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Case report

Second primary pleomorphic carcinoma arising from the pneumonectomy cavity of non-small cell lung cancer: A case report

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ABSTRACT

Here, we report a thirteen years' survivor of initial primary lung cancer, who successfully diagnosed with second primary lung cancer(SPLC). It was arising from the pneumonectomy cavity of a non-small cell lung cancer (NSCLC). Few cases of SPLC associated with the post-pneumonectomy cavity have been reported in the literature. The histologic results of SPLC was metastatic pleomorphic carcinoma. It is a rare type of lung cancer; which incidence has been reported to range from 0.1% to 0.4% among all lung cancers. Based on regular follow-up with chest computed tomography(CT) and an understanding of post-pneumonectomy changes, the second primary pleomorphic carcinoma was correctly diagnosed and appropriately treated.

1. Introduction

Lung cancer is the most common cancer and the leading cause of cancer-related mortality worldwide [1]. With computed tomography (CT) surveillance program and the development of therapeutic approaches for lung cancer, the number of long-term survivors is gradually increasing [2,3]. Improvements in pre- and postoperative care can also improve long-term survival [4]. As the survival time improved and the overall mortality reduced, the risk of second primary lung cancer (SPLC) increased among survivors [5]. Recent studies have shown that long-term survivors of lung cancer have four to six times higher incidence of SPLC [6]. Despite the increasing importance of SPLC, currently, there are no consensus screening guidelines for long-term survivors of lung cancer. Existing guidelines recommend periodic follow-up; however, they differ with respect to surveillance intervals between 3-, 6-, and 12-months and fail to provide specific guidelines on how to extend surveillance intervals as the time after surgery increases [7–10].

Here, we report about a rare case of second primary pleomorphic carcinoma arising from a previous pneumonectomy cavity of non-small cell lung cancer (NSCLC).

2. Case report

A 58-year-old asymptomatic patient with history of NSCLC with subsequent pneumonectomy presented with abnormal shadow in his chest CT. The patient was diagnosed with NSCLC (squamous cell carcinoma, T3N0M0, stage IIB) 13 years ago, and underwent right pneumonectomy with adjuvant chemotherapy. The patient was a past smoker (quit 13 years ago, 25 pack year); however, no respiratory complaints or other physical symptoms were reported.

The patient was performed a regular chest CT after pneumonectomy. The series of chest CTs showed physiological changes following pneumonectomy. The pneumonectomy cavity was replaced with a liquid-filled mass with thick fibrous margins. The large mass was considered as a chronic organizing hematoma or chronic empyema (Fig. 1). In April 2019, chest CT revealed several cystic lesions originated from the large mass replacing the pneumonectomy cavity. One of the cystic lesions protruded into the chest wall and destructed the fifth rib (Fig. 2). The

Abbreviations: NSCLC, non-small cell lung cancer; CT, computed-tomography; SPLC, second primary lung cancer; IPLC, initial primary lung cancer; MRI, magnetic resonance imaging; PET, positron emission tomography.

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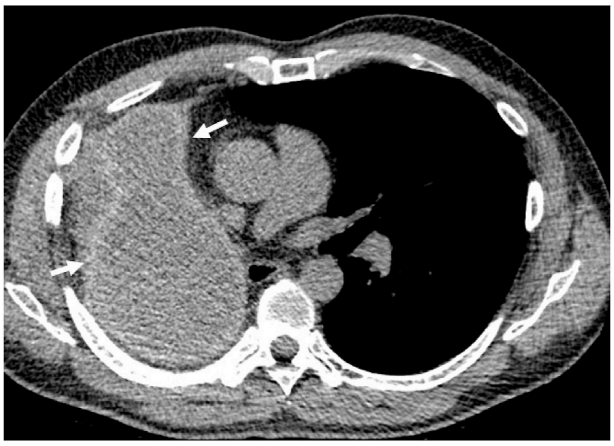

Fig. 1. Axial view of follow-up computed tomography (CT) in March 2016. CT demonstrated that a large snowman shaped mass (white arrow) replacing the right pneumonectomy cavity. The mass was filled with high attenuation material, and the margin of the mass was smooths and separated from chest wall. There was no change in size of the mass compared to the previous CTs. The large mass was considered as a chronic organizing hematoma or chronic empyema.

first percutaneous needle biopsy from the fifth rib was performed, and the pathology showed a few atypical cells. Re-biopsy was recommended, and the patient was referred to our hospital based on the suspicion of recurrence or SPLC.

Re-biopsy from the right fifth rib was performed in May 2019, and pathology showed no evidence of malignancy. Follow-up chest CT performed with short interval (Fig. 3). It revealed that the size of the lesion had increased, thereby suggesting a malignancy. A third biopsy of the right intercostal soft tissue was conducted in January 2020, and pathological examinations of the biopsy showed atypical cells, suggestive of non-small cell carcinoma. In February 2020, a fourth biopsy of the right fifth rib and endobronchial ultrasonography-guided transbronchial needle aspiration from the lymph node 2R were performed for accurate diagnosis. Pathological examinations of the lymph node 2R biopsy revealed the presence of necrotic tissue only; however, poorly differentiated squamous cell carcinoma from the right fifth rib was confirmed. Immunohistochemical analysis revealed negative immunoreactivity for thyroid transcription factor(TTF-1), and a few positive immunoreactive cells of p63 protein.

Brain magnetic resonance imaging (MRI) and positron emission tomography (PET) were performed to rule out the possibility of distant metastasis. Brain MRI did not show any abnormality. PET showed increased ^{18}F-fluorodeoxyglucose uptake in the right level I axillary, supraclavicular, and internal mammary lymph nodes, indicating a possibility for metastasis (Fig. 4). The clinical stage was classified as Stage IV, and surgical treatment was not indicated. However, the salvage operation was planned, because the patient had complained of systemic symptoms such as night sweating. Follow-up chest CT for preoperative evaluation revealed that the protruding lesion grew out of the rib cage (Fig. 5).

Chest wall resection with reconstruction was conducted. The tumor was diagnosed on the fourth-fifth ribs under the pectoralis major muscle. The mass measuring 7 × 7 × 6 cm, including the fourth-fifth ribs, was resected, and the chest wall was reconstructed using Marlex mesh.

The histopathologic diagnosis was different from primary lung cancer showing a well-differentiated squamous cell carcinoma (Fig. 6A). Microscopic images showed a poorly differentiated carcinoma with spindle cell change, extensive necrosis, and acute and chronic inflammation (Fig. 6B). Immunohistochemical analysis revealed positive immunoreactivity for pan-cytokeratin protein (Fig. 6C) and negative immunoreactivity for p63(Fig. 6D) and p40 proteins. The final diagnosis was pleomorphic carcinoma, and the dissected lymph nodes were free of metastasis.

The patient has survived without recurrence for eight months since the surgical treatment.

3. Discussion

We report about a SPLC arising from pneumonectomy cavity, and such cases are rarely reported in the literature. Most of SPLCs are usually developed in remained lung parenchyma, but not in the pneumonectomy cavity. The histopathologic diagnosis was pleomorphic carcinoma, one of the rare type of lung cancer.

A pneumonectomy cavity with chronic empyema may be considered a risk factor for malignancy. It is known that the risk of carcinoma is increased in areas of chronic inflammation [11]. According to Deaton, the long-term inflammation causes metaplasia in the bronchial and pleural epithelium and the epithelium of the skin margins of the tract. Subsequently, metaplastic epithelium extends into the chest cavity where cell proliferation and malignant degeneration occur [12]. In this case, a lesion suspected of malignancy was developed in the adjacent location of the chronic organizing hematoma or chronic empyema.

SPLC was defined according to the criteria of Martini and Melamed [13]. A new distinct pulmonary malignancy is considered an SPLC if any one of the following three criteria are fulfilled: (1) histologic results different from those of the index tumor; (2) same histologic results as those of the index tumor but diagnosed 2 years after the primary tumor; or (3) same histologic results as those of the index tumor diagnosed

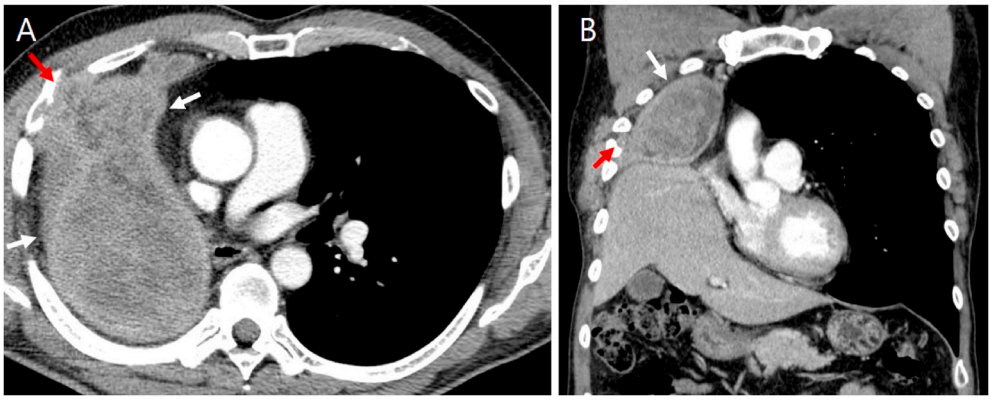

Fig. 2. (A) Axial and (B) Coronal view of follow-up CT in April 2019. The size of large mass replacing the right pneumonectomy cavity was not changed(white arrow). Several cystic lesions originated from the large mass. One of the cystic lesions protruded into the chest wall with bone destruction (red arrow). It was suspected of malignancy. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

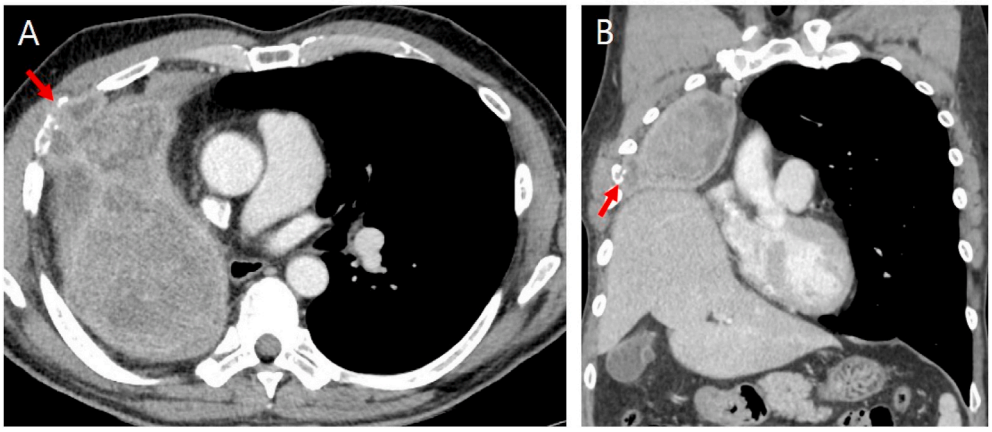

Fig. 3. (A) Axial and (B) Coronal view of follow-up CT in December 2019. The protruding lesion changed its shape like a mass, and the size was increased (red arrow). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

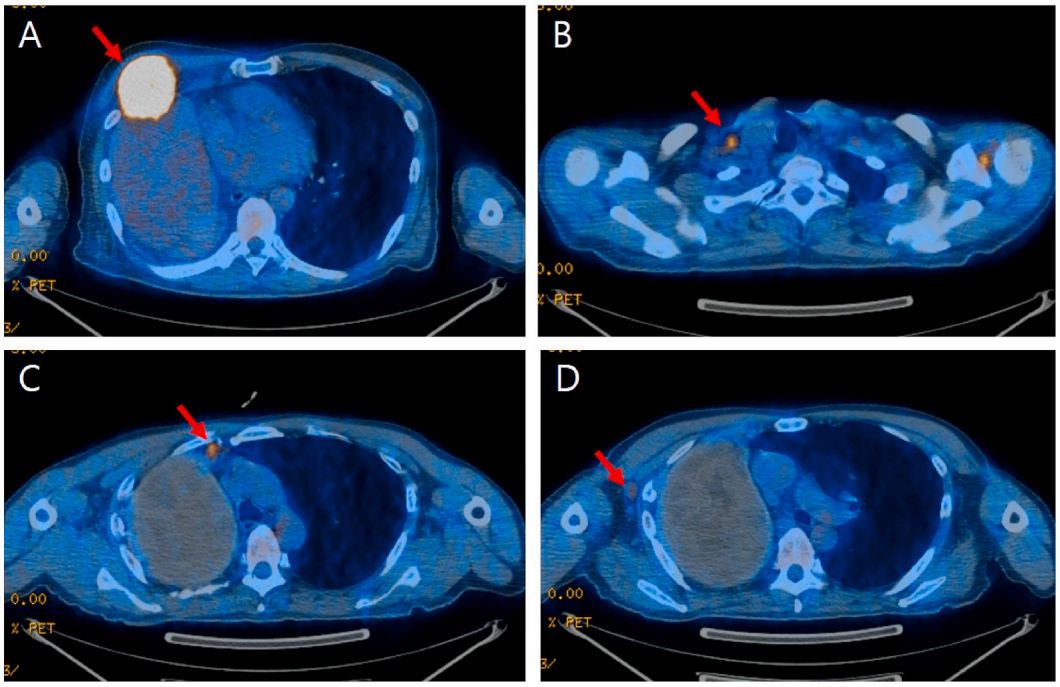

Fig. 4. (A) A biopsy-proven malignant mass in the right 5th rib (arrow). (B) Increased FDG uptakes in the supraclavicular lymph nodes cannot exclude the possibility of metastasis (arrow). (C) Increased FDG uptakes in the internal mammary lymph nodes cannot exclude the possibility of metastasis (arrow). (D) Increased FDG uptakes in the right level I axillary lymph nodes cannot exclude the possibility of metastasis (arrow).

within 2 years of the primary tumor but located in different lobes or segments and with no positive intervening lymph nodes and no evidence of metastasis. In the current case, a tumor was developed from pneumonectomy cavity, 13 years after the IPLC. The primary cancer was completely cured by pneumonectomy in 2007, and there was no evidence of recurrence or metastasis. The histological analysis revealed pleomorphic carcinoma, which was different from squamous cell carcinoma.

Recent improvements in perioperative care and adoption of CT screening could increase long-term survival of NSCLC patients [2–4]. Patients successfully treated for NSCLC have a 2%–5% annual risk of developing SPLC, and the risk of SPLC gradually increases over time without a plateau [6,14–16]. SPLC is a major cause of death among survivors of initial lung cancer; therefore, early detection and management of second primary malignancy are important for survivors [17]. Despite the increasing importance of SPLC, currently, there are no consensus surveillance guidelines for survivors of lung cancer who are at a high risk of developing SPLC [18]. Recent studies support the use of CT surveillance for the diagnosis and treatment of new primary disease with subsequent good survival [19,20]. In the present study, the patient underwent chest CT annually for surveillance after pneumonectomy. Serial chest CTs showed physiological changes following pneumonectomy. The chest CT revealed a newly developed mass involving chest wall 13 years after pneumonectomy. The patient underwent chest CT at shorter intervals, to distinguish whether the mass was malignant. This enabled early detection and proper treatment of SPLC.

In this case, there were several obstacles for confirming the second primary malignancy. First, it was difficult to recognize the progression of malignancy because of post-pneumonectomy changes of the lung [21]. After pneumonectomy, the cavity fills with a fluid [22]. Fibrous contraction results in the displacement and distortion of the mediastinum. Post-pneumonectomy empyema may also develop [23]. Existing

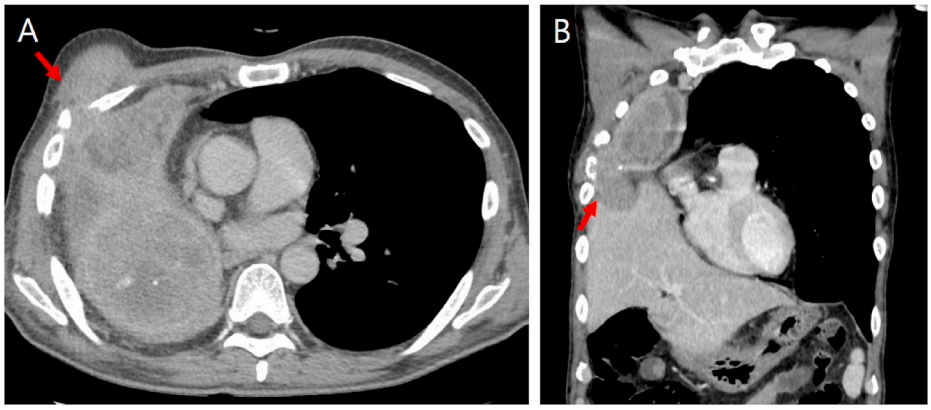

Fig. 5. (A) Axial and (B) Coronal view of follow-up CT in March 2020. The size of large mass replacing the right pneumonectomy cavity was not changed. The protruding lesion grown outside of the rib cage (red arrow). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

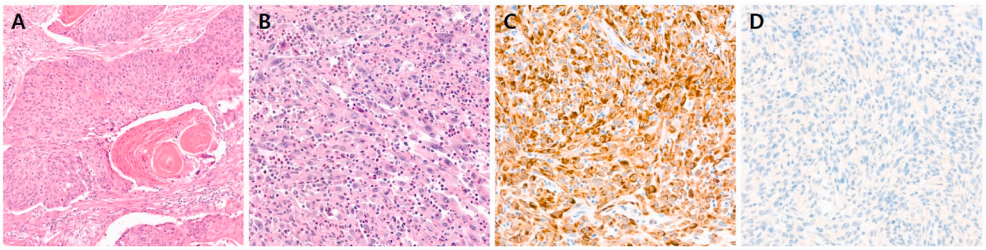

Fig. 6. Histopathological analysis of pneumonectomy and chest wall resection specimens. A: Initial pneumonectomy specimen showing a well-differentiated squamous cell carcinoma with tumor nests and keratinization. B: Tumor cells showing poor differentiation with marked pleomorphic, multinucleated, spindle-shaped, and mitotic figures. C: Positive immunoreactivity for pan-cytokeratin protein, indicating the presence of a carcinoma. D: Negative immunoreactivity for p63 protein. A, × 50; B-D, × 100 magnifications.

data suggest that CT has limited ability in distinguishing between scar tissues after surgery and tumors; however, PET can provide useful information in such situations [24]. In our case, serial chest CTs were performed to distinguish the progression of malignancy. PET could provide additional information about the possibility of metastasis. The pathologic diagnosis was confirmed based on biopsy.

The histopathology of the tumor in this case was a pleomorphic carcinoma. A pulmonary pleomorphic carcinoma is a rare malignant lung tumor, and its incidence has been reported to range from 0.1% to 0.4% among all lung cancers [25]. Pulmonary pleomorphic carcinoma has an aggressive clinical course and poor outcomes compared with other NSCLC [26,27]. Therefore, early detection and proper treatment are important for better prognosis. However, the preoperative diagnosis of pleomorphic carcinoma is rarely confirmed, possibly because of its heterogeneous histopathological characteristics. Pleomorphic carcinoma is a poorly differentiated adenocarcinoma, squamous cell carcinoma, or large cell carcinoma that contains spindle cells and/or giant cells or a carcinoma comprising spindle and giant cells alone, with a sarcomatoid tumor component of at least 10%. It is difficult to diagnose pleomorphic carcinomas based on biopsies or cytology [26,28,29]. In this case report, biopsy was performed four times for different lesions, including the soft tissue of the chest wall, rib, and lymph nodes. Despite multiple biopsies, the pathology showed squamous cell carcinoma; however, a pleomorphic carcinoma was confirmed only after surgical resection.

In conclusion, we reported about a rare case of second primary pleomorphic carcinoma arising from a previous pneumonectomy space of NSCLC. We suggest (1) that post-treatment surveillance is important for detecting the development of an SPLC early enough to allow potentially curative treatment; (2) that the possibility of a malignancy originating from the pneumonectomy cavity should be considered in patients experiencing initial lung cancer with pneumonectomy; and (3) that evaluating the tumor with repeated sampling should be considered to provide an accurate diagnosis, especially when malignancy is strongly suspected.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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