Pulmonary epithelioid hemangioendothelioma misconceived as pulmonary metastasis of other malignancies

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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 metastasis. 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 Enzinger as 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.

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...
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 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 vacuoles 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 IIIIB 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 rosetted 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