CASE REPORT
Yeungnam Univ J Med 2016;33(1):72-75

eISSN 2384-0293
http://dx.doi.org/10.12701/yujm.2016.33.1.72

Pulmonary epithelioid hemangioendothelioma misconceived as pulmonary metastasis of other malignancies

Gi Tark Noh[1], Kyoung Ju Lee[1], Hee Jung Sohn[1], Kyung Han Lee[1], Won Seok Heo[1], Byung Sung Koh[1], Un Mi Han[2], Young A Bae[3]

Departments of [1]Internal Medicine, [2]Pathology, and [3]Radiology, Bundang Jesaeng General Hospital, Seongnam, Korea

Pulmonary epithelioid hemangioendothelioma (PEH) is a rare, low-to-intermediate malignant tumor of endothelial origin. Computed tomography (CT) findings of PEH demonstrate multiple small bilateral nodules; however, to the best of our knowledge, there were no reports on PEH coexisting with other malignancies. Here, we reported on a case involving PEH in a patient with colon cancer and breast cancer which was misconceived as pulmonary meta- stasis. A 63-year-old woman who suffered from constipation for 2 weeks visited our hospital. Colonoscopy showed a large mass with obstruction on hepatic flexure. The histological diagnosis was adenocarcinoma of the ascending colon. Multiple nodules in both lungs and breast were observed on a chest CT scan. A core biopsy of a breast nodule was performed and a diagnosis of invasive ductal carcinoma of the left breast was made. Pulmonary nodules observed on the chest CT scan was considered as pulmonary metastasis from colon or breast cancer. Laparoscopic right hemicolectomy was performed. At the same time, wedge resection of the lung was performed and pathological diagnosis was PEH. Radiologic features of PEH were difficult to distinguish from lung metastasis. Therefore the author reported a rare case involving PEH in a patient with primary malignancy of colon and breast.

Keywords: Hemangioendothelioma; Epithelioid; Metastasis

INTRODUCTION

Pulmonary epithelioid hemangioendothelioma (PEH) is a rare, low-to-intermediate malignant tumor of endothelial origin [1]. The prevalence of epithelioid hemangioendothelioma is less than one in 1 million [2]. PEH was originally reported by Dail and Liebow in 1975 as an "intravascular bronchoalveolar tumor" [3]. The term "epithelioid hemangioendothelioma" was first described by Weiss and Enzingeras a soft tissue vascular tumor of borderline malignancy and features between those of hemangioma and angiosarcoma [4]. Epithelioid hemangioendothelioma can be primary in the lung, pleura, liver, soft tissue, or bone, although other presentations have been reported [1].

Computed tomography (CT) scans of PEH characteristically demonstrate multiple small bilateral nodules measuring 1-2 cm in size. The occurrence of a solitary lung mass is uncommon [1]. The radiographic pattern in PEH may mimic pulmonary metastasis. We report here on a case involving PEH in a patient with colon cancer and breast cancer, which was misidentified as pulmonary metastasis.

Received: June 30, 2015, Revised: August 18, 2015
Accepted: August 28, 2015

Corresponding Author: Kyoung Ju Lee, Department of Internal Medicine, BundangJesaeng General Hospital, 20 Seohyeon-ro 180 beon-gil, Bundang-gu, Seongnam 13590, Korea
Tel: +82-31-779-0200, Fax: +82-31-779-0727
E-mail: lkjmd78@dmc.or.kr

CASE

A 63-year-old woman, who had been suffering from constipation for 2 weeks, visited our hospital in 2013. She was a never-smoker and had no notable past history of disease. A colonoscopy showed a large mass with obstruction of the hepatic flexure. The histological diagnosis of the ascending colon mass was adenocarcinoma. Most of the laboratory data were normal. A chest radiograph showed multiple nodular opacities in both lungs (Fig. 1A). A chest CT scan showed

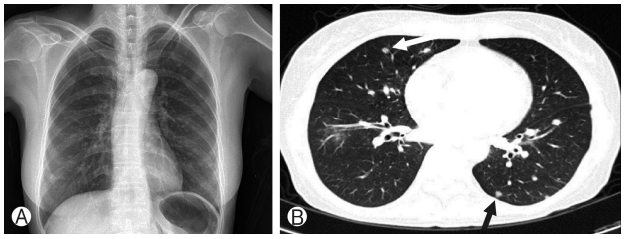

Fig. 1. The initial chest radiography (A) and a chest computed tomography scan (B) showing multiple small bilateral intrapulmonary nodules (arrow).

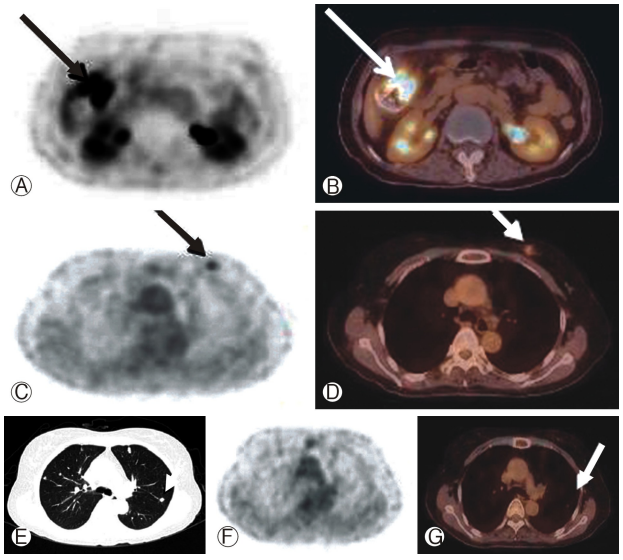

Fig. 2. The fluorodeoxyglucose positron emission tomography (FDG-PET) scan showed an hypermetabolic lesion in the right ascending colon (A, B) and a left breast nodule (C, D), but there was no abnormal FDG uptake in the small pulmonary nodules (E-G).

multiple pulmonary nodules, ranging from 1-8 mm in diameter, scattered throughout both lungs without hilar and mediastinal lymphadenopathy or pleural effusion (Fig. 1B). In addition, the CT scan showed small enhancing nodular lesions in both breasts and a 3-cm irregular mass in the right breast.

A fluorodeoxyglucose positron emission tomography (FDG-PET) scan was performed for evaluation of distant metastasis. The FDG-PET scan showed a hypermetabolic lesion in the right ascending colon mass (Fig. 2A, 2B) and a left breast nodule (Fig. 2C, 2D). There was no abnormal FDG uptake in the small pulmonary nodules (Fig. 2E-2G).

A core biopsy of the left breast nodule was performed, and a diagnosis of invasive ductal carcinoma was made. Therefore, the pulmonary nodules observed on the chest CT scan were considered to be pulmonary metastasis from the colon

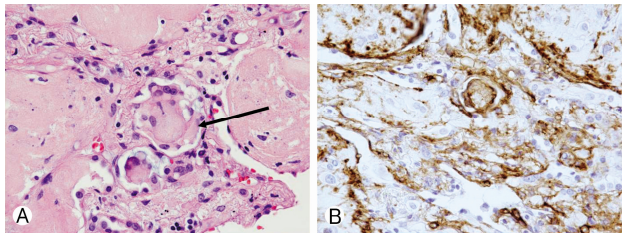

Fig. 3. Histologic findings of the pulmonary nodule. (A) The tumor cells have round to ovoid nuclei and abundant eosinophilic cytoplasm and intracytoplasmic vacuoles. The stroma is sclerotic (H&E stain, ×400). (B) The tumor cells are positive for CD34 (immunohistochemical stain, ×400).

or breast cancer. A laparoscopic right hemicolectomy was performed. At the same time, wedge resection of the lung was performed for diagnosis and staging workup for colon cancer and breast cancer.

Pathologic examination of the pulmonary nodule revealed sclerosis and hypocellularity. The tumor cells were round with abundant eosinophilic cytoplasm and intracytoplasmic vacuolization and mild nuclear atypia (Fig. 3A). In immunohistochemical analysis, the tumor cells were positive for endothelial markers (CD31, CD34) (Fig. 3B) and negative for cytokeratin, smooth muscle actin, and S-100 protein. Based on the examination, the patient was diagnosed with PEH.

Because the patient was diagnosed with stage IIIB colon cancer, she was referred to the oncologic department for adjuvant chemotherapy. A biopsy confirmed that surgery was indicated for the left breast cancer. However, the patient wanted to delay the operation.

We planned a medical follow-up on the PEH and postoperative adjuvant chemotherapy was scheduled for treatment of colon cancer.

Follow-up chest CT scan after chemotherapy showed no significant change in the tumor size and number, thus indicating that PEH was not aggressive. The patient refused further chemotherapy against colon cancer, and we continued medical follow-up for PEH without specific treatment. She still has no symptoms and has survived for 17 months following the initial diagnosis.

DISCUSSION

According to the literature, approximately 248 cases of PEH have been reported [5] and some cases have been diagnosed based on findings of a solitary lung mass or multiple

pulmonary nodules with no other primary malignancy [6,7]. This is the first report of multiple pulmonary nodules found in a patient diagnosed with both colon cancer and breast cancer, which were misidentified as metastasis. However, the final results of the histological analysis concluded that the lesions were PEH, which differed from the existing cases.

In general, chest CT scans of PEH show the presence of multiple small bilateral pulmonary nodules. These findings make PEH difficult to distinguish from metastatic cancer, old granulomatous disease, hemangioma, lymphangioma, sarcoidosis, vasculitis, or malignant conditions such as mesothelioma, primary adenocarcinoma, and angiosarcoma [1]. One study reported unusual radiologic findings of PEH. Ground-glass opacities and irregular interstitial thickening were the predominant findings, mimicking the appearance of diffuse interstitial lung disease [6]. In this case, the patient was diagnosed with PEH, colon cancer, and breast cancer at the same time, as it was not easy to distinguish the PEH from metastatic lesions.

The FDG-PET scan has become an important imaging tool for PEH diagnosis. One study showed that a FDG-PET scan sometimes fails to detect a malignant lesion of less than 6 mm in diameter. However, FDG uptake may reflect the activation of PEH tumor cells, which is a sign of a poorer prognosis [7]. A previous study reviewed FDG-PET scan findings of eight cases of PEH [8]. Among the eight cases, five cases showed increased FDG uptake, however, three cases were negative for FDG uptake, suggesting that a negative FDG-PET scan cannot completely exclude PEH. In our case, the FDG-PET scan did not show any pathological FDG uptake in the pulmonary nodules. This outcome is thought to be caused by small nodules, little FDG activity in the tumor, or low cellular density.

The histological characteristics of the previously mentioned case are common cytomorphologic features－abundant eosinophilic cytoplasm and intracytoplasmic vacuolization-also found in primary adenocarcinoma, mesothelioma, and large-cell lymphoma. Therefore, immunohistochemical studies such as those for the endothelial markers CD31, CD34, and factor VIII are necessary for final diagnosis.

Similar to most PEH cases, this case was histologically confirmed by surgical biopsy. To date, only a few reports on fine needle aspiration (FNA) findings of PEH have been published. Nevertheless, there has been some research reporting that when FNA is performed, a large rosettoid pattern with a central hyalinized core may be a key cytologic feature in PEH diagnosis, suggesting possible findings for PEH diagnosis in the future [9].

No standard therapy for PEH has been established. Surgery is the approach of choice, and is indicated by the presence of a single pulmonary nodule, or multiple unilateral nodules when the number of lesions is limited [10]. Various chemotherapies have been reported and certain patients with bilateral multiple nodules may benefit from chemotherapy and immunotherapy [5,8]. Because PEH is a vascular tumor, the use of antiangiogenic therapy may be suggested. Several studies have shown that a partial remission could be achieved with carboplatin, paclitaxel, and bevacizumab, a monoclonal antibody that blocks human vascular endothelial growth factor-A [11]. A partial response of the pulmonary lesions was obtained with interferon α-2a, probably due to its antiangiogenic activity [12].

Follow-up chest CT scan after chemotherapy showed no significant change in the tumor size and number. The reason may be that the disease entity was stable, not that chemotherapy had an effect.

The prognosis of PEH is uncertain. Some studies have reported a 5-year survival probability of 60% (range, 47-71%) [13] and median survival of asymptomatic PEH patients was 180 months [5]. The prognostic factors of PEH have not yet been established either. Several studies have reported various prognostic factors. Some prognostic factors of PEH such as hemorrhagic symptoms (pleural effusion, alveolar hemorrhage, anemia, and hemoptysis) can reveal markers of vascular aggressiveness [5,12].

In our case, the patient had no pleural effusion or chest symptoms. Several studies reported that lack of these symptoms was associated with a lower risk for cancer progression [5,12].

Diagnosis of PEH is difficult. Given that the radiological features of PEH are similar to those of pulmonary metastasis, diagnosis of cases involving coexistence of a solid tumor and pulmonary nodules can be difficult. In general, when the patient has a single malignant disease, physicians do not confirm the pathology of the multiple lung nodules coexisting with malignancy. Our patient was 63 years old, and she had double primary malignancies. Therefore we considered the possibility of metastasis of the multiple lung lesions from either colon or breast cancer.

To the best of our knowledge, the current case report is the first to describe PEH coexisting with other primary solid

tumors. We report our experience with a case involving a PEH misconceived for pulmonary metastasis in a 63-year-old female patient diagnosed with colon cancer and breast cancer concurrently, along with a review of the relevant literature.

REFERENCES

1. Travis WD, Tazelaar HD, Miettinen M. Epithelioid haemangioendothelioma/angiosarcoma. In: Travis WD, Brambilla E, Konrad Müller-Hermelink H, Harris CC, editors. World health organization classification of tumours: pathology and genetics of tumours of lung, pleura, thymus and heart. Lyon: IARC Press; 2004. p. 97-8.
2. Amin RM, Hiroshima K, Kokubo T, Nishikawa M, Narita M, Kuroki M, et al. Risk factors and independent predictors of survival in patients with pulmonary epithelioid haemangioendothelioma. Review of the literature and a case report. Respirology 2006;11:818-25.
3. Dail D, Liebow A. Intravascular bronchioloalveolar tumor. Am J Pathol 1975;78:6a-7a.
4. Weiss SW, Ishak KG, Dail DH, Sweet DE, Enzinger FM. Epithelioid hemangioendothelioma and related lesions. Semin Diagn Pathol 1986;3:259-87.
5. Sardaro A, Bardoscia L, Petruzzelli MF, Portaluri M. Epithelioid hemangioendothelioma: an overview and update on a rare vascular tumor. Oncol Rev 2014;8:259.
6. Mukundan G, Urban BA, Askin FB, Fishman EK. Pulmonary epithelioid hemangioendothelioma: atypical radiologic findings of a rare tumor with pathologic correlation. J Comput Assist Tomogr 2000;24:719-20.
7. Okamura K, Ohshima T, Nakano R, Ouchi H, Takayama K, Nakanishi Y. A case of pulmonary epithelioid hemangioendothelioma surviving 10 years without treatment. Ann Thorac Cardiovasc Surg 2010;16:432-5.
8. Yi L, Cheng D, Shi H, Zhang K, Liao Y, Ao Q, et al. Pulmonary epithelioid hemangioendothelioma coexisting with pulmonary nodular amyloidosis: case discussion and review of the literature. Int J Clin Exp Med 2014;7:1891-7.
9. QHan KM, Kim DH, Myong NH. Fine needle aspiration cytology of pulmonary epithelioid hemangioendothelioma with prominent hyaline degeneration: a case report. Korean J Pathol 2010;44:554-7.
10. Ye B, Li W, Feng J, Shi JX, Chen Y, Han BH. Treatment of pulmonary epithelioid hemangioendothelioma with combination chemotherapy: report of three cases and review of the literature. Oncol Lett 2013;5:1491-6.
11. Radzikowska E, Szczepulska-Wójcik E, Chabowski M, Oniszh K, Langfort R, Roszkowski K. Pulmonary epithelioid haemangioendothelioma--interferon 2-alpha treatment--case report. Pneumonol Alergol Pol 2008;76:281-5.
12. Bagan P, Hassan M, Le Pimpec Barthes F, Peyrard S, Souilamas R, Danel C, et al. Prognostic factors and surgical indications of pulmonary epithelioid hemangioendothelioma: a review of the literature. Ann Thorac Surg 2006;82:2010-3.
13. Ye B, Li W, Liu XY, Sun KL, Yang LH, Ma K, et al. Multiple organ metastases of pulmonary epithelioid haemangioendothelioma and a review of the literature. Med Oncol 2010;27:49-54.