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Case Report

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Cardiac Metastases from Mucosal Head and Neck Squamous Cell Carcinoma

Courtney B Shires[1*], Karuna Dewan[2], Allen Ardestani[1]

Abstract

Objectives: To understand that cardiac metastasis of mucosal head and neck squamous cell carcinoma (SCCa) is rare and carries a poor prognosis. To acknowledge the possibility of cardiac metastasis in patients with mucosal head and neck SCCa. This condition is usually asymptomatic, but it can present with EKG changes, syncope, or even sudden death.

Methods: A single case report of a 55-year-old female with a history of T2N1M0 oral tongue SCCa treated with surgery and postoperative radiation is presented. The patient went on to develop a cardiac septal metastasis. To date, fewer than 35 documented cases of mucosal head and neck SCCa metastasizing to the heart are present within the literature. This is an uncommon but life-threatening condition.

Results: In our case, the patient was placed on hospice and passed away in her home 11 months later. A literature review over 35 years (1985-2020) of the incidence, presentation, diagnosis, treatment, and outcome of patients with Head and Neck Mucosal Squamous Cell Carcinoma (HNMSCC) and cardiac metastasis (CM) was performed. CM of HNMSCC occurs on rare occasion, with 33 other documented cases. The most common primary tumor sites were oral tongue (33.3%), and larynx (27.8%). The most common presenting symptoms were dyspnea (16.7%) and chest pain (16.7%).

Conclusions: Cardiac metastasis is uncommon but life-threatening long-term sequelae of mucosal head and neck SCCa without any effective treatment options.

Keywords: Cardiac metastasis; Head and neck cancer; Squamous cell carcinoma.

Introduction

Cardiac metastasis (CM) of mucosal head and neck squamous cell carcinoma is an incredibly rare but universally fatal phenomenon. The incidence of cardiac metastasis of all squamous cell carcinoma has been found to be between 5 and 10 percent when examining autopsies. The incidence of cardiac metastases is substantially higher in malignancies from other sites such as melanoma, lung, breast, esophagus, and lymphoma. There are 12 reported cases of cardiac metastasis from squamous cell carcinoma of the tongue in the English-language medical literature [1-6]. There are 34 cases of cardiac metastasis (CM) from multiple locations of mucosal head and neck squamous cell carcinoma (HNMSCC) [2-18]. When distant metastases of HNMSCC occur, they most often involve the lung, skin, liver or bone. The mechanism of metastasis from the head and neck to the myocardium is poorly understood. Pathways that have been proposed are hematogenous

Affiliation:

[1]West Cancer Center & Research Institute, Germantown, TN, USA.

[2]Division of Laryngology, Otolaryngology Head and Neck Surgery, Louisiana State University, Shreveport, LA, USA.

***Corresponding author:**
Courtney Shires, MD 7945 Wolf River Blvd Germantown, TN 38138 West Cancer Center & Research Institute, Germantown, TN, USA.

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spread through the coronary arteries, direct extension, and retrograde dissemination through lymphatic channels [5, 12, 13]. Involvement of the cardiac conduction system is much less common. In decreasing order of frequency, tumors usually metastasize to the pericardium, myocardium, epicardium, endocardium, and intracavitary regions [14]. Clinical manifestations of CM are rare and nonspecific therefore they are often not detected until an advanced stage or at autopsy [5]. Symptoms can include sudden onset heart failure and new arrhythmia. In those patients with advanced HNMSCC and new onset cardiac symptoms, metastatic cardiac lesion should be suspected. Helpful diagnostic testing includes electrocardiogram, echocardiography, computed tomography, and magnetic resonance imaging [19]. Cardiac biopsy providing histologic diagnosis is the gold standard; however myocardial biopsy is often a perilous undertaking. Despite advances in cancer treatment, management of metastatic cardiac lesions remains challenging. Currently, there is no standardized therapeutic approach. Options include palliative chemotherapy and radiation, and for specific cases surgical resection.

Case Presentation

A 55-year-old female presented in October 2012 with a tender right floor of mouth/ventral tongue lesion that was present for one month. She had difficulty tolerating oral feeds secondary to the tenderness. Over the previous month she had lost 10 pounds. The patient reported persistent right otalgia, treated regularly with hydrocodone. Her speech changed slightly. The patient denied any shortness of breath, hemoptysis, or aural fullness. She smoked 10 cigarettes daily and drank 4 beers daily for many years. Biopsy and imaging revealed squamous cell carcinoma. On November 16, 2012 she underwent composite resection of right floor of mouth/ventral tongue cancer and right hemiglossectomy, right selective neck dissection, tracheotomy, and reconstruction with anterior lateral thigh flap. Pathology results described a T2N1N0 squamous cell carcinoma of the right floor of mouth and tongue. Margins were negative, but lymphovascular and perineural invasion were identified. After multidisciplinary tumor board discussion, it was recommended that she receive adjuvant radiation therapy (RT). She was not compliant with this recommendation.

Eight months after surgery, on June 27, 2013, the patient underwent a combined positron emission tomography (PET)/computed tomography (CT) scan (Figure 1a, 1b, 1c) for follow up of disease which noted a 2.7-cm mass in the right floor of mouth as well as several enlarged lymph nodes with hypermetabolic activity in the right level 2B region, the largest of which was 3 cm. The patient was subsequently taken to the operating room for radical right neck dissection. Significant disease was noted in right neck areas level 2B, as well as a soft tissue mass that extended through the mylohyoid and into the base of the tongue musculature. Multiple areas were biopsied and surgical pathology showed moderate to poorly differentiated squamous cell carcinoma diffusely invading soft tissue with tumor present at cauterized excision margins. Postoperatively the Medical Oncology Service was consulted, and plans were made for the patient to follow up for chemotherapy and radiation in light of positive surgical margins. On the third postoperative day, a CT scan of the abdomen and thorax was obtained which showed no evidence of metastatic disease involving the abdomen or pelvis. The patient's postoperative course continued uneventfully. The patient was discharged home. The patient failed to present for multiple Medical Oncology and Radiation Oncology appointments. Several months later, she presented in October 2013 and underwent a PET scan. Unfortunately, this showed interventricular septum metastasis of the heart. No biopsy was attempted. She was placed on hospice and passed away in her sleep 11 months later. She never experienced any cardiac symptoms. She denied chest pain, dyspnea, and palpitations.

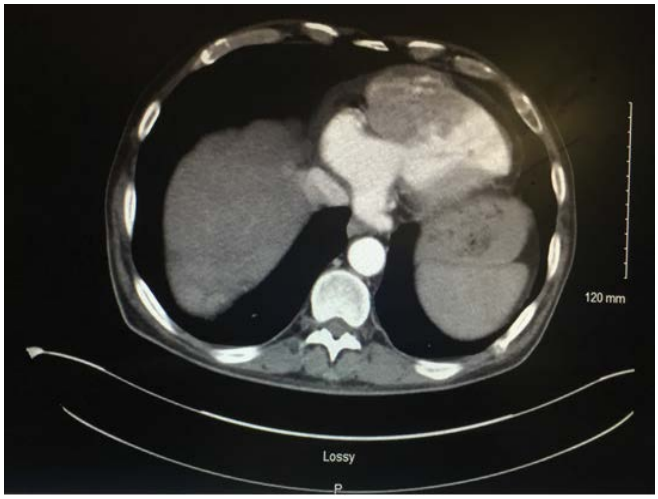

Figure 1a: Axial view of interventricular septum mass filling most of right ventricle

Figure 1b: Coronal View

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Figure 1c: Sagittal View

Discussion

In the last 35 years (1985 – 2020) this is the 34th reported case of CM from HNMSCC (Table 1) and only the 25th diagnosed in a living patient. Ages ranged widely from 32 to 73 years old (mean 60.0±13.5 years), with a slight male predominance (57%). These tumors represent uncommon and late stage sequelae of HNMSCC. CM from HNMSCC does not seem to have geographic distribution, as they have been reported across the world in our series. Previously published reports were from the United States, Asia, and Europe. In the reviewed literature sites of initial head and neck malignancies included: tongue (12), larynx (6), oral cavity (9), oropharynx (4), hypopharynx (2), and unknown primary (1). Interestingly, none of the patients in this series had a nasopharynx primary, even though nasopharynx malignancy is reported to metastasize more often than other head and neck mucosal malignancies. Hypopharynx cancer tends to have a worse prognosis that other HNMSCC but has not been found to have more cardiac metastasis. Oral tongue cancer is reported to have skip metastasis in the neck. It is also found to have a higher incidence of CM as well. Fittingly this was the most common primary tumor site in this review. Cardiac metastasis of tumors arising from head and neck and particularly of the larynx are reported to be extremely rare [14]. In this cohort of patients TNM stage at initial presentation was mostly advanced: stage I (1), stage II (4), stage III (5), stage IV (7). The staging was unknown for 19 of the patients. Initial treatment for the primary lesions included: surgery (3), surgery then postoperative radiation or chemoradiation (3), concurrent chemoradiation (2), concurrent chemoradiation then surgery then chemotherapy (2), concurrent chemoradiation then surgery (1), induction chemotherapy then surgery then radiation (1), and radiation then surgery (1).

Patients with CM are most often asymptomatic. The most common presenting symptoms were chest pain (16.7%), dyspnea (16.7%), EKG changes (13.9%), and edema (13.9%). Other reported symptoms included syncope and fatigue. Initial, nonspecific symptoms include syncope, dizziness, and dyspnea. Three of the CM was noted as incidental findings on routine surveillance imaging. The CM ranged from being asymptomatic to causing heart failure to causing sudden death. Symptoms varied widely, including dyspnea, lower extremity edema, substernal pressure, arrhythmia, and sudden death. Twenty-two of the 34 patients in this series were symptomatic. Two of the previous reports of tongue cancer involved patients who presented with arrhythmias due to conduction disturbances from tumor invasion of the septum [6, 9]. In a 3rd case, a patient presented with angina decubitus due to the presence and location of her cardiac tumors [10]. Another presented with a large pericardial effusion [2]. One patient's syncopal episodes could be attributed to an uncontrolled seizure disorder that resulted from extensive brain metastases [5]. Another patient's palpitations were due to atrial fibrillation that was most likely caused by widespread pulmonary disease [5]. Symptomatic cardiac metastases from squamous cell carcinoma are an uncommon situation [5]. Cardiac metastasis should be suspected when new cardiovascular symptoms are observed in patients with a history of head and neck malignancy [13]. Length of time from initial cancer diagnosis to discovery of CM averaged 24.5 months (10 patients), and the time from initial cancer treatment to CM averaged 15.6 months (14 patients).

The development of symptoms depends on the size and location of the tumor. As the mass grows patients can develop chest pain, valvular abnormalities, heart failure, pericardial effusion, cardiogenic shock, or tamponade. Symptoms, when present, depend upon the location and size of the mass. Location of CM was: ventricle (10), pericardium (7), interventricular septum (6), atrium (3), septum (3), atrium and ventricle (2), ventricle and intraventricular and epicardium (2), all 4 chambers (1), intra- and extracardiac (1). This is in contrast to prior studies to reported the most common sites in descending order as the pericardium, myocardium, epicardium, endocardium, and intracavitary regions [14]. Initial diagnostic modality in all cases was an electrocardiogram (EKG) [13]. In several cases, the EKG demonstrated non-specific changes including ST- elevation in the absence of troponin elevation, development of atrial fibrillation [17], or complete AV block [20]. In one particular case the patient demonstrated right bundle branch block seven months before diagnosis of the cardiac metastasis [21]. Imaging that was pertinent in diagnosing CM in our series was: echocardiogram (38.9%), CT (19.4%), PET (11%), and cardiac MRI (5.6%). Previously, cardiac imaging to detect malignancy included CT, magnetic resonance imaging, 3-dimensional transthoracic echocardiography, and PET [2-

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5, 16]. The use of PET/CT yields functional and morphologic information with excellent resolution, and valuable follow-up information in difficult cases [22]. To date, no study has shown the superiority of a single imaging technique in this patient group. Echocardiography is relatively inexpensive, readily available, repeatable, and portable. Onwuchekwa recommended that patients with head and neck malignancies undergo early echocardiographic evaluation when cardiac symptoms arise [5]. The patient presented in this case report underwent a PET scan at the time of CM diagnosis. Within the literature 7 cases (19.4%) of CM diagnoses were made at the time of autopsy.

CM diagnosis is confirmed by at least one of the following methods: myocardial biopsy (1), pericardial fluid drainage (2), CT guided pericardial biopsy (2), and surgical excision of CM (2). Seven underwent biopsy postmortem. Only 3 of these patients had other known sites of metastasis prior to discovery of their CM. With imaging, 15 patients (41.7%) were found to have other sites of metastases in addition to CM. Diagnosis relies primarily on clinical suspicion and imaging. Most physicians do not biopsy these. While histologic examination is the gold standard for diagnosis, cardiac biopsy is fraught with risk [23]. It offers no benefit in patients with cardiac metastasis. Nagata (2012), Suda (2007), and Werbel (1985) did obtain a biopsy [4, 6, 12]. Tsai (2010) performed pericardial drainage, and Ito (2008) performed autopsy [2, 9]. Treatment options for patients with cardiac metastases are limited. Due to the extent and location of the intracardiac lesions, most patients are not candidates for surgical resection [5]. In this series, 6 patients were placed on hospice, 4 were administered palliative chemotherapy, 2 were medically managed for heart failure, 2 underwent immunotherapy, 2 underwent surgical resection, 1 had a pacemaker placed, and 1 was administered radiation. There is no support to placing these patients on cardiac medications, as only two patients in this series were placed on cardiac medication. Treatment is usually palliative and the prognosis is poor [3]. The prognosis of HNMSCC typically is fatal [10]. The 34 patients uniformly died of this disease, with the longest survival after diagnosis of CM of 26 months. The patient presented here passed away 11 months after diagnosis.

Table 1: Cases of cardiac metastasis of mucosal head and neck squamous cell carcinoma between 1985 and 2020.

Author (year)	Age	Gender	Primary site	Stage	Primary Treatment	Symptom	Diagnostic Method	Cardiac Metastasis Location	Metastasis Treatment	Outcome
Alhakeem (2008)	49	M	Larynx		Surgery	Right leg ischemia, Left chest pain, hypotension, tachycardia	Echo, CT	All 4 chambers, Intraventricular septum		
Browning (2015)	50	M	Tongue	T4aN2c	Surgery, Radiation	none	PET	Right ventricle	Palliative care	
Cho(2018)	70	M	Oral Cavity		Surgery, Chemo-XRT	Dizziness	EKG, Echo	Right ventricle, Intraventricular septum	Pacemaker, Palliative chemotherapy	
Chua (2017)	63	M	Tongue		Surgery, Chemo-XRT	Dyspnea	Echo	Right atrium, Pericardium	Medical management of heart failure	
Shires (2020)	55	F	Tongue	T2N1M0	Surgery	Asymptomatic	CT	Intraventricular septum	Palliative care	Death
Duband (2010)	57	F	Tongue	T3N2b	Surgery, Chemo-XRT	Sudden Death	Autopsy	Right atrium		Death
Fouladi (2013)	56	F	Unknown Primary	TxN3M1		Right neck swelling	Chest CT, PET	Intraventricular septum	None	
Fujio (2019)	66	F	Oral Cavity	T3N0M0	Surgery, Radiation	malaise, Loss of appetite, dyspnea, edema	CT, Biopsy	Right ventricle	Palliative care	Death
Gullulu (2006)			Larynx							
Hans (2009)	54	M	Base of Tongue	T2N2M0	Chemotherapy, Surgery, Radiation	Dyspnea, edema,	CT, echo, EKG	Right ventricle	None	
Ito (2008)			Tongue		Surgery, Radiation	Sudden death, Arrythmia	Autopsy	Conducting system	none	Death
Iyer (2002)			Pyriform sinus					Pericardium		
Kamatani(2015)	90	M	Buccal Mucosa	T4aN1M0	Surgery (cyberknife)	Dyspnea, weakness	Autopsy	Right ventricle	None	
Kavanagh (2012)			Larynx			Nonspecific symptoms	Echo, MRI			
Kawamoto (2001)	71	M	Tongue	T2N2M0	Surgery	Loss of Appetite	Autopsy	Left ventricle	None	Death

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Larkin (1994)			Larynx			Syncope				
Malekzadeh	58	F	Tongue	T2N2cM0	Surgery, Radiation	Chest pain	PET	Right ventricle	Palliative Chemotherapy	
Mark-Adjeli(2019)	60	M	Tonsil	T4aN1M0	Chemo-XRT	Fatigue	PET, MRI	Right Ventricle	Surgery, Palliative XRT, Immunotherapy	Death
Martell (2016)	62	M	Retromolar Trigone	T42N2M0	Surgery, Chemo-XRT	Dyspnea, A fib	Biopsy	Right ventricle	None	
Mckeag (2013)	77	M	Tongue			Syncope, Fever, PNA, A fib	Echo	Right atrium, Right ventricle	None	Death
Nagata (2012)	60	M	Tongue	T2N1M0	Chemo-XRT, Surgery		CT	Left atrium	Surgical excision	Death
	60	M	Soft Palate	T2N1M0	Chemo-XRT, Surgery		CT	Right atrium and ventricle	None	Death
Onwuchekwa (2012)	45	F	Tongue		Surgery	Syncope	Echo	Right ventricle, Intraventricular septum	Palliation	
	36	F	Tongue		Chemo-XRT, Surgery	A. fib	Echo	Left ventricle	Chemotherapy, Radiation, Medical management of heart failure	Death
Pattni (2015)	89	F	Oral Cavity	T4N2M0	Radiation	EKG changes- ST elevation, tachycardia	Echo	Right ventricle	Palliative care	
Renders (2005)			Larynx			Myocardial infarct	EKG	Right ventricle		
Rivkin (1999)	57	M	Base of Tongue	T1N0M0	Surgery, Radiation	Myocardial infarct, Chest pain, ST elevation, Edema	EKG, Echo	Right ventricle	Palliative Chemotherapy	Death
Schwender (2002)	73	F	Buccal Mucosa	T4N0M0	Chemo-XRT	Weakness, lightheadness, dyspnea, Afib	CT, Echo, biopsy	Anterior pericardium		Death
Shafiq (2019)	43	M	Tongue	T2N2M0	Surgery, Chemo-XRT	Asymptomatic	CT, EKG, Echo, MRI, biopsy	Left Ventricle	Immunotherapy, Chemotherapy,	
Suda (2007)	63	M	Hypopharynx	T4N2bM0	Chemo-XRT	Asymptomatic	EKG, Echo, Myocardial biopsy			
Tandon (2019)	25	F	Tongue	T2N0M0	Surgery, Radiation	Chest pain, Dyspnea, Cough	Echo	Right ventricle, Left Ventricle	Hospice	Death
Tsai (2010)	62	F	Retromolar Trigone			Cardiac Tamponade	Echo		Pericardial effusion drainage	
Werbel (1985)	60	F	Base of Tongue	T2N0M0	Surgery, Radiation	Chest pain, Angina, ST changes	EKG, Echo, Biopsy	Right Atrium, Mediastinal mass	Palliative radiation	Death
Zemann (2006)	58	F	Oral Cavity		Surgery, Radiation	Dyspnea	CT	Right ventricle, pericardium	None	Death

Conclusion

CM from the head and neck most often originates from primary tongue and larynx malignancies. Most patients initially have stage IV HNMSCC. Initial treatment in 79% of patients included surgery, and 67% of patients underwent combined surgery with nonsurgical therapy. CM does not necessarily present in patients with other known local, regional, or distant disease. CM usually occurs in the ventricle or interventricular septum. Echocardiogram and CT have most commonly been used for diagnosis. CM usually presents around 1 year after diagnosis/treatment of HNMSCC. Cardiac metastasis should be suspected in any patient with HNMSCC in whom new cardiac symptoms develop. Most physicians do not obtain premortem tissue diagnosis of CM. Presentation of CM varies widely, from an asymptomatic incidental finding to sudden death. Death occurs within months of diagnosis of CM. This entity is distributed evenly across the world. It is advisable to consider cardiac metastasis in the differential diagnosis when a patient with a history of HNMSCC presents with new onset cardiac symptoms including EKG changes or syncope. It may be worth considering adding routine EKG to the annual surveillance regimen for patients who have been treated for HNMSCC.

Abbreviations

squamous cell carcinoma (SCCa); Head and Neck Mucosal Squamous Cell Carcinoma (HNMSCC); cardiac metastasis (CM); radiation therapy (RT); positron emission tomography (PET); computed tomography (CT); electrocardiogram (EKG)

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