Title: Coexistence of a pulmonary adenocarcinoma with a focal organizing pneumonia

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Abstract:

We report a case of a pulmonary adenocarcinoma in coexistence with an organizing pneumonia. A 73-year old man presented with an abnormal shadow on a chest X-ray. The pathological diagnosis, made via a partial resection, was a focal organizing pneumonia with reactive proliferation of the bronchial epithelium. Three years later, two tumors adjacent to the staple line were revealed by computed tomography. A left lower lobectomy was performed and both tumors were diagnosed as an adenocarcinoma. Because the histological findings for the atypical epithelial areas of the previous tumor were similar to the two new lesions in this patient, we regarded these tumors as a marginal recurrence.

Text:

Introduction:

As it is difficult to distinguish a pulmonary carcinoma from a focal organizing pneumonia (OP) by radiological imaging. A pulmonary resection is therefore needed in many cases to enable a definitive diagnosis. A histopathological differential diagnosis of these two lesions can usually be made without difficulty. We here present a case of a lung tumor that had been histopathologically diagnosed as a focal organizing pneumonia via a partial resection of the lung, but for which a coexisting adenocarcinoma was revealed via a marginal occurrence three years later.

Case report:

A 73- year old man presented with an abnormal shadow on a chest X-ray during a check-up. He had no history of any major disease. Chest computed tomography (CT) revealed a 3 cm lesion in the peripheral area of the left lower lobe (Figure 1a). Positron emission tomography with fluorin-18 fluorodeoxyglucose further revealed a strong accumulation of this agent at this tumor mass and a maximum standardized uptake value of 10.8 was measured. A pulmonary cancer was strongly suspected and a surgical

procedure was performed for the diagnosis and treatment of this tumor. To enable an intraoperative diagnosis during surgery, we performed a partial resection of the left lower lobe that included the tumor mass using an endoscopic linear cutter. The histological findings obtained from our analysis of a frozen section of this tumor showed infiltration by numerous inflammatory cells but no apparent malignancy. We therefore did not perform an additional pulmonary resection. Subsequent pathological examinations revealed marked interstitial inflammation and the presence of granulation tissue in the air space. In addition, areas of atypical epithelial proliferation were found to be scattered diffusely throughout the tumor (Figure 1b). A definitive diagnosis of a focal organizing pneumonia with reactive changes of the epithelium was made.

Three years after this operation, two small nodules adjacent to the staple line were revealed in this same patient by chest CT during a medical checkup. These lesions had increased in size six months later and a malignancy was suspected (Figure 2a, 2b). We subsequently performed a left lower lobectomy with a mediastinal lymphadenectomy. Pathological examinations revealed a papillary proliferation of the tumor cells with a mild

nuclear atypia and abundant intracellular mucin, but no lymph node metastases. Histologically, the two lesions were not connected but showed similar characteristics. The definitive diagnosis at this juncture was a well differentiated adenocarcinoma of the lung (Figure 2c). A reexamination revealed that the pathological findings of the atypical epithelial areas of the previously resected tumor were similar to the two additional adenocarcinomas. We therefore concluded that an adenocarcinoma had already coexisted with an organizing pneumonia in the lesion resected in the first operation, and regarded the two new lesions as a marginal recurrence of this adenocarcinoma. The patient has since been followed up for one year with no evidence of recurrence.

Discussion:

Focal OP is one of the known clinical variants of OP, is usually detected via chest radiograph screening, and is most often diagnosed after an excision in cases of suspicious lung cancer (1). The causes of focal OP are mostly cryptogenic, but *Hemophilus influenzae*, *Streptococcus pneumoniae*, and others have been identified as the etiologic agents in some reported cases (2,

3), consistent with our current findings.

A differential diagnosis of focal OP versus lung cancer is currently difficult to make as CT findings show that focal OP may simulate lung cancer (4). Moreover, a pathologic OP pattern is commonly found adjacent to lung cancer (5, 6). Surgical lung resections are thus performed in most cases to enable a pathological diagnosis. Wu and colleagues have previously reported that an intraoperative frozen section diagnosis has utility in preventing an underdiagnosis in cases of lung neoplasm.

In our present case, we made a diagnosis of focal OP following an initial operation but did not find any evidence of adenocarcinoma either via the analysis of frozen sections or through a postoperative pathological examination. Atypical epithelial proliferation was recognized but we considered this to be an inflammatory reaction because it was scattered diffusely. In reexamination of the specimen from the first operation, no obvious adenocarcinoma without interstitial inflammation was recognized. However, two adenocarcinomas which were discontinuous but pathologically equivalent subsequently arose in the staple line and showed pathological findings that were similar in some respects to those of the initial tumor that

was resected in the first operation. This included the epithelial architecture, the presence of cellular atypia, and other characteristics. These findings led us to speculate that the lesion resected in the first operation was a mixture of an OP and an adenocarcinoma and that some components of the adenocarcinoma had remained around the staple line.

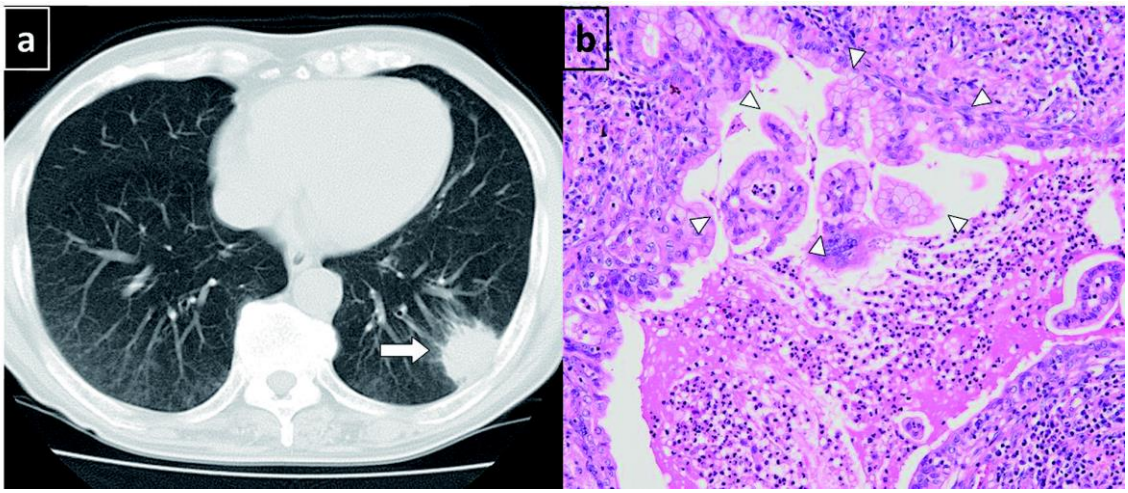
The mechanism by which a mixture of an adenocarcinoma and OP arose in our present case is unknown. The concept of a "scar" carcinoma might help to explain the origin of these two lesions (7) but some studies have suggested that the scarring associated with pulmonary neoplasia is not a predisposing factor in the development of a carcinoma, but is a host response to the tumor (8). Moreover, if the new adenocarcinomas arose from the precedent OP, the area of these carcinomas should be localized in part of the inflammatory tumor. In our present case however, the areas of atypical bronchial epithelia were scattered around the whole of the tumor. We therefore speculate that an infection occurred in the precedent adenocarcinoma and that the pathological OP pattern was then formed due to a delayed resolution reaction. Romero, et al. have previously reported in their clinicopathological assessment of peripheral OP in patients with

resected lung tumors that OP in the vicinity of the tumor was present in 37% of all patients analyzed. These authors concluded that a bronchial obstruction is one of the possible mechanisms underlying OP formations adjacent to lung tumors (5). Although our present case differs from these reported cases because the OP lesion did not occur in the vicinity of the tumor but was mixed with the tumor, it is possible that bronchial obstruction due to carcinoma could be related to the occurrence of OP.

In conclusion, if a focal organizing pneumonia is accompanied by atypical epithelial areas, the coexistence of pulmonary adenocarcinoma should be considered and periodic follow-ups must be undertaken.

Figure legends:

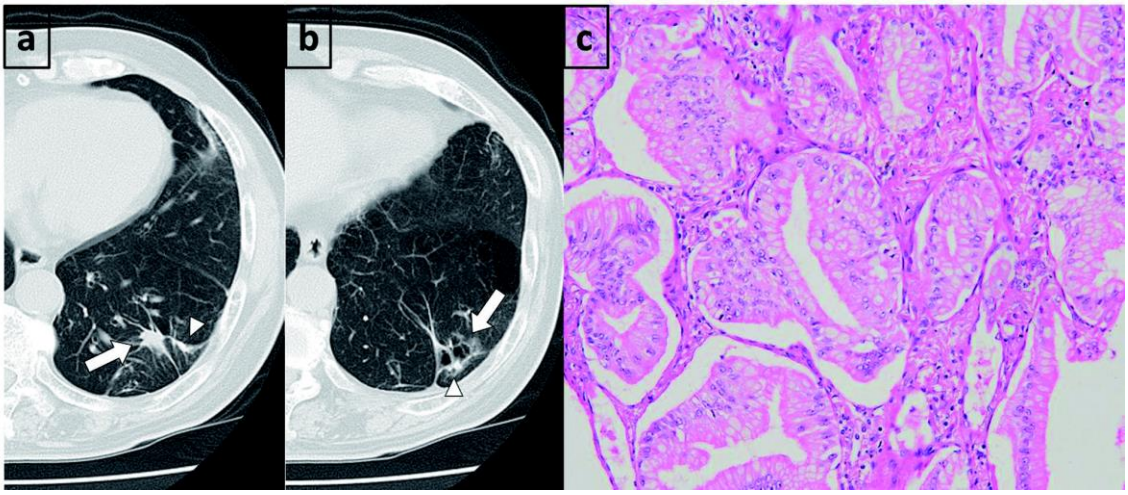
Figure 1



a: Chest CT revealing a solid tumor in the left lower lobe (arrow).

b: High magnification analysis of the lung tumor resected in the first surgery (H&E staining, original magnification x 400) showing marked interstitial inflammation and granulation tissue in the air space, and also revealing atypical epithelial proliferation with abundant intracellular mucin (arrowhead).

Figure 2



a: Chest CT performed three years after the first operation revealing a solid tumor (arrow) adjacent to the staple line (arrowhead).

b: Caudal side slice of the solid lung tumor showing another tumor with a cavity formation (arrow) adjacent to the staple line (arrowhead).

c: High magnification analysis of the lung tumor in our present case resected in the second surgery (H&E staining, original magnification x 400) showing papillary proliferation of tumor cells with mild nuclear atypia and abundant intracellular mucin. These findings of atypical epithelia are similar to those of Figure 1.

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