biopsy (EMB) in cases of possible chemotherapy-induced myocarditis is not well defined and is likely underused in current clinical practice. Performing EMB requires an experienced operator and a skilled pathologist to correctly interpret the biopsy, which may not be available at all sites. Although tissue diagnosis remains a gold standard, especially when the result of CMR is suboptimal or nondiagnostic, the practical limitations often restrict the use of EMB. Although our patient had mild troponin elevation, in the majority of published cases no distinct biochemical abnormalities are noted.

Cardiac metastases are most commonly found in the pericardium, followed by the myocardium, although they can be seen in the epicardium, endocardium, and intracavitary regions as well.[1] In fact, pericardial effusion has been recognized as a direct indication of cardiac metastases, occasionally serving as the initial manifestation.[4] Our patient had a small amount of loculated pericardial effusion, as seen on his images.

Limited treatment options are available for oral SCC with cardiac metastases. The majority of patients are not surgical candidates because of the location of the disease. In our case, surgical resection was not feasible because of the extent of cardiac involvement. In a palliative care context, radiotherapy or chemotherapy may be considered for patients with symptomatic metastases. Furthermore, immunotherapeutic approaches with the use of agents like pembrolizumab or nivolumab (anti-programmed death ligand-1 antibodies) have the potential to enhance survival outcomes for these patients,[8,9] which was the initial treatment modality for our patient. However, despite the treatment, the outcome remains poor. In our case, the patient had known lung metastases followed by hepatic, kidney, and cardiac involvement and was given palliative therapy (carboplatin, pembrolizumab, and paclitaxel).

FOLLOW-UP

The patient was given the triple chemotherapeutic agents mentioned above.

CONCLUSIONS

Cardiac metastases are rare among patients with oral cavity cancers, and there is a lack of established guidelines for diagnosis and management. The diagnostic process is challenging because cardiac metastases often do not present with noticeable symptoms, and the value of routine surveillance imaging remains uncertain. In both symptomatic and asymptomatic individuals, a multimodality imaging approach involving advanced echocardiography, PET/CT, and CMR should be implemented to confirm the presence and extent of the metastatic disease, which can assist in tailored management and individualized clinical decision making for each specific patient.

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