Primary pleural epithelioid hemangioendothelioma

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Abstract

Epithelioid hemangioendothelioma (EHE) is a rare vascular tumor exceptionally involving the pleura with less than 30 cases reported in literature. We herein describe another case of pleural EHE in a 79-year-old man with medical history of chronic obstructive pulmonary disease and high blood pressure. He presented right-sided pleural effusion. Computerized tomography revealed multifocal pleural thickening and effusion. Pleural biopsy was performed. Microscopically, the tumor showed a biphasic pattern with cords and nests of epithelioid cells showing mild atypia and rare mitosis with intracytoplasmic lumina containing red blood cells. The second pattern is composed of spindle-shaped cells with occasional necrosis. The tumor cells were positive for CD34 and focally with CK7. The diagnosis of EHE was made.

Introduction

Epithelioid hemangioendothelioma (EHE) is a rare vascular tumor that might develop in any tissue but which has predilection for the liver, heart, lung and bone. Pulmonary epithelioid hemangioendothelioma (PEH) was first described in 1975 by Dail and Leibow, it was considered as an aggressive bronchoalveolar cell carcinoma.¹ Primary pleural location is extremely rare with less than 30 cases reported in the literature as analyzed in Table 1.²⁻¹⁹ The aim of this report is to present the case of a 79-year-old man who was diagnosed with pleural EHE and summarize the limited published data concerning this rare neoplasm in order to improve the diagnosis and its management.

Case Report

A 79-year-old man with a family history of colorectal cancer and past medical history of chronic obstructive pulmonary disease (COPD) and high blood pressure presented with right-sided chest pain and breathlessness associated to a recent weight loss. On physical examination there was dullness to percussion and decreased breath sounds over the right hemithorax with signs of right heart failure. Chest radiography confirmed the presence of a moderate right pleural effusion. A Computerized tomography (CT) of the thorax, abdomen and pelvis was performed and revealed a mild right pleural effusion with multifocal pleural thickening. No pulmonary nodules were seen. Three enlarged iliac lymph node were observed. Based on the family history of colorectal cancer, pleural and lymph node metastasis from a primary gastrointestinal cancer were highly suspected. However, no abnormalities were noted on fibro-colonoscopy. Image-guided pleural biopsy was performed. Microscopically, the tumor showed a biphasic pattern with cords and nests of epithelioid cells set in a myxoid stroma. Some cells show mild atypia and rare mitosis with intracytoplasmic lumina containing red blood cells. The diagnosis of EHE with high-grade pattern was made. Although, no codified therapies for this cancer have been established yet, the patient was not candidate for surgery considering the extent and bilaterality of the nodules and his hard medical history. Several cycles of chemotherapy with Etoposide and Cisplatin were decided as the lesions were diffuse and bilateral with suspicion of lymph node involvement.

Unfortunately, during his stay in the hospital, the patient developed acute decompensation of his COPD which required mechanical ventilation and intensive care. He sadly died one month later because of cardiac and respiratory failure.

Discussion

The accumulation of fluid in the pleural space is a common and non-specific manifestation of a wide range of diseases which could be pulmonary, pleural or extrapulmonary. Lung cancer (40%) and breast cancer (25%) are the most common metastatic tumors to the pleura. About 10% of all malignant pleural effusions are due to primary cancers arising from the pleura mainly represented by malignant mesothelioma (>90%) followed by other rare neoplasms.²

EHE is an extremely rare tumor affecting the pleura with less than thirty cases described in literature.² Analysis of these cases revealed a variable epidemiologic profile. Patients diagnosed with EHE of the pleura are mostly men with a gender ratio of 2, 75. The mean age at onset of symptoms is 46, 84. No particular family or past medical history is associated to EHE, one case have been reported in a patient with a history of exposure to asbestos.³ The main complaints of patients in this analysis are non-specific symptoms such as dyspnea, cough, chest pain and weight loss.³⁻¹⁰ Only two cases have been discovered incidentally on routine chest radiography.⁵⁻⁹ Imaging shows in all cases either effusion or thickening of the pleura associated in some cases to lung nodules.²⁻⁸ As EHE is a very rare cause of pleural disease, more common etiology need to be ruled out firstly. In our case, the pleural effusion was thought to be resulting from metastasis of digestive cancer and so the patient underwent useless investigations leading to a delay in the proper diagnosis. Thus, considering the aggressive nature of this tumor, a quick and collaborative move of the medical team should be made in order to establish an early diagnosis. Pleural biops with pathological examination is the key for diagnosis. Microscopically, the tumor is intermediate between angiosarcoma and hemangioma.¹ It is characterized by nests and cords of spindle to epithelioid cells

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embedded in a hyaline, myxoid, chondroid or collagenous stroma. The cells show prominent cytoplasmatic vacuoles containing red blood cells (reminiscent of primitive vascular channels). In some cases there are solid nests of tumor cells displaying cytological atypia together with increased mitotic activity (more than 1 per 10 HPF) and areas of necrosis. On immunohistochemical analysis, the tumor cells express endothelial markers: CD31, CD34 and factor VIII. In some cases, they are positive for smooth muscle actin and cytokeratin. Epithelial membrane antigen (EMA) is negative unlike other epithelial tumours. EHE of the pleura may be confused with mesothelioma, however positive staining for vascular markers on immunohistochemistry is helpful to distinguish EHE from mesothelioma. Depending on the degree of atypia and the presence of necrosis, EHE can mimic angiosarcoma especially when the tumor is highly aggressive. Immunohistochemistry do not contribute much to distinguish between EHE and epithelioid angiosarcoma. However, it is not well defined whether EHE is a distinctive entity or an intermedi-

Table 1. Primary pleural location: 30 cases reported in the literature. Modified from tables in previous reports by Lee et al., Marquez-Medina et al., and Salijevska et al.

| Authors                      | Age/Gender | Clinical presentation | Radiological findings | Treatment                                      | Survival (months) |
|------------------------------|------------|-----------------------|-----------------------|------------------------------------------------|-------------------|
| Pinet, 1999                  | 50/F       | Incidentally on chest Radiography | Pleural effusion     | Carboplatin, etoposide                         | >18               |
| Crotty et al., 2000          | 51-71/M (n=4) | Chest pain, dyspnea, cough, fever, weight loss | Pleural effusion     | Carboplatin, etoposide                         |                   |
| Lee et al., 2008             | 31/F       | Chest pain            | Pleural thickening    | Adriamycin, MAID                              | 10                |
| Lazarus, 2011               | 42/M (n=2) | Cough, dyspnea, chest pain, fever | Pleural effusion     | *Taxol, bevacizumab                           | *8                |
| Yousem and Hochholzer, 1987 | 4/M        | Dyspnea               | Pleural effusion      | None                                           | 3                 |
| Lin, 1996                    | 36-58/M (n=6) | Incidentally          | Pleural effusion      | INF-alpha                                      | >24               |
| Al Sharim et al., 2005       | 51/M       | Cough, dyspnea        | Pleural effusion      | INF-alpha                                      |                   |
| Vittorio, 2004              | 61/M       | Chest pain            | Pleural effusion      | Cisplatin, etoposide                          | 3                 |
| Saqi, 2007                   | 37/M       | Dyspnea, chest pain   | Pleural effusion      | Not specified                                  | Not specified     |
| Liu et al., 2010             | 50/M       | Dyspnea               | Pleural effusion      | Surgery + chemotherapy (not specified)        | 6                 |
| Bocchino, 2010              | 58/F       | Cough, dyspnea, chest pain | Pleural nodule       | None                                           | 3                 |
| Andre, 2010                 | 65/F       | Chest pain            | Pleural effusion      | Carboplatin, etoposide                        | 6                 |
| Kim et al., 2011            | 46/F       | Chest, discomfort     | Pleural effusion      | Surgery, Carboplatin, Etoposide               | >22               |
| Marquez-Medina, 2011        | 85/M       | Chest, fatigue, weight loss | Pleural effusion      | None                                           | 7                 |
| Bansal, 2012                | 51/F       | Chest pain, weight loss | Pleural effusion      | Doxorubicin                                    | 4                 |
| Yu, 2013                    | 39/F       | Dyspnea               | Pleural mass          | Surgery, Carboplatin, etoposide               | >14               |
| Ha, 2014                    | 71/M       | Cough, dyspnea, fatigue | Pleural effusion      | Not specified                                  | Not specified     |
| Salijevska 2015             | 36/F       | Chest pain            | Whiteout              | Paclitaxel                                      | 6                 |
| This case                   | 79/M       | Chest pain, dyspnea   | Pleural effusion      | None                                           | 1                 |

M, male; F, female; LN+: Lymph node metastasis.
Conclusions

It is worth bearing in mind that pleural EHE may reveal itself as pleural effusion. Considering the rarity and the aggressive behavior of this neoplasm, it is important we continue to collect data through case reporting in order to establish clinical and prognostic profile of this tumor and standardize its management.

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