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Short Communication

3-Cases of Lung Adenocarcinoma: Confused by High Serum CA19-9 Levels and Interstitial Changes on Chest CT

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2. Key words

Serum tumor markers, interstitial lung diseases, lung adenocarcinoma

1. Abstract

1.1. Objective: To explore the clinical characteristics and cause of misdiagnosis of 3 cases of lung cancer, and to provide evidence for limiting the risk for misdiagnosis of similar cases in the future.

1.2. Materials and Methods: The medical record and clinical data of three patients with lung adenocarcinoma were analyzed retrospectively. Initially these patients were diagnosed as interstitial pneumonia complicated by infection in outside hospitals because the CT scans showed pulmonary fibrosis or interstitial pulmonary changes with diffuse opacity or massive consolidation. Subsequently, because their serum levels of CA19-9 were markedly elevated, gastroscopy, enteroscopy and even PET/CT were performed at hospitalization in our unit.

1.3. Results: These 3 patients were finally diagnosed as stage IV lung carcinoma by means of bronchoscopy and lung biopsy.

1.4. Conclusion: The serum level of CA199 can be increased significantly in patients with lung adenocarcinoma other than in digestive tract tumors. Also, lung cancers in pulmonary fibrosis patients may show diffuse opacity and massive consolidation.

3. Introduction

Recently, physicians have recognized that interstitial pneumonia, especially idiopathic pulmonary fibrosis (IPF), and lung cancer can present concurrently. Also, mild to moderate elevations of serum tumor markers have been reported in patients with IPF [1, 2]. Maher et al [3] reported that CA19-9 and CA125, markers of epithelial injury, increased significantly as IPF progressed, and these elevations were associated with an increased risk of IPF death.

CA19-9 and CA125 are commonly used circulating markers of cancer, and they have high predictive value for gastrointestinal and gynecological tumors, especially for pancreatic and ovarian malignancies [4, 5]. Here, three cases of lung adenocarcinoma diagnosed in our unit from 2017 to 2019 were reported, whose serological features were high level of CA19-9 and imaging features were interstitial pulmonary changes.

4. Materials and Methods

From July, 2017 to February, 2019, 3 patients (2 males and 1 female) were diagnosed and treated as stage IV stage of lung adenocarcinoma at Drum Tower Hospital affiliated to Medical School of Nanjing University. The entire medical record and clinical data were analyzed retrospectively. In brief, they were all misdiagnosed as interstitial lung disease (ILD) with infection and treated by antitussives, expectorants, and bronchodilators, and antibiotics without improvement. The period from onset of symptoms to diagnosis was between 12 to 36 months. And the period from diagnosis to death ranged between 4 to 19 months (Table 1).

Table 1: General features

	CASE1	CASE2	CASE3
Gender	male	male	female
Age(year)	54	60	73
Duration(month, from onset to diagnosis)	12	36	18
Duration(month, from diagnosis to death)	19	12	4
smoker	Y	Y	N

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5. Results

Cough and dyspnea on exertion were the main symptoms. In two cases the cough was (add whether productive or not) the third patient had moderate amounts of sputum (80-100mL per day) production. In all cases crackles were heard on physical examination.

The serum level of CA19-9 in all three patients was markedly elevated (>1000 U / mL), and CA 125 was slightly elevated in two patients (Table 2). Autoantibodies, and anti- neutrophil cytoplasmic antibodies were negative. EGFR gene mutation was negative in three patients. Because of the high serum level of CA19-9, gastroscopy and enteroscopy were performed in two patients, and Positron Emission Tomography / computerized Tomography (PET/CT) was performed in one patient (Table 2).

Interstitial changes were present on chest CT scan in three patients. Also, diffuse opacity with consolidation was present in the lung fields (Figure 1-3).

Three cases were diagnosed as lung adenocarcinoma by bronchoscopy in one patient and by percutaneous needle biopsy in two patients. For managemenet, one patient received chemotherapy and antiangiogenic therapy, a second patient received oral amlotinib, and the patient did not receive any cancer-directed treatment. All the three patients succumbed to their disease.

Table 2: Clinical manifestations

	CASE1	CASE2	CASE3
Symptoms	short of breath on exertion valcros	Cough,short of breath and intermittent fever	Cough and short of breath
Signs	crackles	crackles	bubbles
CA19-9 (U/ml,<30)	**>1000.0**	**>1000.0**	**>1000.0**
CA125(U/ml, <27)	78.75	27.1	3.9
ANA (-)	(±)	(-)	(-)
Diagnostic method	PPP guided by Doppler	PPP guided by CT	BAL
Other inspection methods	Ultrasound Gastroscop+ Enteroscope	Gastroscop+ Enteroscope	PET/CT+ Ultrosonic Bronchoscope
Histopathology	Adenocarcinoma	Adenocarcinoma	negative
Cytopathology	Adenocarcinoma cells	Adenocarcinoma cells atypia, Adenocarcinoma cells	(-)
EGFR mutated	(-)	(-)	

CA: carbohydrate antigen. ANA: antinuclear antibodies. PPP: percutaneous pulmonary puncture. EGFR: epidermal growth factor receptor gene. BAL: bronchoalveolar lavage. PET/CT: positron emission tomography/ computed tomography

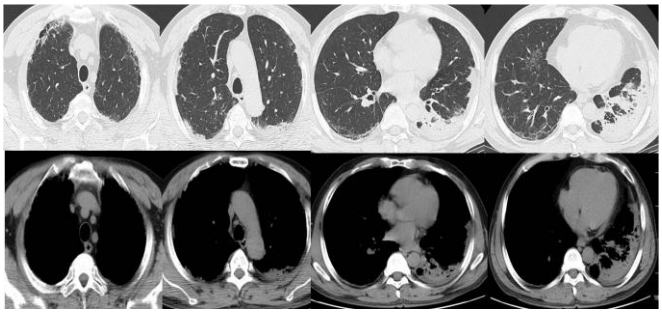

Figure 1: Radiological features of Case 1

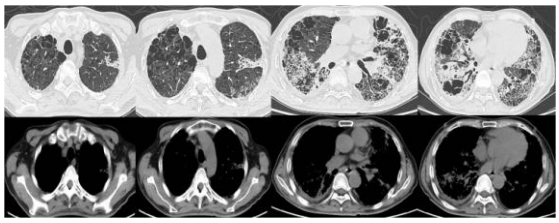

Figure 2: Radiological features of Case 2

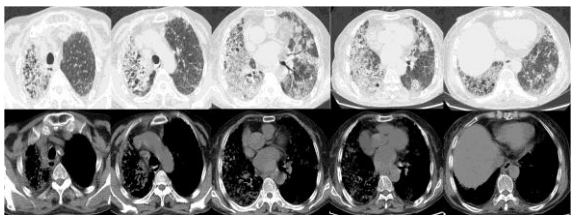

Figure 3: Radiological features of Case 3

6. Discussion

CA19-9 and CA125 are commonly used as cancer biomarkers. Undoubtedly, high levels of CA19-9 and CA125 are useful in supporting the diagnosis of cancer. Goonetilleke KS et al. [4] systematically reviewed the value of CA19-9 in diagnosing pancreatic cancers and found a sensitivity of 79 (70%- 90%) and specificity of 82 (68%-91%). CA19-9 is the most widely used biomarker for diagnosis of pancreatic cancers. Medeiros et al. [6] did the similar work for CA125 and found a sensitivity of 80 (76%- 82%) and specificity of 75 (73%- 77%) ovarian cancers. CA125 was regarded as a powerful marker in ovarian tumors with high accuracy, and even a helpful marker for surgeons to decide what kind of surgery to perform [6]. In addition, CA19-9 and CA125 have diagnostic relevance in lung cancer. Up to 60% of patients with large cell carcinoma had elevated CA125 levels (mean 176 U/ml), while only 15.4% of patients with other types of lung cancer had elevated CA125 levels (54.3U/ml) [7]. The concentration of serum CA19-9 in advanced lung cancer was also increased, especially in lung adenocarcinoma and bronchioloalveolar cell carcinoma [8].

Mild to moderate elevations of tumor markers are also found in patients with pulmonary fibrosis. Studies suggest that CA19-9 and CA125 have important prognostic value for IPF [3]. The reason may be that there are many similarities in the pathogenesis of pulmonary fibrosis and lung cancer [9-12]. In recent years, there is increasing awareness that lung cancer may coexist in patients with ILD. Of ILDs, IPF accounts for more than 50% of the cases. It has been reported that roughly 1/10 of IPF patients develop lung cancer [13-15]. Most cases of the lung cancer associated with IPF develop as nodular lesions in the surrounding areas of fibrosis, mainly in reticular or honeycomb lesions [16].

Reviewing the three cases in this report, the diagnosis was full of challenge. First of all, tumor markers were increased significantly.

Considering the diagnostic value of CA19-9 in digestive system tumors, gastroscopy, colonoscopy, and even PET/CT were necessary diagnostic measures, but despite these tests, no cancer was detected. Additional considerations were whethers the cases were ILD with digestive system tumor or ILD with lung cancer? Secondly, the CT findings of these three patients had diffuse opacity and consolidations in addition to findings consistent with pulmonary fibrosis. The presentation of cancer as consolidations was inconsistent with the solitary nodules in lung cancer prior reports. If ILD combined with infection was considered, why did the opacity or consolidation was persistent and cannot be absorbed after a long time of anti-infection treatment? If not an infection, what were the possibilities? Was it organizing pneumonia besides pulmonary fibrosis? Or was it ILD complicated with tumor? Therefore, biopsies, or even repeated biopsies, are necessary for diagnosis.

The significance of this study lies: on one hand, in a small number of patients with lung adenocarcinoma, the serum level of CA199 can be increased significantly other than in digestive tract tumors. On the other hand, lung cancers happened in pulmonary fibrosis can show diffuse opacity and massive consolidation in CT scan.

In conclusion, high serum CA19-9 levels can happen in some subtype of lung adenocarcinoma. Besides solitary nodules, diffuse opacity and massive consolidation in CT scan can happen in lung cancer over ILD.

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References

1. S Takayama, N Kataoka, Y Usui, N Inase, Y Natori, M Nakayama, et al. CA 19-9 in patients with benign pulmonary diseases. Nihon Kyobu Shikkan Gakkai Zasshi. 1990; 28(10): 1326-31.
2. Victoria Rusanov, Mordechai R Kramer, Yael Raviv, Benjamin Medalion, Alexander Guber, David Shitrit. The significance of elevated tumor markers among patients with idiopathic pulmonary fibrosis before and after lung transplantation. Chest. 2012; 141(4): 1047-1054.
3. Toby M Maher, Eunice Oballa, Juliet K Simpson, Joanne Porte, Anthony Habgood, William A Fahy, et al. An epithelial biomarker signature for idiopathic pulmonary fibrosis: an analysis from the multicentre PROFILE cohort study. Lancet Respir Med. 2017; 5(12): 946-955.
4. Goonetilleke KS, Siriwardena AK. Systematic review of carbohydrate antigen (CA 19-9) as a biochemical marker in the diagnosis of pancreatic cancer. Eur J Surg Oncol. 2007; 33(3): 266-70.
5. Bottoni P, Scatena R. The Role of CA 125 as Tumor Marker: Biochemical and Clinical Aspects. Adv Exp Med Biol. 2015; 867: 229-44.
6. Medeiros LR, Rosa DD, da Rosa MI, Mary Clarisse Bozzetti, et al. Accuracy of CA 125 in the diagnosis of ovarian tumors: a quantitative systematic review. Eur J Obstet Gynecol Reprod Biol. 2009; 142(2): 99-105.
7. R Molina, P Santabarbara, X Filella, P Mengual, A M Ballesta, A Balague. Relationship of CA 125 and CA 19-9 with lung carcinoma histological subtype: preliminary study. Int J Biol Markers. 1989; 4(4): 215-20.
8. L Heikkilä, R J Suomalainen, J Lindgren, H Jalanko, A Harjula, S Mattila. Carcinoembryonic antigen (CEA) and gastrointestinal cancer associated antigen CA 19-9 in bronchioloalveolar carcinomas and pulmonary adenocarcinomas. Ann Chir Gynaecol. 1986; 75(5): 260-5.
9. Calado RT, Young NS. Telomere diseases. N Engl J Med. 2009; 361(24): 2353-2365.
10. Vancheri C, Failla M, Crimi N, Raghu G. Idiopathic pulmonary fibrosis: a disease with similarities and links to cancer biology. Eur Respir J. 2010; 35: 496-504.
11. Vancheri C, Du Bois RM. A progression-free end-point for idiopathic pulmonary fibrosis trials: lessons from cancer. Eur Respir J. 2013; 41: 262-269.
12. Vancheri C. Idiopathic pulmonary fibrosis: an altered fibroblast proliferation linked to cancer biology. Proc Am Thorac Soc. 2012; 9: 153-157.
13. Ivan Le Jeune 1, Jonathan Gribbin, Joe West, Chris Smith, Paul Cullinan, Richard Hubbard, et al. The incidence of cancer in patients with idiopathic pulmonary fibrosis and sarcoidosis in the UK. Respir Med. 2007; 101(12): 2534-2540.
14. H Matsushita, S Tanaka, Y Saiki, M Hara, K Nakata, S Tanimura, et al. Lung cancer associated with usual interstitial pneumonia. Pathol Int. 1995; 45(12): 925–932.
15. M Turner-Warwick, M Lebowitz, B Burrows, A Johnson. Cryptogenic fibrosing alveolitis and lung cancer. Thorax 1980; 35(7): 496-499.
16. Antoniou KM, Tomassetti S, Tsitoura E, Vancheri C. Idiopathic pulmonary fibrosis and lung cancer: a clinical and pathogenesis update. Curr Opin Pulm Med. 2015; 21(6): 626-33.