

A Case of Pulmonary Epithelioid Hemangioendothelioma with Surgical Resection

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Abstract

A 65-year-old female patient was found to have a nodular shadow on a chest X-ray. Computed tomography showed a well-defined tumor measuring 1.8 cm in diameter in the right middle lobe that was diagnosed to be adenocarcinoma by a transbronchial lung biopsy. The patient underwent right middle lobectomy and hilar and mediastinal lymph node dissection for stage IA primary lung cancer. The pathological diagnosis was pulmonary epithelioid hemangioendothelioma (PEH), which is a rare tumor of the lung. The postoperative course was uneventful, and she remains free of PEH recurrence at 26 months after the surgery. PEH is the currently preferred term for the neoplastic process originally described as intravascular bronchioloalveolar tumor in the lung. The estimated prevalence of epithelioid hemangioendothelioma is less than 1 in 1 million, PEH is a rare tumor derived from vascular endothelial cells, and it is difficult to diagnose it preoperatively. PEH is considered to have low-to-intermediate grade malignancy, but the tumor predominantly involves the liver, lungs, soft tissues, and can be multicentric, even resulting in systemic metastasis. We described a case of a single PEH found at a medical checkup that was treated with complete resection. Active surgical treatment is considered desirable for single cases.

Keywords: Pulmonary epithelioid hemangioendothelioma (PEH); Intravascular bronchioloalveolar tumor (IVBAT); Factor VIII-related antigen

Introduction

Pulmonary epithelioid hemangioendothelioma (PEH) is a rare tumor of vascular endothelial origin with an epithelioid appearance that was initially referred to as an intravascular bronchioloalveolar tumor (IVBAT) [1]. Despite having low-to-intermediate malignant potential, bilateral and/or multiple pulmonary nodules and systemic metastases have been reported, but there is no standard treatment. Depending on intrathoracic tumor spread and systemic metastases, surgical resection and chemotherapy should be considered [2].

We herein report a surgically resected case of PEH that was diagnosed to be primary lung cancer before surgery.

Case Presentation

A 65-year-old female with a history of papillary thyroid cancer and uterine fibroid treatment was found to have a nodular shadow on a chest X-ray. She was a never-smoker and had no significant abnormalities on a physical examination except for an abdominal scar related to the treatment of her uterine fibroid. Chest computed tomography (CT) showed a well-defined nodule, 1.8 cm in diameter, in the right middle lobe (Figure 1), and adenocarcinoma, which was different from papillary thyroid cancer, was observed in the transbronchial lung biopsy (TBLB) performed by the referral hospital. No significant hilar or mediastinal lymph node swelling was observed. 18-fluorodeoxyglucose positron emission tomography (FDG-PET) showed no abnormal accumulation except in the nodule in the right middle lobe (SUV max: 6.09). The levels of tumor markers, such as CEA and SCC, were within the normal range. Since the preoperative diagnosis was stage IA primary lung cancer, the patient underwent right middle lobectomy with hilar and mediastinal lymph node dissection. A histopathological examination revealed that the tumor cells had intracytoplasmic vacuoles, and the centers of the tumor were hyaline hypocellular while the peripheral areas consisted of epithelioid-like cells. Immunohistochemistry

showed positive staining for CD31 and CD34, but negative staining for AE1/AE3, CAM5.2 and TTF-1 (Figure 2). The pathological diagnosis was PEH. The postoperative course was uneventful, and the patient was followed up without recurrence at 26 months post operation.

Discussion

PEH is the currently preferred term for the neoplastic process originally described as intravascular bronchioloalveolar tumor in the lung. PEH is considered to have low-to-intermediate grade malignancy, but the tumor predominantly involves the liver, lungs, soft tissues, and can be multicentric, even resulting in systemic metastasis [1-4]. The estimated prevalence of epithelioid hemangioendothelioma is less than 1 in 1 million [5], and only such 95 cases have been reported in the literature [6].

PEH typically occurs in young females as bilateral multiple nodules and has a variable clinical course [7]. PEH likely develops at a median onset of 36 years of age [8]. The incidence of PEH is four times higher in women than in men. Approximately 50% of patients are asymptomatic. Some patients have chest pain, pleuritic pain, cough, dyspnea, or rarely. Although the typical CT findings are multiple small unilateral (23.7%) or bilateral (76.2%) pulmonary nodules, PEH can also present as diffuse infiltrative pleural thickening [6].

The differential diagnosis of PEH includes metastatic lung tumor,

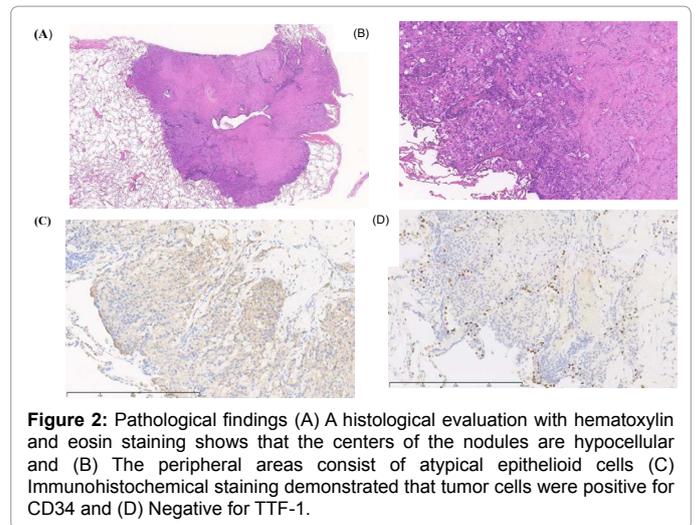
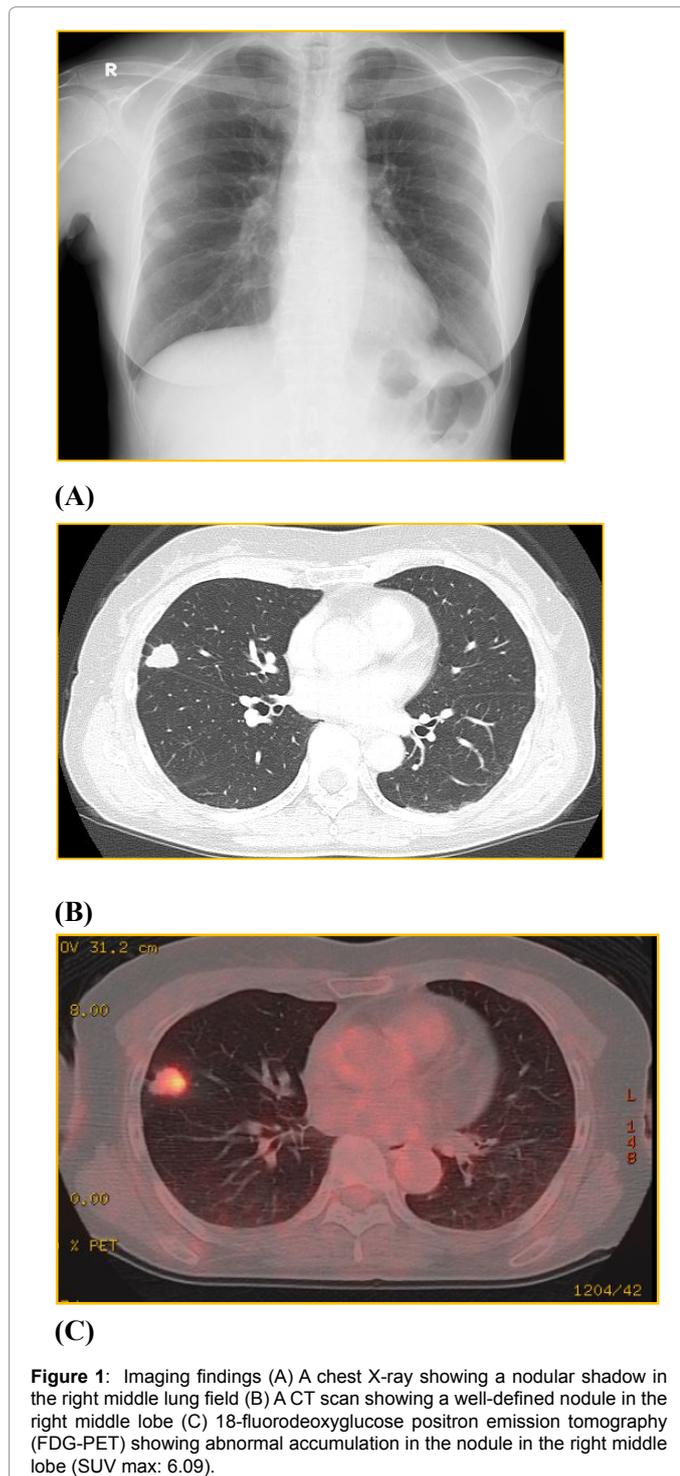
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granulomatous disease, silicosis, multiple hamartoma, sarcoidosis, nodular amyloidosis, and lung cancer, but it is difficult to make a precise diagnosis based only on imaging findings. Since PEH is rarely diagnosed by bronchoscopy, a surgical lung biopsy often obtains a definite diagnosis [9]. For this reason, a surgical lung biopsy by video-assisted thoracoscopic surgery (VATS), which is capable of reducing the surgical invasion in a patient and obtaining a reliable diagnosis, is an important diagnostic tool. In this case, the patient was diagnosed



with lung adenocarcinoma by a bronchoscopic lung biopsy; however, the final pathological diagnosis was PEH after surgical resection. The reason for the diagnosis of adenocarcinoma before surgery was likely because the marginal epithelial-like cells of PEH were biopsied and diagnosed as adenocarcinoma or the specimens biopsied by TBLB were very small and could not be tested adequately.

A diagnosis is mainly achieved by a pathological examination of the surgical biopsy specimen and is based on immunohistochemistry showing diffuse factor VIII-related antigen, CD31, and CD34 cytoplasmic staining in the malignant cells, confirming an endothelial lineage for the tumor cells [10-12].

Despite the fact that PEH has intermediate malignant potential, therapeutic methods have not been established. Cases with single nodules undergo surgical resection, while asymptomatic multiple nodular cases are followed up, and symptomatic multiple nodular cases are treated. Although steroid administration, anti-tuberculosis drug administration, radiation therapy, and anticancer drug therapy have been performed, none were effective treatments [1,13,14]. Disease progression can reportedly be suppressed by interferon α -2A administration or bevacizumab administration [15,16], but there have been reports of cases of spontaneous remission [14]. Thus, the biological behavior of PEH is still unknown and further clinical studies are needed.

The progression of PEH is usually considered to be slow, but it varies from rapid growth resulting in death in weeks after a diagnosis to the long-term survival of more than 10 years, with life expectancy ranging from 1 to 15 years [3,14] Dail et al. reported such poor prognostic factors for PEH as the presence of respiratory symptoms, extensive lymphangitic spread, pleural effusion on chest radiography, extensive intravascular, endobronchial, interstitial tumor spread, hepatic metastases, and peripheral lymphadenopathy [1]. Due to the unpredictable prognosis, if possible, curative resection should be considered to maximize the possibility of a good outcome [11].

Conclusion

We herein described a case of a single PEH found at a medical check-up that was treated with complete resection. PEH is a rare tumor derived from vascular endothelial cells, and it is difficult to diagnose it preoperatively. Active surgical treatment is considered desirable for single cases.

Declarations

Dr. Shimamatsu and Dr. Edagawa were received personal fees from Ono Pharmaceutical, outside the submitted work; Dr. Takenoyama was received personal fees from Takeda Pharmaceutical, Pfizer Japan, Kyowa Hakko Kirin, AstraZeneca and Taiho Pharmaceutical, grants from Nippon Boehringer Ingelheim, Daiichi Sankyo, Novartis Pharma and Bristol-Myers, grants and personal fees from Eli Lilly Japan, Ono Pharmaceutical, and Chugai Pharmaceutical, outside the submitted work; Dr. Toyozawa was received personal fees from Ono Pharmaceutical and Kyowa Hakko Kirin, outside the submitted work; Dr. Nosaki was received personal fees from Ono Pharmaceutical, Kyowa Hakko Kirin, AstraZeneca, Chugai Pharmaceutical, Eli Lilly Japan and Nippon Boehringer Ingelheim, grants from MSD, outside the submitted work; Dr. Hirai was received personal fees from Ono Pharmaceutical, Kyowa Hakko Kirin, AstraZeneca, Chugai Pharmaceutical and Eli Lilly Japan, grants and personal fees from Novartis Pharma, outside the submitted work; Dr. Yamaguchi was received personal fees from Ono Pharmaceutical, Kyowa Hakko Kirin, Chugai Pharmaceutical, and Eli Lilly Japan, grants from AstraZeneca, outside the submitted work; Dr. Taguchi was received personal fees from Taiho Pharmaceutical, Ono Pharmaceutical, MSD, Pfizer Japan and Chugai Pharmaceutical, outside the submitted work; Dr. Seto was received personal fees from Daiichi Sankyo, Fuji Pharma, Hisamitsu Pharmaceutical, Kyowa Hakko Kirin, Mochida Pharmaceutical, Nippon Kayaku, Ono Pharmaceutical, Roche Diagnostics, Showa Yakuhin Kako, Sumitomo Dainippon Pharma and Takeda Pharmaceutical, grants from Astellas Pharma, Bayer Yakuhin, Merck Serono, MSD, Verastem and Yakult, grants and personal fees from AstraZeneca, Chugai Pharmaceutical, Eisai, Eli Lilly Japan, Nippon Boehringer Ingelheim, Novartis Pharma, Pfizer Japan, Sanofi and Taiho Pharmaceutical, outside the submitted work; Dr. Ichinose was received personal fees from Pfizer Japan, Ono Pharmaceutical, Eli Lilly Japan, Kaketsuken, Chugai Pharmaceutical, Kyowa Hakko Kirin and Taisho Toyama Pharmaceutical, grants from Takeda Bio Development Center, grants and personal fees from Taiho Pharmaceutical, outside the submitted work. Dr. Fushimi has nothing to disclose.

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