

CASE REPORT

Epithelial-to-mesenchymal transition (EMT) to sarcoma in recurrent lung adenosquamous carcinoma following adjuvant chemotherapy

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Keywords

Adenosquamous lung carcinoma; adjuvant chemotherapy; epithelial-to-mesenchymal transition; lung cancer; sarcoma.

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Abstract

Adjuvant chemotherapy has long been indicated to extend survival in completely resected stage IB to IIIA non-small cell lung cancer (NSCLC). However, there is accumulating evidence that chemotherapy or chemoradiotherapy can induce epithelial-to-mesenchymal transition (EMT) in disseminated or circulating NSCLC cells. Here, we describe the first case of EMT as the cause of recurrence and metastasis in a patient with resected stage IIB lung adenosquamous carcinoma after adjuvant chemotherapy. We review the literature and explore the possible mechanisms by which EMT occurs in disseminated tumor cells (DTC) or circulating tumor cells (CTC) in response to adjuvant chemotherapy (cisplatin) as a stressor. We also explore the possible therapeutic strategies to reverse EMT in patients with recurrence. In summary, although adjuvant cisplatin-based chemotherapy in resected NSCLC does extend survival, it may lead to the adverse phenomenon of EMT in disseminated tumor cells (DTC) or circulating tumor cells (CTC) causing recurrence and metastasis.

Introduction

There is accumulating evidence that chemotherapy or chemoradiotherapy can induce epithelial-to-mesenchymal transition (EMT) in non-small cell lung cancer cells. Here, we describe the first case of EMT as the cause of recurrence and metastasis in a patient with resected stage IIB lung adenosquamous carcinoma after adjuvant chemotherapy.

Case report

A 72-year-old man who had never smoked underwent a right upper lobectomy for adenosquamous carcinoma. A preoperative fluorine-18 fluorodeoxyglucose positron emission tomography-CT scan did not show any metastasis (Fig 1). The resected specimen showed adenosquamous carcinoma without any sarcomatous

component measuring 6.5 cm x 4 cm x 3.5 cm with visceral pleural invasion and lymphovascular permeation (Fig 2). The surgical margins were clear and the resected intrathoracic lymph nodes were free of metastasis (pathological stage IIB [pT3N0M0]). Adjuvant chemotherapy consisted of four cycles of cisplatin 75 mg/m² on day 1 and vinorelbine 25 mg/m² on days 1 and 8 every three weeks. A repeat CT examination eight months post-surgery showed a recurrent tumor at the apex of the remaining right lung measuring 7.0 cm x 6.6 cm x 3.7 cm. He underwent a surgical resection of the tumor and reconstruction of the chest wall. Histopathological examination of the tumor revealed a high grade pleomorphic sarcoma with no epithelial elements. The tumor cells were strongly positive for vimentin and negative for cytokeratin (CK) 5 and 6, and thyroid transcription factor-1 (TTF-1) (Fig 3). A CT scan two months later showed multiple new metastatic lung nodules.