Primary Undiagnosed Adenocarcinoma of Lung Presenting as Acute Respiratory Distress Syndrome

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Neoplastic pulmonary infiltration is an unusual but recognized cause of acute respiratory distress syndrome (ARDS). However, its occurrence with primary undiagnosed adenocarcinoma of lung has never been reported in previous instance. We herein report a 54-year-old patient who developed ARDS after ten days of respiratory symptoms and died within three weeks from his initial presentation. High-resolution computed tomography (CT) of his chest showed diffuse patchy infiltration and areas of ground-glass attenuation. Adenocarcinoma was diagnosed by open lung biopsy. Although the clinical manifestation of lung cancer is somewhat variable, rapid deterioration with ARDS is uncommon. The reports in which ARDS developed as a result of neoplastic infiltration of the lungs is reviewed briefly. We also stress the fact that neoplasm should be considered as a possible etiology of unexplained ARDS.

Key words: ARDS; Biopsy; Lung, adenocarcinoma; Lung, diffuse infiltrative disease

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dyspnea still persisted. Meanwhile, no suspected pathogens were isolated by sputum, urine, and blood cultures, as well as acid-fast stain and culture for tuberculosis. Following laboratory examinations demonstrated marked leukocytosis (WBC 24000/mm$^3$) with left shift (neutrophil 80.6%). Other autoimmune profiles and serum electrophoresis were within normal limits, except elevated carcinoembryonic antigen (CEA 17.87ng/mL). A series of the chest radiographs revealed more serious patchy infiltrations. High-resolution CT of the chest was then performed, which demonstrated diffuse patchy infiltrative pattern with widespread geometric ground-glass attenuation over both lungs (Fig 1). The mediastinum and bilateral hilar regions show clear appearance without evidence of abnormal masses or enlarged lymph nodes. No evidence of pleural or pericardial effusion noted.

Ten days after admission, progressively worse clinical course was noted and severe hypoxemia was developed abruptly. Endotracheal intubation was carried out immediately and the patient was transferred to the intensive care unit. Assist controlled mandatory ventilator support was given with the following values: fraction of inspired oxygen (FiO$_2$)

![Figure 1](image1.png)

**Figure 1.** a. High-resolution CT of the chest at the level of right pulmonary artery demonstrated diffusion patchy infiltration and geographic ground-glass attenuation, mimicking infectious pneumonia. b. Some areas of patchy infiltration revealed high attenuation (arrow), measuring about 39 in Hounsfield units, on soft tissue window settings.

![Figure 2](image2.png)

**Figure 2.** a. The tumor was composed of nests of glandular cells, which grew along the bronchial epithelium and infiltrated into the lung parenchyma. The cells showed increased nuclear/cytoplasmic ratio and conspicuous nucleoli with squamous metaplasia. (Hematoxylin and eosin, X 200) b. These tumor cells showed reactivity to immunohistochemical stain: CK-18.
Arterial blood gas analysis showed: pH 7.368, PaCO$_2$ 44 mmHg, PaO$_2$ 75 mmHg, bicarbonates 24.7 mmol/L, BE 0.3. The Swan-Ganz catheter was inserted for monitoring the pulmonary artery pressure, which was revealed to be within the normal limit (about 5 to 7 mmHg).

Because of the unknown etiology of ARDS and elusive clinical manifestation, emergent open lung procedure with tissue biopsy was then performed. Adenocarcinoma of lung with focal squamous cell differentiation was proven by the pathological examination (Fig 2). Clinically, the patient did not respond to any medical treatment, and his family refused to receive more aggressive chemotherapy. We tried our effort to stop the ongoing clinical deterioration, but the patient still expired about ten days later.

**DISCUSSION**

Neoplasm can cause diffuse tumor infiltration of lung and lead to the development of subsequent ARDS. A review of the English literature revealed that most common neoplasm which may cause ARDS from pulmonary neoplastic infiltration were leukemia and lymphoma. They develop the acute onset of pulmonary failure, which was described as leukostasis syndrome [5]. Other malignancies, including malignant histiocytosis, testicular choriocarcinoma with pulmonary metastasis, and metastatic thyroid cancer, have been reported to have pulmonary neoplastic infiltration and thus result in ARDS [6-8]. These malignant cells may presumably direct hinder or have a tendency of hemorrhage to destroy the normal gas exchange and cause subsequent respiratory failure. However, our patient developed typical clinical symptoms of ARDS during hospitalization, which included sudden onset of dyspnea, labored cracked breathing sound on chest auscultation, diffuse patchy alveolar infiltrates and ground-glass attenuation on the high-resolution CT. The Swan-Ganz catheter was inserted to exclude cardiogenic pulmonary edema. All medical therapy and supportive treatment were useless to reverse the progressive hypoxemia caused by abnormal gas exchange. Any recognizable possibilities were excluded and no clinical etiology could be traced to explain the existing ARDS until pathologically proven adenocarcinoma of lung.

High-resolution CT of our patient showed the typical appearance of diffuse infiltrative pattern, manifesting as multifocal patchy infiltrates and ground-glass opacities throughout both lung fields. By frequency, this pattern has often been regarded as infectious pneumonia[9]. In other words, diffuse infiltrative disease related to neoplasm always has a long and slow evolution and did not response to standard medical treatment. Our case of diffuse pulmonary adenocarcinoma with acute exacerbation had a strikingly similar radiological appearance which initially caused diagnostic confusion. No possible distinguishing imaging features in our case should have suggested a diagnosis rather than infectious pneumonia. Even though it was not possible to make an early correct diagnosis in our case, CT still plays the potential role in many cases in distinguishing the possible etiology of diffuse air-space consolidations.

The clinical presentation of diffuse adenocarcinoma of lung can be associated with a rapidly progressive fatal course, but with ARDS as a contributory factor to sudden death has never been reported. Furthermore, multicentric bronchogenic carcinoma mimicking pulmonary infiltrative disease has been most frequently regarded as squamous and broncholoalveolar cell types [10]. It is also the most important feature in predicting prognosis on broncholoalveolar carcinoma [11]. In our patient, pathologic sections showed malignant cells chiefly involving the interstitial and alveolar spaces could possibly explain the difficulty with oxygen transport and eventually lead to respiratory failure.

Broncholoalveolar lavage, transbronchial bronchoscopic biopsy, percutaneous needle biopsy or open lung biopsy has higher accurate rate in the diagnosis of diffuse pulmonary infiltrates than high-resolution CT [3, 12]. These interventional techniques may be chosen to provide more precise diagnosis of diffuse infiltrative disease, especially when clinical presentation and radiological evidences can not make an unquestionable diagnosis. Selecting the most appropriate method will depend upon the anatomic location and likely entity of the pulmonary lesion. Among these invasive techniques, open lung biopsy is indicated for diffuse infiltrative lung disease, as our patient, whom is critically ill suffering from respiratory failure.

We concluded that, in some cases of refractory ARDS, neoplastic infiltration should be considered as the cause of diffuse infiltrative lung disease. Early awareness of the etiology of acute lung injury is important since ARDS due to neoplastic infiltration has high mortality rate. CT is advocated to show the site, size, and possible nature of the pulmonary lesion, but limited to recognize precise pathological diagnosis. Therefore, interventional tissue proof is still
absolutely necessary in these patients to provide the correct diagnosis and therapeutic planning.

REFERENCE

病例報告：未診斷出的肺腺癌以急性呼吸窘迫症為臨床表現

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在臨床上惡性腫瘤導致成人呼吸窘迫症的例子是很少見的，而由肺腺癌造成成人呼吸窘迫的案例更是沒有被報告過。因此，我們報告一個54歲的男性病人，於住院十天內發展出成人呼吸窘迫症，並於三個禮拜內死亡。他的肺部電腦斷層顯示廣泛性非對稱性的浸潤及毛玻璃狀病兆，而肺腺癌診斷是靠開胸組織切片手術確立的。雖然臨床上肺腺癌的表現可以是非常多變，但是急進惡化的現象卻非常罕見。這篇文章主要是探討惡性腫瘤導致成人呼吸窘迫症的可能原因及案例，當臨床上遇到難治、無法解釋的成人呼吸窘迫症時，必須把惡性腫瘤列為鑑別診斷；一經診斷確定後，我們可以預期此類病人的預後會很差。

關鍵詞：急性呼吸窘迫症；組織切片；肺腺癌；廣泛性浸潤性肺病