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CASE REPORT

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Fluorodeoxyglucose positron emission tomography/computed tomography identifying pericardial metastasis from early-stage p16-positive oropharyngeal cancer

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Abstract

Pericardial metastasis from HPV-positive oropharyngeal squamous cell carcinoma (OPSCC) without local recurrence is extremely rare. We report about a 69-year-old man exhibiting pericardial metastasis on positron emission tomography/computed tomography (PET/CT). There are currently no reports on the use of PET/CT in patients with pericardial metastasis from p16-positive OPSCCs.

KEYWORDS

FDG positron emission tomography/computed tomography, head and neck squamous cell carcinoma, oropharyngeal squamous cell carcinoma, P16-positive, pericardial metastasis

1 | INTRODUCTION

Pericardial metastasis from oropharyngeal squamous cell carcinomas (OPSCCs) is a very rare occurrence, especially from human papillomavirus (HPV)-positive squamous cell carcinomas. OPSCCs are strongly associated with HPV infection, with a prevalence of approximately 80%.[1] The tumor suppressor p16 is a surrogate marker for HPV, and HPV-related head and neck squamous cell carcinomas are associated with more favorable prognoses and better responses to therapy.[2,3] The gold standard for HPV detection is p16 immunohistochemistry, which reportedly has 100% sensitivity and 79% specificity.[1,2] To the best of our knowledge, the present case is the first of pericardial metastasis without local recurrence in the early stage of p16-positive OPSCC reported in the English literature. There have only been two recent case reports of pericardial metastasis from advanced-stage OPSCCs.[4,5] There have been no previous reports of the use of fluorodeoxyglucose (FDG) positron emission tomography (PET)/computed tomography (CT) in patients with pericardial metastasis from p16-positive OPSCCs. Herein, we report the case of a 69-year-old man diagnosed with p16-positive OPSCC exhibiting rare pericardial metastasis on PET/CT.

2 | CASE REPORT

A 69-year-old man without any relevant medical history visited our hospital outpatient clinic with right throat discomfort. He reported that he currently consumed alcohol in social situations and used to be a smoker (1 pack/day for 30 years), but had quit smoking 5 years ago and was

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currently a nonsmoker. Otorhinolaryngologic examination revealed a right palatine tonsillar mass, and no other abnormal lesions were observed. Histological examination of a right palatine tonsil biopsy revealed p16-positive squamous cell carcinoma. Results of ultrasound-guided fine needle aspiration biopsy (US-FNAB) of bilateral neck lymph nodes were negative. He was diagnosed with OPSCC of the right palatine tonsil and underwent right oropharyngectomy with right selective neck dissection, including levels I–III (supraomohyoid neck dissection). Pathology revealed a 2.5-cm-sized mass with invasion of the superior constrictor muscle and no metastatic lymph nodes in the dissected neck. The tumor was a moderately differentiated squamous cell carcinoma with p16 overexpression, and all resection margins were clear. The pathologic stage was T2N0M0 (stage I according to AJCC TNM cancer staging, 8th edition).[6] The patient's case was then discussed by a multidisciplinary oncology team to review the radiology and histopathology results and develop a treatment plan. He underwent adjuvant radiotherapy (6600 cGy, 30 fractions) to the head and neck area.

A follow-up neck CT performed 4 years later revealed multiple borderline size enlarged lymph nodes in his right axilla. PET/CT was performed with integrated PET/CT scanners (Biograph mCT; Siemens Medical Solutions) and depicted mild FDG uptake in the right axilla lymphadenopathy. US-FNAB of the right axilla lymph nodes was negative for malignancy. Eight months later, he was admitted to our hospital with fatigue and dyspnea, and a follow-up PET/CT was performed. There was no evidence of local recurrence, but PET/CT revealed diffuse hypermetabolic irregular nodular thickening in the pericardium and hypermetabolic supraclavicular, mediastinal, and aortocaval lymph nodes (Figure 1A-E). The previously noted right axillary lymphadenopathy was not visualized on this scan. The maximum standardized uptake value of hypermetabolic pericardial thickening was 14.2 and that of the lymph nodes was 6.0. Chest CT also depicted pericardial thickening and mediastinal lymphadenopathy (Figure 2A and B). There were no significant fluctuations in his blood pressure, pulse rate, or body temperature (37°). Laboratory tests including complete blood count, erythrocyte sedimentation rate, and C-reactive protein were within normal limits. The patient was diagnosed with pericardial metastasis accompanied by multiple lymph node metastases determined via chest CT and PET/CT. Thereafter, he received palliative chemotherapy for treatment of the pericardial metastasis.

3 | DISCUSSION

The incidence of cardiac metastasis ranges from 0.7% to 3.5% in healthy individuals but is reportedly up to 9.1% in autopsied oncology patients.[5] The most common primary malignancies accompanying pericardial metastasis include lung cancer, breast cancer, leukemia/lymphoma, esophageal cancer, mesothelioma, colon cancer, and undifferentiated cancer of unknown origin.[7-10] Primary pericardial tumors, including malignant mesothelioma and fibrosarcoma, are much less common.[11]

HPV-positive OPSCCs tend to follow different clinical courses than HPV-negative OPSCCs related to smoking and/or alcohol consumption. HPV-positive OPSCCs are associated with better prognoses and better responses to radiotherapy and chemotherapy than their HPV-negative counterparts.[12] While HPV-negative OPSCCs usually exhibit locoregional failure, distant metastasis is a relatively common cause of treatment failure in HPV-positive OPSCCs.[3] Although the rates of distant metastasis are similar regardless of HPV infection, distant metastasis in HPV-positive OPSCC patients may develop more than 2 years after treatment, but in HPV-negative OPSCC patients, it commonly develops within 2 years after treatment.[3] Long-term clinical and radiography follow-up is recommended. After distant metastasis, patients with HPV-positive OPSCC that is appropriately treated may exhibit prolonged survival compared to patients with HPV-negative OPSCC.[3]

HPV-positive OPSCCs with extensive primary tumor and/or extranodal extension conglomerated metastatic lymph nodes, multiple neck lymph node metastases, and neck level IV and V lymph node involvement are associated with a higher risk of distant metastasis.[3,13] The most common sites of distant metastases are the lung, followed by the bone and the liver.[4,5] Patterns of distant metastasis of HPV-positive cancer may include heterogeneous and disseminated involvement of multiple organs and unusual sites.[3] Distant metastasis to the pericardium from head and neck squamous cell carcinomas is rare, especially in cases of HPV-positive primary cancer without local recurrence.

The clinical manifestations of pericardial metastasis range from no symptoms to sudden death. With regard to primary head and neck squamous cell carcinomas, several cases of pericardial metastasis due to tongue cancer have been reported.[14,15] There are two case reports pertaining to OPSCCs: Pericardial metastasis from locoregionally advanced p16-positive OPSCC (pT3N2M0, extranodal extension-positive)[4] and an unusual case of cardiac metastasis in locoregionally advanced p16-negative OPSCC detected via autopsy.[5] Although the present patient underwent appropriate treatment based on the pT2N0M0 (stage I) and was categorized as being at low risk of distant metastasis, multiple disseminated metastasis including the unusual site of the pericardium developed 5 years later. This is the first case of an early-stage p16-positive OPSCC with diffuse pericardial metastasis reported in the English literature and the first reported patient to be investigated via PET/CT and diagnosed

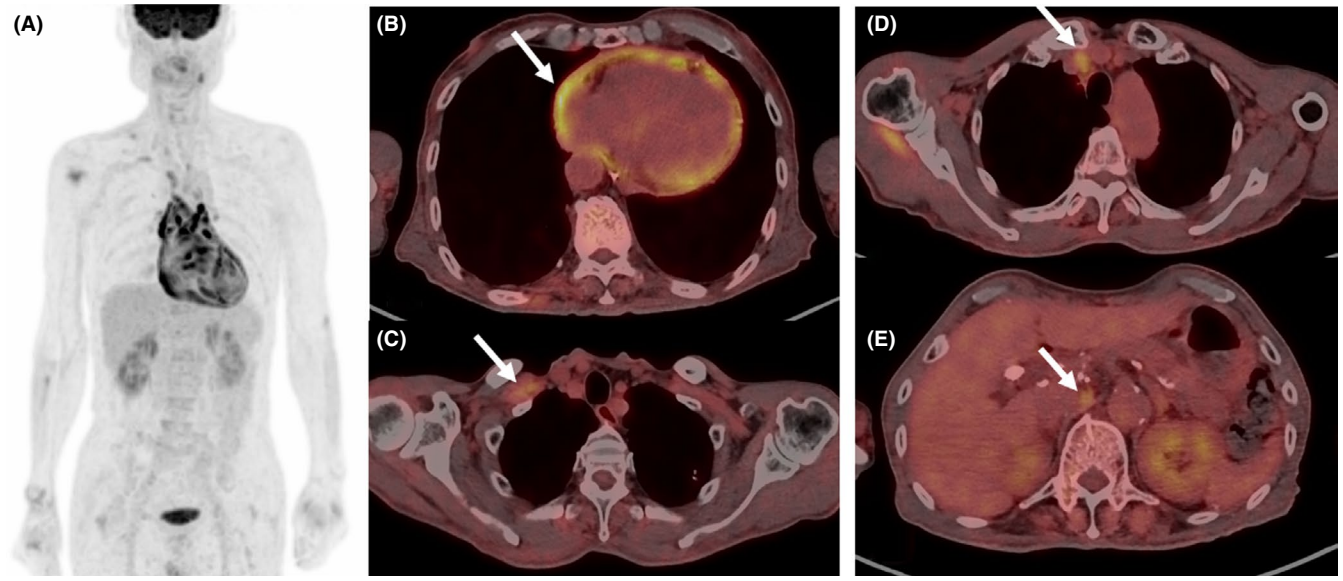
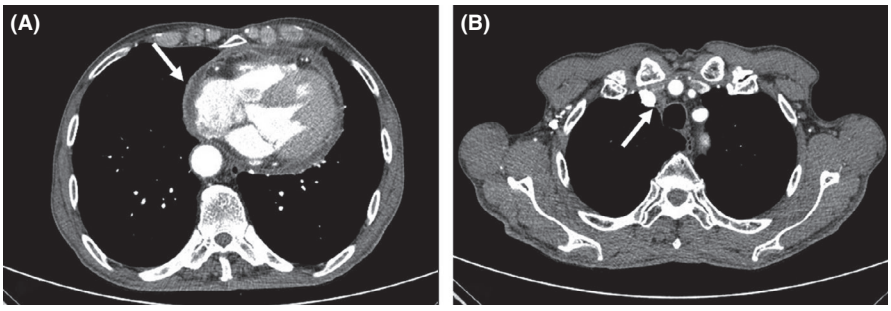


FIGURE 1 A, Positron emission tomography (PET)/computed tomography (CT) maximum intensive projection imaging revealed diffuse heterogeneous hypermetabolic thickening in the pericardium. B, Axial PET/CT imaging revealed diffuse hypermetabolic nodular thickening with a maximum standardized uptake value (SUV_{max}) of 14.2 in the pericardium (arrow). C-E, Axial PET/CT imaging depicted multiple hypermetabolic supraclavicular, mediastinal, and aortocaval lymphadenopathy with an SUV_{max} of 6.0 (arrow)

FIGURE 2 A and B, Axial enhanced chest computed tomography revealed irregular pericardial thickening and mediastinal lymphadenopathy (arrow)



with the primary tumor long before the appearance of pericardial metastasis with no definite local recurrence during the preceding interval.

Unfortunately, pathologic confirmation was not obtained in the current patient. Notably, however, PET/CT is well known to be helpful in the presumptive diagnosis of malignancy, considering the downfalls of repetitive nondiagnostic pericardial effusion or technically tricky pericardial biopsy.[7] In addition, irregular pericardial thickening and mediastinal lymphadenopathy are reliable CT indicators of pericardial metastasis.[16] Infectious or inflammatory pericardial disease could also be ruled out in the present patient because there were no related signs or symptoms such as fever or inflammatory markers.

4 | CONCLUSION

The current patient exhibited an unexpected clinical course despite early staging of HPV-positive OPSCC at initial diagnosis. The possibility of pericardial or cardiac metastasis should not be ruled out in patients with head and neck malignancy who have nonspecific or newly developed cardiac symptoms. Clinicians should be alert to this potential situation and perform appropriate management accordingly.

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CONFLICT OF INTEREST

The authors declare that there are no conflicts of interest with respect to the research, authorship, and/or publication of this article.

AUTHOR CONTRIBUTIONS

Hye-kyung Shim, Mi Ra Kim, and Hongje Lee: made major contributions to the writing of this manuscript. All authors: read and approved the final manuscript.

ETHICAL APPROVAL

The study was conducted in compliance with the Institutional Review Board (IRB) regulations (approval ID: IRB 2019-08-043-001) and the Declaration of Helsinki. The IRB approved a request to waive the documentation of informed consent.

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REFERENCES

1. Ang KK, Sturgis EM. Human papillomavirus as a marker of the natural history and response to therapy of head and neck squamous cell carcinoma. *Semin Radiat Oncol*. 2012;22(2):128-142.
2. Kobayashi K, Hisamatsu K, Suzui N, Hara A, Tomita H, Miyazaki T. A review of HPV-related head and neck cancer. *J Clin Med*. 2018;7(9):241.
3. Huang SH, Perez-Ordonez B, Weinreb I, et al. Natural course of distant metastases following radiotherapy or chemoradiotherapy in HPV-related oropharyngeal cancer. *Oral Oncol*. 2013;49(1):79-85.
4. Kuta V, Rigby M, Hart R, Trites J, Taylor SM. Pericardial metastasis from p16 positive oropharyngeal squamous cell carcinoma. *Otolaryngology Case Reports*. 2018;6:25-26.
5. Ferrari D, Codeca C, Viale G, et al. An unusual case of tracheo-pleural fistula and cardiac metastases in oropharyngeal carcinoma: a case report and review of the literature. *Cancers Head Neck*. 2016;1:16.
6. Amin MB, Edge SB, Edge SB, et al. *AJCC cancer staging manual* (8th ed.). New York, NY: Springer; 2017.
7. Kim MS, Kim EK, Choi JY, Oh JK, Chang SA. Clinical utility of [(18)F]FDG-PET /CT in pericardial disease. *Curr Cardiol Rep*. 2019;21(9):107.
8. Maisch B, Ristic A, Pankuweit S. Evaluation and management of pericardial effusion in patients with neoplastic disease. *Prog Cardiovasc Dis*. 2010;53(2):157-163.
9. Yi JE, Yoon HJ, O JH, Youn HJ. Cardiac and Pericardial (18)F-FDG Uptake on Oncologic PET/CT: Comparison with Echocardiographic Findings. *J Cardiovasc Imaging*. 2018;26(2):93-102.
10. Maleszewski JJ, Anavekar NS. Neoplastic pericardial disease. *Cardiol Clin*. 2017;35(4):589-600.
11. Burazor I, Imazio M, Markel G, Adler Y. Malignant pericardial effusion. *Cardiology*. 2013;124(4):224-232.
12. Guo T, Rettig E, Fakhry C. Understanding the impact of survival and human papillomavirus tumor status on timing of recurrence in oropharyngeal squamous cell carcinoma. *Oral Oncol*. 2016;52:97-103.
13. Nishijima W, Takooda S, Tokita N, Takayama S, Sakura M. Analyses of distant metastases in squamous cell carcinoma of the head and neck and lesions above the clavicle at autopsy. *Arch Otolaryngol Head Neck Surg*. 1993;119(1):65-68.
14. Ito T, Ishikawa N, Negishi T, Ohno K. Cardiac metastasis of tongue cancer may cause sudden death. *Auris Nasus Larynx*. 2008;35(3):423-425.
15. Browning CM, Craft JF, Renker M, Schoepf UJ, Baumann S. Squamous cell carcinoma of the tongue with metastasis to the right ventricle. *Am J Med Sci*. 2015;349(5):461-462.
16. Sun JS, Park KJ, Kang DK. CT findings in patients with pericardial effusion: differentiation of malignant and benign disease. *AJR Am J Roentgenol*. 2010;194(6):W489-W494.

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