Extraskelatal Myxoid Chondrosarcoma-like Features in Metastasizing Lung Adenocarcinoma: Unique Morphological Changes after Chemo-radiotherapy

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Abstract

Lung cancer closely resembling Extraskelatal Myxoid Chondrosarcoma (EMC), called “primary pulmonary myxoid sarcoma (PPMS),” is an extremely rare tumor. This report is presented here of a unique case showing EMC-like changes only in metastases from conventional lung adenocarcinoma in an 81-year-old man. After lung tumor resection and chemo-radiotherapy, he underwent the resection of right adrenal metastasis composed of carcinomatous and EMC-like components. There were multifocal transitions between these components. He was treated with additional chemo-radiotherapy for newly developed liver and brain metastases, but he died 3.3 years after the initial surgery. Autopsy revealed EMC-like tumors, with or without minute adenocarcinomatous components, extensively involving widespread organs. Reverse transcription-polymerase chain reaction did not detect EWSR1-CREB1 fusion in the primary tumor or metastases. These features indicated that the current tumor was different from PPMS characterized by EWSR1-CREB1 fusion. We concluded that such EMC-like features represent morphological changes of metastatic lung adenocarcinoma. We believe that this possible occurrence should be recognized for accurate diagnosis of metastatic lung carcinoma.

Keywords: Chemo-radiotherapy; Extraskelatal Myxoid Chondrosarcoma; EWSR1-CREB1; Lung; Adenocarcinoma

Introduction

Extraskelatal Myxoid Chondrosarcoma (EMC) is an uncommon soft-tissue tumor usually originating in the deep tissues [1]. Primary lung cancers resembling EMC have been rarely reported as "primary pulmonary myxoid sarcoma (PPMS)" [2,3]. Recently, we encountered a unique autopsy case of lung carcinoma showing EMC-like features only in metastases after chemo-radiotherapy. To our knowledge, such EMC-like changes have not been mentioned previously in metastases of lung carcinoma, although therapy-induced myxomatous or colloid-like changes have been reported in some other site cancers [4,5]. We herein described this case to expand our knowledge of morphological changes in metastasizing lung carcinoma.

Case Report

An 81-year-old man underwent the left upper lobectomy for a 2 cm-sized lung tumor. Before the lobectomy, the whole-body examination using X-ray computed tomography (CT) scan and bone scintiscan could not reveal any metastases, and the removed tumor was classified as Stage IA (pT1N0cM0). The patient did not receive additional chemo-radiotherapy, and was followed up with laboratory examination of serum tumor markers and chest radiologic examination. About 1.5 years later, abdominal X-ray CT scan was performed for his progressive weight loss in a year, and revealed a right adrenal metastasis. He was treated with local radiotherapy and chemotherapy using gemcitabine, vinorelbine, and tegafur. Because of its progressive increase 1.2 years after the beginning of chemo-radiotherapy, the right adrenal metastasis was performed. Thereafter, for newly developed liver and brain metastases, he received additional chemotherapy using gemcitabine, vinorelbine, and paclitaxel, and radiotherapy for brain metastasis. However, he died 3.3 years after the initial surgery.

The well-demarcated primary lung tumor showed features of poorly differentiated adenocarcinoma (histological grade 3) composed of nested polygonal cells occasionally showing papillary or mucin-positive glandular features (Figure 1). Sarcomatous features were not identified. The surgically removed right adrenal metastasis included adenocarcinomatous components and myxoid areas (Figure 2a).

Figure 1: Primary lung adenocarcinoma (a) showing a well demarcated nodule. Low-power view (b) showing nested and vague papillary cancerous growth and high-power view (c) demonstrating polygonal cancer cells (c) with alcin blue+ lumina (c, inset). Primary carcinoma cells expressing strong positivity for cytokeratin 7 (d).

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response in prostatic and rectal adenocarcinomas [4,5], clear cell carcinoma-like features in ovarian carcinoma [8], and granulosa cell tumor-like pattern in ovarian sex cord tumor with annular tubules [9]. However, therapy-induced EMC-like changes have not been previously mentioned in lung or other site carcinoma. Moreover, in the current case, the histology of metastatic sites before chemoradiotherapy was unknown. Widespread metastatic lesions without radiotherapy also showed EMC-like changes. Hence, the current study could not determine whether EMC-like changes in this case were a chemo-radiotherapy-induced condition or a simply manifestation of metastases themselves.

Primary lung tumors resembling EMC include PPMS [2,3], pulmonary angiomatoid fibrous histiocytoma (AFH) [10], and pulmonary microcystic fibromyxoma [11]. PPMS is a rare tumor of uncertain differentiation, characterized by EMC-like histology and EWSR1-CREB1 fusion [2,3], and this entity would encompass "low-grade pulmonary myxoid sarcoma" [12] and "primary pulmonary EMC" [13]. The currently presented primary and secondary tumors showed pan-CX7+ and no EWSR1-CREB1 fusion, which could rule out a diagnosis of PPMS. Similarly, CX7+ in the current case is distinctly different from no CX expression in pulmonary AFH and microcystic fibromyxoma [10,11]. No EWSR1-ATF1 fusion in the present case can rule out a diagnosis of AFH [10]. Lung myoepithelioma with extensive myxoid changes may be another differential diagnosis of this case. However, most cases of myoepithelioma were S-100 protein+ and/or SMA+ [3,14], whereas such expressions were not observed in the current case. Hence, the present case would represent no myoepithelial differentiation in primary or secondary lesions.

Thus, EMC-like changes can occur in metastasizing lung adenocarcinoma. Consideration of this possible occurrence would be useful for accurate diagnosis and therapeutic management of patients with lung carcinoma, although it may be a rare phenomenon.

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**References**


