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Case Report

An Advanced-stage Large-cell Neuroendocrine Lung Carcinoma with Intramedullary Spinal Metastases Detected by Positron Emission Tomography

Shao-Ming Yu[1]*, Yu-Chuan Chang[2,3], Wen-Chi Chou[1,4]

[1]Department of Hematology and Oncology, Chang Gung Memorial Hospital at Linkou, Taoyuan, Taiwan
[2]Department of Nuclear Medicine, Chang Gung Memorial Hospital at Linkou, Taoyuan, Taiwan
[3]Department of Medical Imaging and Radiological Sciences, College of Medicine, Chang Gung University, Taoyuan, Taiwan
[4]Department of Internal Medicine, College of Medicine, Chang Gung University, Taoyuan, Taiwan

Abstract

Large-cell neuroendocrine carcinoma (LCNEC) is a rare form of lung cancer with an aggressive behavior that frequently metastasizes to liver, brain, and bone. Intramedullary spinal cord metastasis (ISCM) is a rare clinical presentation of solid cancer and always indicates a dismal prognosis. This article presents a 72-year-old male patient diagnosed with an advanced-stage LCNEC who initially presented with ISCM that was diagnosed by positron emission tomography-computed tomography (PET-CT). This case demonstrates the diagnostic performance of PET-CT for ISCM. PET may be an alternative diagnostic modality for patients intolerant or unable to receive magnetic resonance imaging study to detect ISCM in those with LCNEC.

Keywords: Intramedullary spinal cord metastasis, large-cell neuroendocrine lung carcinoma, positron emission tomography

Introduction

Large-cell neuroendocrine carcinoma (LCNEC) of the lung is a rare form of lung cancer, with an aggressive disease behavior and extensive metastases to multiple organs.[1] For patients with spinal cord compression, the most common metastatic sites are the vertebral bone with cord compression, followed by epidural metastases, and most uncommonly by intramedullary spinal cord metastasis (ISCM).[2] The gold standard diagnostic modality for ISCM is magnetic resonance imaging (MRI). However, the use of MRI is limited by the time-consuming examination, need for patient cooperation in the examination room, and inability to perform whole-body examinations. A few cases of ISCMs have been detected by fluorine-18- fluorodeoxyglucose-positron emission tomography (FDG-PET). Herein, we present a case with

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Address for correspondence: Dr. Shao-Ming Yu, Department of Hematology and Oncology, Chang Gung Memorial Hospital at Linkou, No. 5 Fu-Hsing Street, Kwei-Shan Hsiang, Taoyuan 333, Taiwan.
E-mail: soundysm@gmail.com

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advanced-stage LCNEC of the lung with ISCMs, which was diagnosed by PET-computed tomography (PET-CT).

Case Report

A 72-year-old male smoker presented with a history of hypertension and type 2 diabetes mellitus. He had been diagnosed with unresectable locally advanced intrahepatic cholangiocarcinoma in the late 2019. Therefore, systemic chemotherapy with gemcitabine plus oxaliplatin was given every 2 weeks. He achieved a partial tumor response with chemotherapy until May 2020. He then started to experience mild left leg weakness, right chest pain, and dry cough. The chest pain intensity progressed gradually and extended to his upper back and sternal area in the following weeks. A CT scan in May 2020 showed that his intrahepatic cholangiocarcinoma was stable; however, one spiculated mass over the right upper lung field with hilum encasement and prominent mediastinal and left supraclavicular (supraclavicular nodal failure [SCF]) lymphadenopathies were found, which suggested second primary lung cancer. At the same time, his left lower limb weakness deteriorated rapidly, associated with limb numbness, pain sensation, and acute urine retention in May 2020. He was admitted as a medical emergency under the suspicion of cauda equina syndrome. Laboratory tests revealed neither leukoerythroblastic anemia nor disseminated intravascular coagulopathy [Table 1] at admission. Lumbar spine MRI was arranged first, which showed degenerative change with spurs over the lumbar vertebrae and sacrum with neural foramen encroachment but without definite evidence of spinal cord compression over the lumbar region or cauda equina syndrome. His neurologic signs then progressed again with weakness involving bilateral lower limbs and loss of sensation over his abdomen in a few days. After a review of the image by a radiologist and consultation with a neurologist, myelopathy above the T6 level over the thoracic spine was impressed. An excisional biopsy of left SCF lymphadenopathy showed metastatic LCNEC. PET-CT for tumor staging disclosed right lung cancer with multiple lymph nodes and spinal cord metastases at the T1–T3 level [Figure 1]. The maximum standardized uptake values (SUVs) of FDG–avidity lesions of the primary lung tumor, lymph node, and ISCM metastases were 12.4, 11.3, and 8.0, respectively. Intravenous corticosteroids with dexamethasone were prescribed from the day of admission to reduce cord edema. Palliative radiotherapy was delivered to the spinal metastases but with a poor clinical response. Due to rapidly worsening clinical condition and performance status, systemic palliative chemotherapy was not feasible, and best supportive care was provided. The patient died about 2 weeks after the diagnosis of lung cancer.

Table 1: Patient's hemogram and prothrombin time

WBC	10.3 (*1000/uL)	**Segment**	65.9 %
RBC	3.62 (*10^6/uL)	**Lymphocyte**	22.6 %
Hb	10.0 (g/dL)	**Monocyte**	8.5 %
Hematocrit	31.5 %	**Eosinophil**	2.2 %
MCV	89.2 (fl)	**Basophil**	0.8 %
RDW	17 %	**PT**	11.7 (seconds)
Platelet	217 (*1000/uL)	**PT (INR)**	1.1

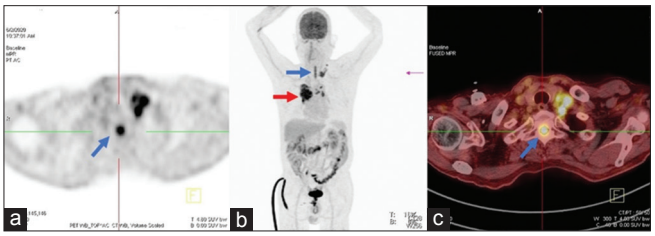

Figure 1: (a) Positron emission tomography axial view, (b) positron emission tomography coronal view, (c) positron emission tomography-computed tomography axial view. Positron emission tomography-computed tomography for evaluating tumor status showing fluorodeoxyglucose-uptake lesions over right hilar area (red arrow; main tumor of large-cell neuroendocrine carcinoma and hilar lymphadenopathy (LAPs)) and T1–T3 level (blue arrow; intramedullary spinal cord metastasis). The maximum standardized uptake values of main tumor, LAPs, and the spinal cord metastases was 12.4, 11.3, and 8.0, respectively

Discussion

LCNEC has a low incidence in primary lung cancer and mainly occurs in older males and heavy smokers.[3] With an aggressive clinical behavior, the 5-year overall survival rate of LCNEC ranges from 15% to 40%, with frequent metastases to the liver, brain, and bone.[1,3] ISCMs are an uncommon clinical presentation but are more frequently being diagnosed, due to therapeutic advances and improvements in cancer-specific survival.[2] Lung cancer is the most common primary site of ISCMs, accounting for nearly 50% of cases of ISCMs. The clinical presentations of ISCMs may manifest as back pain and hemicord syndrome with or without autonomic dysfunction.[4] ISCM has been reported to be the initial presentation at the diagnosis of cancer in 10% to around 20% of ISCM cases.[2,4] The reported median survival after a diagnosis of ISCMs is only 3.6 months.[2] MRI has been widely used to evaluate malignancy with central nervous systemic involvement. Contrast-enhanced MRI with gadolinium is sufficiently sensitive for intramedullary spinal lesions and can demonstrate ISCMs from surrounding cord edema.[4] A small proportion of patients are asymptomatic or have nonspecific back pain at the intramedullary lesion, which is incidentally disclosed on MRI examination.[2] Early diagnosis and treatment rather than a radiosensitive histology are paramount in determining the outcome.[4] In a retrospective review, surgical management may have contributed to improved survival and neurologic outcomes in selected patients with solitary lesions without brain metastasis.[2]

PET is commonly used in lung cancer staging and evaluation in the current clinical practice, especially in detecting distant metastases. In prior studies, differences in FDG–avidity have been reported in different types of lung cancer.[5,6] According to Aquino *et al*., the average SUVs of squamous

cell carcinoma (SUV: 9.2 ± 1) and large-cell carcinoma (SUV: 7.5 ± 1.5) were higher than that of adenocarcinoma (SUV: 4.6 ± 0.8 in the nonbronchioloalveolar [bronchioloalveolar carcinoma (BAC)] subtype and 1.6 ± 1.2 in the BAC subtype).[5] In another analysis, the maximum SUV value was significantly higher for squamous cell carcinoma than small-cell carcinoma and adenocarcinoma.[6] For pulmonary neuroendocrine tumors, the maximum SUV has been reported to be significantly different for carcinoids (mean, 4.0; median, 3.4), LCNECs (mean, 12.0; median, 10.7), and small-cell carcinomas (mean, 11.6; median, 11.7).[7] In another study, the mean SUV_{max} of LCNECs was around 9.0,[8] and a higher SUV_{max} has been shown to be a poor prognostic factor in patients with LCNECs.[7,8]

Nevertheless, only a few cases of lung cancer with ISCMs detected by PET have been reported. These cases reported different histological subtypes of lung cancer, including squamous cell carcinoma,[9] adenocarcinoma,[10] small-cell carcinoma,[11] and large-cell carcinoma[12] and one case only being described as nonsmall-cell lung cancer.[13] In the case of large-cell carcinoma, there was no further description about the subgroup histology.[12] ISCM was found in one case by PET at the same time as the primary cancer was diagnosed;[13] however, in other four cases, ISCMs were revealed on PET during the subsequent follow-up for re-evaluation of disease status. Two cases had multifocal FDG-uptake lesions along the spinal cord, suggesting diffuse ISCMs.[10,12] In other three cases, PET revealed focal FDG–avid lesions over upper cervical, lower cervical, and thoracic areas, respectively.[9,11,13] The SUVs of ISCMs in different types of lung cancer have not been clearly elucidated, probably due to the rarity of cases. In a small analysis of FDG-PET evaluation in patients with active myelopathy, the mean value of SUV_{max} detected in neoplastic lesions was significantly higher than in inflammatory lesions (3.3 vs. 1.9, $P < 0.001$), and half of the ISCMs in patients with solid tumors originated from lung cancer.[14] The SUV of ISCM in our case was 8.0. Compared with MRI, FDG-PET or PET-CT has relatively limited spatial resolution in detecting intramedullary lesions. One retrospective study tried to evaluate the visibility of ISCMs on PET compared with MRI. The results suggested that most ISCMs can be detected on PET when performed near the time of pretreatment MRI.[15] Several factors were reported to cause false-negative PET resulting in detecting ISCMs and should be kept in mind, including small lesion size, distracting uptake by adjacent bony vertebrae or disseminated systemic metastases, and lack of specific attention to the spinal cord. The authors concluded that PET can be considered as an option to evaluate ISCMs in some settings, such as for patients in whom MRI is contraindicated or PET has been done for tumor staging.[15] In conclusion, since the early management of ISCMs benefits survival and neurologic function, the use of PET as a widely used tool for tumor staging and re-evaluation might be helpful in the early detection of ISCMs.

Declaration of patient consent

The authors certify that they have obtained appropriate patient's family consent form. In the form, the patient's family has given the consent for the patient's images and other clinical information to be reported in the journal. The patient's family understands that the patient's name and initial will not be published and due efforts will be made to conceal the identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

References

1. Hung YP. Neuroendocrine tumors of the lung: Updates and diagnostic pitfalls. Surg Pathol Clin 2019;12:1055-71.
2. Goyal A, Yolcu Y, Kerezoudis P, Alvi MA, Krauss WE, Bydon M. Intramedullary spinal cord metastases: An institutional review of survival and outcomes. J Neurooncol 2019;142:347-54.
3. Hiroshima K, Mino-Kenudson M. Update on large cell neuroendocrine carcinoma. Transl Lung Cancer Res 2017;6:530-9.
4. Schiff D, O'Neill BP. Intramedullary spinal cord metastases: Clinical features and treatment outcome. Neurology, 1996;47:906-12.
5. Aquino SL, Halpern EF, Kuester LB, Fischman AJ. FDG-PET and CT features of non-small cell lung cancer based on tumor type. Int J Molecular Med 2007;19:495-9.
6. Sunnetcioglu A, Arısoy A, Demir Y, Ekin S, Dogan E. Associations between the standardized uptake value of 18F-FDG PETCT and demographic, clinical, pathological, radiological factors in lung cancer. Int J Clin Exp Med 2015;8:15794-800.
7. Chong S, Lee KS, Kim BT, Choi JY, Yi CA, Chung MJ, *et al*. Integrated PET/CT of pulmonary neuroendocrine tumors: Diagnostic and prognostic implications. AJR Am J Roentgenol 2007;188:1223-31.
8. Lee KW, Lee Y, Oh SW, Jin KN, Goo JM. Large cell neuroendocrine carcinoma of the lung: CT and FDG PET findings. Eur J Radiol 2015;84:2332-8.
9. Jayasundera MV, Thompson JF, Fulham MJ. Intramedullary spinal cord metastasis from carcinoma of the lung: Detection by positron emission tomography. Eur J Can 1997;33:508-9.
10. Nguyen NC, Sayed MM, Taalab K, Osman MM. Spinal cord metastases from lung cancer detection with F-18 FDG PET/CT. Clin Nucl Med 2008;33:356-8.
11. Bhatt G, Jain A, Bhatt A, Civelek AC. Intramedullary spinal cord metastases and whole body ^{18}F-FDG PET-CT-A case report. Quant Imaging Med Surg 2019;9:530-4.
12. Komori T, Delbeke D. Leptomeningeal carcinomatosis and intramedullary spinal cord metastases from lung cancer detection with FDG positron emission tomography. Clin Nucl Med 2001;26:905-7.
13. Sari O, Kaya B, Kara Gedik G, Ozcan Kara P, Varoglu E. Intramedullary metastasis detected with 18F FDG-PET/CT. Rev Esp Med Nucl Imagen Mol 2012;31:299-300.
14. Flanagan EP, Hunt CH, Lowe V, Mandrekar J, Pittock SJ, O'Neill BP, *et al*. [(18) F]-fluorodeoxyglucose-positron emission tomography in patients with active myelopathy. Mayo Clin Proc 2013;88:1204-12.
15. Mostardi PM, Diehn FE, Rykken JB, Eckel LJ, Schwartz KM, Kaufmann TJ, *et al*. Intramedullary spinal cord metastases: Visibility on PET and correlation with MRI features. AJNR Am J Neuroradiol 2014;35:196-201.