Mod Rheumatol (2007) 17:262–264
DOI 10.1007/s10165-007-0579-6

CASE REPORT

Yohei Kida · Etsuko Maeshima · Kanako Furukawa
Tomohiro Ichikawa · Mikako Goda · Masakazu Ichinose

A case of polymyositis with a significantly high level of KL-6 associated with pancreatic cancer

Received: July 28, 2006 / Accepted: February 27, 2007

Abstract A 53-year-old man was diagnosed with polymyositis (PM) in 1997 and treated with prednisolone. The subjective symptoms of pneumonitis were poor. However, the KL-6 values were elevated to 2230 IU/l in March 2001. Abdominal computer tomography findings revealed a pancreatic-tail tumor and multiple liver nodules, diagnosed as primary pancreatic adenocarcinoma with multiple liver metastasis. The stage of the pancreatic cancer was IV, and curative surgery of the tumor was not indicated. Chemotherapy and radiotherapy were administered for the liver metastasis. However, these therapies were ineffective against the tumors. The patient died on 12 September 2001. If a high level of KL-6 is found without the increasing activity of lung disease containing interstitial pneumonia in PM patients, examination for the internal malignancies including pancreatic cancer should be performed, although cases of PM with a significantly high level of KL-6 associated with pancreatic cancer are rare.

Key words KL-6 · Pancreatic cancer · Polymyositis

Introduction

Polymyositis/dermatomyositis (PM/DM) is an inflammatory connective tissue disease predominantly involving skeletal muscle.[1] Patients with PM/DM are reported to have higher incidences of malignancies.[2] Generally, KL-6 is known as a useful marker for diagnosis and evaluation of the activity of interstitial pneumonitis.[3] We report a case of PM with a significantly high level of KL-6 associated with pancreatic cancer.

Y. Kida[1] (✉) · E. Maeshima · K. Furukawa · T. Ichikawa · M. Goda · M. Ichinose
Third Department of Internal Medicine, Wakayama Medical University, 811-1 Kimiidera, Wakayama 641-8509, Japan

Present address:
[1] Department of Inernal Medicine, Kainan City Hospital, 272-3 Hikata, Kainan 642-0002, Japan
Tel. +81-73-482-4521; Fax +81-73-482-9551
e-mail: yofactory@yahoo.co.jp

Case report

A 53-year-old man was diagnosed with PM in February 1997. Arthralgia, muscular pain, and weakness, elevated creatine kinase isozyme (CK) (1745 IU/l), anti-Jo-1 antibody positive, and the pathology findings of muscle biopsy (lymphoid inflammatory infiltrates) accorded with the 1975 revised criteria for the classification of PM.[1] No abnormal findings were revealed by digestive endoscopy, or chest and abdominal computed tomography (CT). KL-6 values were within normal limits (322 U/ml) at this time. Other laboratory findings are given in Table 1. The administration of prednisolone (PSL) 60 mg/day after intravenous methylprednisolone pulse therapy (1 g/day for 3 days) was started afterwards. The dosage of PSL was reduced gradually to 5 mg every other day with the recovery of the symptoms. There were no abnormalities in CK value until March 2001. During this period CK changed from 89 to 190 IU/l, aspartate aminotransferase (AST) from 22 to 35 IU/l, and lactate dehydrogenase (LDH) from 150 to 185 IU/l. The KL-6 value had not been even measured once because there were no subjective symptoms and the breast sound was clear. On regular blood test, the KL-6 values were elevated to 3971 U/ml in March 2001. At first, increased activity of interstitial pneumonitis was suspected, and chest X-ray and chest CT were performed. No deterioration of interstitial pneumonitis was seen. However, abdominal CT findings revealed a pancreatic tail tumor (Fig. 1a) and multiple liver tumors (Fig. 1b). The patient was admitted to our hospital for treatment of the tumors in April 2001. There were no subjective symptoms at that time of PM including arthralgia and muscular pain. On admission, body temperature was 37.5°C, blood pressure 110/70 mmHg, and heart rate 60 beats/min. The patient was completely awake and alert. There was no anemia or jaundice. One of the liver tumors was palpable in the epigastric region, but there was no tenderness or

Table 1. Laboratory findings on admission

Blood count		**Serology**	
WBC	8800/μl	C-reactive protein	0.38 mg/dl
RBC	458×10^4/μl	IgG	1169 mg/dl
Hemoglobin	12.0 g/dl	IgA	163 mg/dl
Hematocrit	37.5%	IgM	438 mg/dl
Platelet	20.9×10^4/μl	Antinuclear antibody	Negative
Chemistry		Anti-Jo-1 antibody	Negative
Total protein	7.0 g/dl	HBs-antigen	Negative
Albumin	4.4 g/dl	HCV-antibody	Negative
Blood urea nitrogen	14 mg/dl		
Creatinine	0.6 mg/dl	**Tumor markers**	
Uric acid	7.0 mg/dl	AFP	5.6 ng/ml
Sodium	141 mEq/l	CEA	8.0 ng/ml
Potassium	4.0 mEq/l	CA19-9	2181 ng/ml
Chloride	103 mEq/l	KL-6	3191 U/ml
AST	49 IU/l		
ALT	45 IU/l		
LDH	228 mg/dl		
ALP	166 IU/l		
Total bilirubin	0.2 mg/dl		
Amylase	95 IU/l		
Glucose	102 mg/dl		
Total-cholesterol	196 mg/dl		
Triglyceride	62 mg/dl		
Creatine kinase	189 IU/l		
Aldolase	3.5 IU/l		

AST, aspartate aminotransferase; ALT, alanine aminotransferase; ALP, alkaline phosphatase; LDH, lactate dehydrogenase; AFP, α-fetoprotein; CEA, carcinoembryonic antigen; CA19-9, carbohydrate antigen

muscular reflex in this region. White blood cells, hemoglobin, and hematocrit were 8800/μl, 12.0 mg/dl, and 37.5%, respectively, indicating slight anemia. Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) had increased to 42 IU/l and 41 IU/l, respectively. Carcinoembryonic antigen (CEA) and carbohydrate antigen 19-9 (CA19-9), as tumor markers, were elevated at 8.0 ng/ml and 2181 U/ml, respectively. Abdominal CT findings showed a 2-cm-diameter pancreatic-tail tumor and multiple liver tumors. There were no abnormal findings on digestive endoscopy and other examinations. The tumor was diagnosed as primary pancreatic adenocarcinoma with multiple liver metastases. The stage of the pancreatic cancer was IV, and the curative surgery of the tumor was not indicated.

Chemotherapy (fluorouracil 600 mg/day, orally) and radiotherapy (total 45 Gy) were performed for the liver metastasis. However, these therapies were ineffective against the tumors. The patient died on 12 September 2001.

Discussion

Polymyositis/dermatomyositis is strongly associated with malignant disease. Sigurgeirsson et al.[2,13] reported that 1.77% (3/146) PM patients occurred for pancreatic cancer. The malignant diseases most associated with PM were, in descending order: lung cancer, rectum and colon cancer, pancreatic cancer, kidney cancer, stomach cancer, breast cancer.

14.9% of cases of PM show cancer, which develops after diagnosis of PM. There has been only one report where KL-6 was measured for a case of PM with pancreatic cancer.[3] However, in that case the serum KL-6 was not elevated.

Generally, KL-6 is a useful marker of the activity of interstitial pneumonia;[4] additionally, it is expressed in various kinds of malignant tissue, including lung adenocarcinoma [52% (17/33)], pancreatic cancer [44% (4/9)], breast cancer [40% (8/20)], lung squamous cell carcinoma [18% (4/22)], lung small cell carcinoma [8% (1/13)], and hepatocellular carcinoma [13% (1/8)].[5] There have been some cases associated with malignancy other than lung cancer with significantly high level of KL-6.[6,7]

KL-6 is a mucin-like high-molecular weight glycoprotein classified as Cluster 9 (MUC-1). LISA 101 and 201 constitute a part of KL-6. The KL-6 associated mucin LISA 101 is increased by more than 50% only in pancreatic cancer.[8] A pancreatic cancer patient with MUC-1 and small intestinal mucin antigen (SIMA) stromal expression around cancer cells was reported to have died within 25 months after surgery. The expression of MUC-1 and SIMA stromal around cancer cells is a sensitive prognostic marker.[9] Unfortunately, SIMA was not examined in the present case.

It has been suggested that KL-6 might be useful in PM/DM patients as an indication of an internal malignancy or interstitial lung disease[10]. It would therefore seem reasonable to continue surveillance for at least the first 2 or 3 years after a diagnosis of PM.[11] However, in this case the subjective symptoms of pneumonia were not significant, and pan-

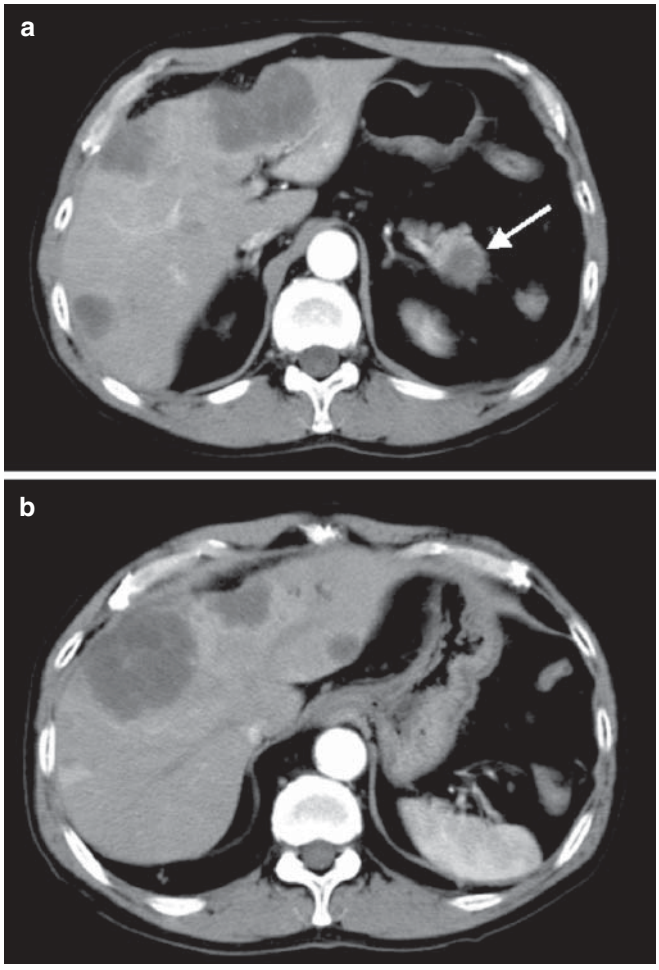

Fig. 1a,b. Abdominal computed tomography findings revealed a pancreatic-tail tumor (**a**, *arrow*) and multiple liver tumors (**b**)

creatic cancer occurred 4 years after PM was diagnosed. There are some case reports of malignancies occurring 5 years after diagnosis of PM.[12] There is no consensus in the standard that should suspect the malignancies. In general, an abnormal value of KL-6 is above 500 IU/l. Actually, there are often many cases with an exacerbation of interstitial pneumonia. If there is a high level of KL-6 without exacerbation of interstitial pneumonia or other tumor markers except KL-6 were elevated, internal malignancies should be suspected. To search for malignancies in PM/DM patients would therefore have to be followed up for at least 5 years after PM is diagnosed.[13] In conclusion, if there is a high level of KL-6 without evidence of lung disease including interstitial pneumonia in PM/DM patients, internal malignancies should be suspected.

References

1. Bohan A, Peter JB. Polymyositis and dermatomyositis. N Engl J Med 1975;292:344–7.
2. Hill CL, Zhang Y, Sigurgeirsson B. Frequency of specific cancer types in dermatomyositis and polymyositis: a population-based study. Lancet 2001;357:96–100.
3. Inarte LM, Lozano de LF, Carcia-Bragodo F. Trigeminal sensory neuropathy with dermatomyositis associated with a pancreatic malignancy. J Rheumatol 1990;17:276–7.
4. Ohnishi H, Yokoyama A, Kondo K, Hamada H, Abe M, Nishimura K, et al. Comparative study of KL-6, surfactant protein-A, surfactant protein-D, and monocyte chemoattractant protein-1 as serum markers for interstitial lung diseases. Am J Respir Crit Care Med 2002;165:378–81.
5. Kohno N, Akiyama M, Kyoizumi S, Hakoda M, Kobuke K, Yamakido M, et al. Detection of soluble tumor associated antigens in sera and effusions using novel monoclonal antibodies, KL-3 and KL-6, against lung adenocarcinoma. Jpn J Clin Oncol 1988;18: 203–16.
6. Kodera M, Usuda T. A case of dermatomyositis with significantly high level of KL-6 associated with ovarian cancer. Ryumachi 2002; 42:694–8.
7. Kawata T, Tsukagoshi H, Mashimo T, Kakizaki S, Kasahara T, Iwasaki J, et al. KL-6-producing invasive thymoma. Intern Med 2002;41:979–82.
8. Kohno N, Inoue Y, Hamada H, Fujioka S, Fujino S, Yokoyama A et al. Difference in sero-diagnostic values among KL-6 associated mucins classified as cluster 9. Int. J Cancer Suppl 1994;8:81–3.
9. Yamasaki H, Ikeda S, Okajima M, Miura Y, Asahara T, Kohno N, et al. Expression and localization of MUC-1, MUC-2, MUC5AC, and small intestinal mucin antigen in pancreatic tumors. Int J Oncol 2004;24:107–13.
10. Kubo M, Ihn H, Yamane K, Kiuchi K, Yazawa N, Soma Y, et al. Serum KL-6 in adult patients with polymyositis and dermatomyositis. Rheumatology 2000;39:632–6.
11. Chow WH, Gridley G, Mellemkjaer L, McLaughlin JK, Olsen JH, Fraumeni JF Jr, et al. Cancer risk following polymyositis and dermatomyositis: A nationwide cohort study in Denmark. Cancer Causes Control 1995;6:9.
12. Whitmore SE, Rosenshein NB, Provost TT. Ovarian cancer in patents with dermatomyositis. Medicine (Baltimore) 1994;73:153.
13. Sigurgeirsson B, Lindelof B, Edhag O, Allander E. Risk of cancer in patients with dermatomyositis or polymyositis. A population-based study. N Engl J Med 1992;326:363–7.