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Serum mucin-like glycoprotein antigen (KL-6) as a specific marker of interstitial pneumonia: a case report

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Introduction

It is often difficult to diagnose interstitial pneumonia (IP) in critically ill patients or in patients with acute respiratory failure, because specific hematological and serological findings are limited. In a patient with refractory IP, we determined the concentration of a mucin-like glycoprotein antigen (KL-6) over time as a serum marker specific to IP. We report a case to emphasize the diagnostic importance of KL-6, citing the relevant literature.

Case report

The patient was a 72-year-old man with a height of 153 cm and a weight of 40.2 kg.

Medical history

The patient underwent surgery for ascending colon adenocarcinoma in 1996. In 1998 he underwent microwave coagulation therapy of the liver for metastatic hepatic cancer, segmentectomy in the right lung for metastatic lung cancer, and segmental resection of the liver, for a total of three surgeries.

Present illness

On February 4, 1999, the patient underwent lower lobectomy and segmentectomy in the right lung for a metastatic tumor. Postoperatively, he was admitted to the ICU and was discharged on February 8 with a good clinical course. Hypoxemia (PaO_2 50 mmHg on room air) appeared immediately after discharge. He was readmitted to the ICU on February 12 after endotracheal intubation. Since chest computed tomographic (CT) examination showed pneumonia in the upper left lung and pyothorax in the right thoracic cavity, combined antibiotic treatment with imipenem/cilastatin and sulbactam/ampicillin was started. Fever, hypotension, and tachycardia occurred on February 15 (0 postoperative day; POD). We suspected that the symptoms were due to sepsis caused by pyothorax or pyopoiesis in the right lung and conducted pyothorax drainage by thoracotomy, followed by continuous hemodiafiltration (CHDF) conbined with endotoxin removal therapy (polymyxin B removal, PMX) for 2 consecutive days. Methicillin-resistant *Staphylococcus aureus* (MRSA) was detected in the pleural exudate collected at chest drainage, and intrathoracic lavage with physiological saline was started on February 16 (1 POD). Despite the administration of antibiotics (imipenem and vancomycin), no improvement was seen in the inflammatory findings or respiratory distress. The retiform shadow was revealed in the left lung on chest radiography, and neutrophils and lymphocytes increased in the bronchoalveolar lavage (BAL) fluid. Therefore, we suspected IP and prescribed steroid pulse therapy (methylprednisolone 500 mg·day^{-1}) for 3 days starting on March 4 (17 POD). CPR decreased, MRSA disappeared, and respiratory distress improved. *Pseudomonas aeruginosa* was detected in the sputum and pleural exudate on March 10 (23 POD), and lung infection symptoms were repeatedly exacerbated. Although chest radiography findings of IP in the left lung tended to improve, hypercapnia persisted. We conducted steroid pulse therapy (methylprednisolone 500 mg·day^{-1}) again between March 24 (37 POD) and March 26 (39 POD) and began oral administration of

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Table 1. Time course of serum KL-6 concentrations, CRP, WBC, and PaO_2/FiO_2

Postoperative day	KL-6 ($U \cdot ml^{-1}$)	CRP ($mg \cdot dl^{-1}$)	WBC ($10^2 \cdot \mu l^{-1}$)	PaO_2/FiO_2 (mmHg)
0	210	20.9	137	127.9
1	201	22.2	74	175.5
2	205	25.1	130	234.7
4	287	13.5	150	264.5
6	594	23.9	145	202.7
8	612	21.4	156	165.4
11	892	14.0	115	140.6
15	1230	11.6	99	98.5
18	721	9.6	159	154.8
23	681	26.7	204	239.0
28	564	11.6	97	201.0
33	349	7.3	333	213.5
37	895	10.6	92	204.7
40	1142	12.9	147	114.4
43	596	10.8	136	214.9
47	498	9.2	187	265.9
50	409	13.3	111	312.6

KL-6, serum mucin-like glycoprotein antigen; CRP, c-reactive protein; WBC, white blood cells.

prednisolone at $5\,mg \cdot day^{-1}$ on alternate days. Respiratory distress improved, and the patient was discharged from the ICU on April 7 (51 POD).

The KL-6 was analyzed by enzyme immunoassay (Eitest KL-6, Sanko Junyaku, Tokyo, Japan). The normal range of serum KL-6 concentration was below $400\,U \cdot ml^{-1}$ in our laboratory.

The serum concentration of KL-6 was in the normal range on admission to the ICU but increased to $1230\,U \cdot ml^{-1}$ when chest X-ray findings showed signs of IP, then decreased gradually after steroid pulse therapy. The variation in serum KL-6 concentration was closely correlated with the improvement of the patient's distress (Table 1). Pearson's correlation coefficient was calculated to assess the correlation between serum concentrations of KL-6 and the partial pressure of arterial oxygen/fraction of inspired oxygen (PaO_2/FiO_2) (Fig. 1). A high correlation was found between them ($r^2 = 0.292$, $P = 0.0251$).

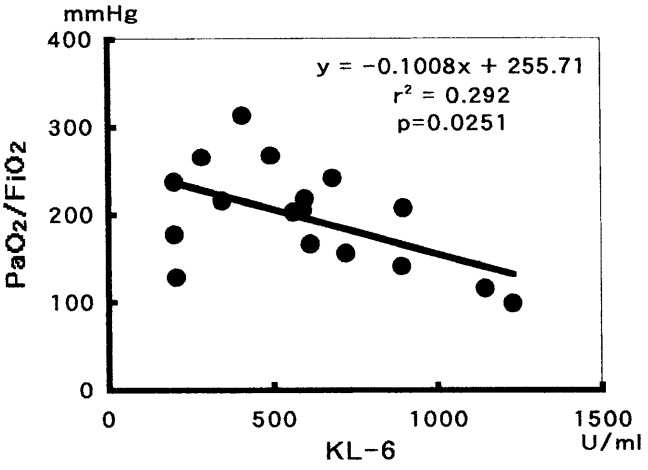

Fig. 1. Correlation analysis between serum concentrations of mucin-glycoprotein antigen (KL-6) and partial pressure of arterial oxygen/fraction of inspired oxygen (PaO_2/FiO_2)

Discussion

Interstitial pneumonia, a serious respiratory complication in the ICU, is difficult to diagnose and treat. Objective, rapid evaluation is required at the acute stage, or exacerbation may result. Conventional indicators used to diagnose IP are clinical symptoms, chest radiography, CT, gallium (Ga) scintigraphy, increased neutrophils and lymphocytes in the bronchoalveolar lavage (BAL) fluid, and increased lactate dehydrogenase (LDH), carcinoembryonic antigen (CEA), and CRP as determined hematologically and serologically. However, no indicator that is highly sensitive and specific to IP is available to allow easy and rapid determination to monitor the disease activity.

KL-6, discovered by Kohno et al. in 1988, is a glycoprotein antigen expressed in type II alveolar and bronchiolar epithelial cells and bronchial gland serous cells [1]. It is markedly expressed in type II alveolar cells in patients with IP, showing a high concentration. KL-6 was originally studied as a tumor marker but is presently being evaluated as an indicator of IP activity [2–6].

In our patient, the KL-6 concentration was low after admission to the ICU but increased when a retiform shadow appeared in the left lung on the chest X-ray, gradually peaking just before the first administration of steroid pulse therapy. After steroid pulse therapy, the KL-6 concentration normalized as the chest radiography retiform shadow and respiratory symptoms improved and CRP decreased. KL-6 thus appears to be a useful indicator to monitor IP.

In previous reports, KL-6 reflected the activity and disease in patients with idiopathic IP and with secondary IP, such as drug-induced pneumonia and radiation pneumonitis and with hypersensitivity pneumonitis [7–10]. It is thus very useful for the early detection of IP. KL-6 thus appears to be a useful indicator of IP, especially if it becomes urgent to decide whether treatments requiring careful consideration, such as steroid pulse therapy, should be applied, because the treatment protocols for interstitial and bacterial pneumonia differ.

In conclusion, we treated a case of IP in which the serum marker KL-6, which is reported to be highly specific to IP, was monitored over time. KL-6 was very useful for the diagnosis of IP and as an indicator of its activity.

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