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CASE REPORT

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Cyclosporin-A ameliorated interstitial pneumonitis in a patient with amyopathic dermatomyositis

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Abstract A 40-year-old woman with amyopathic dermatomyositis (ADM) developed acute pneumonitis. Despite pulse methylprednisolone therapy, the pneumonitis worsened. We therefore initiated cyclosporin-A (Cy-A) therapy with success, although *Pneumocystis carinii* (PC) pneumonia occurred. Coexistence of dermatomyositis (DM)-related pneumonitis and PC pneumonia was diagnosed by means of chest X-ray findings, KL-6, and polymerase chain reaction (PCR) for PC. We thus continued Cy-A therapy to ameliorate the pneumonitis. Cy-A appeared to be effective for corticosteroid-resistant pneumonitis in a patient with DM.

Key words Cyclosporin-A (Cy-A) · Dermatomyositis (DM) · Interstitial pneumonitis (IP) · KL-6 · *Pneumocystis carinii* (PC)

Introduction

Interstitial pneumonitis (IP) is a major complication among patients with dermatomyositis (DM) and polymyositis (PM). This condition contributes to the high mortality rate in patients with DM/PM; second only to malignant diseases.

In recent decades, amyopathic DM (ADM), a subgroup of DM that lacks the myositic features but manifests dermatitis signs, has been reported.[1–3] Patients with ADM are likely to develop severe IP, resulting in high mortality rates.[4] Thus, an effective treatment against DM-related IP is needed to save lives and to maintain quality of life. At present, cyclosporin-A (Cy-A) is considered effective against IP in patients with DM.[2–6]

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KL-6, a glycoprotein in the MUC-1 mucin family, is a newly established parameter for interstitial pulmonary fibrosis. It does not show elevated levels in the sera of patients with pulmonary infection except for *Pneumocystis carinii* (PC) peumonia.[7,8] We successfully treated an ADM patient with IP by Cy-A.

Case report

A 40-year-old woman developed a nonproductive cough and dyspnea in March 1998 and was referred to Nihon University Itabashi Hospital on 1 April 1998. On admission, erythema was verified in the first, second, and third metacarpophalangeal joints and the whole proximal interphalangeal joints bilaterally, which were findings compatible with Gottron's sign. Heliotrope erythema and Raynaud's phenomenon were absent, although poikiloderma was confirmed in the forearms. She did not exhibit myopathic signs: findings of manual muscle test were normal. Fine crackling sounds were audible in both lung fields. Chest X-ray and computed tomography (CT) revealed diffuse granular shadows in the bilateral lung fields (Fig. 1a, b). Blood gas analysis at rest breathing room air showed minimal hypoxemia: 80.4 mmHg PaO_2, 36.0 mmHg $PaCO_2$, and 96.2% SaO_2. Pulmonary function testing disclosed the presence of restricted diffusion capacity: 80.3% %DLCO, 59.9% %VC, and 96.2% $\%FEV_{1.0}$. Serum levels were elevated for ALT (130 IU/l), AST (121 IU/l), and aldolase (7.5 IU/l), whereas levels of creatinine phosphokinase (CK) and myoglobulin were normal. No abnormal immunologic parameters were observed except for ANA 1:20, C-reactive protein (CRP) 2.5 mg/dl, and CH50 63.4 U/ml. Electromyographic findings manifested short duration and low amplitude in the right biceps, suggesting a limited myogenic pattern, although the findings of the manual muscle test were normal in all of the muscles. Specimens obtained by skin biopsy from the right hand and forehead were compatible with dermatitis: liquefaction degeneration, hypogranulation of the epidermis,

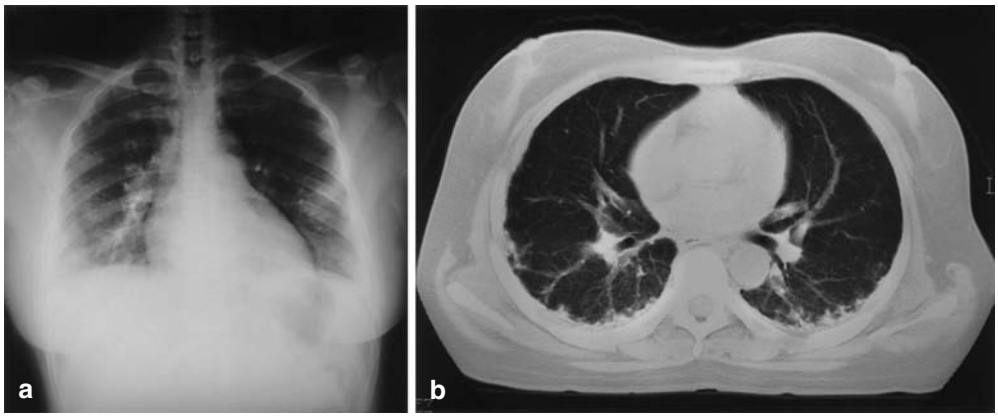


Fig. 1. Findings of chest X-ray (**a**) and CT on admission (**b**)

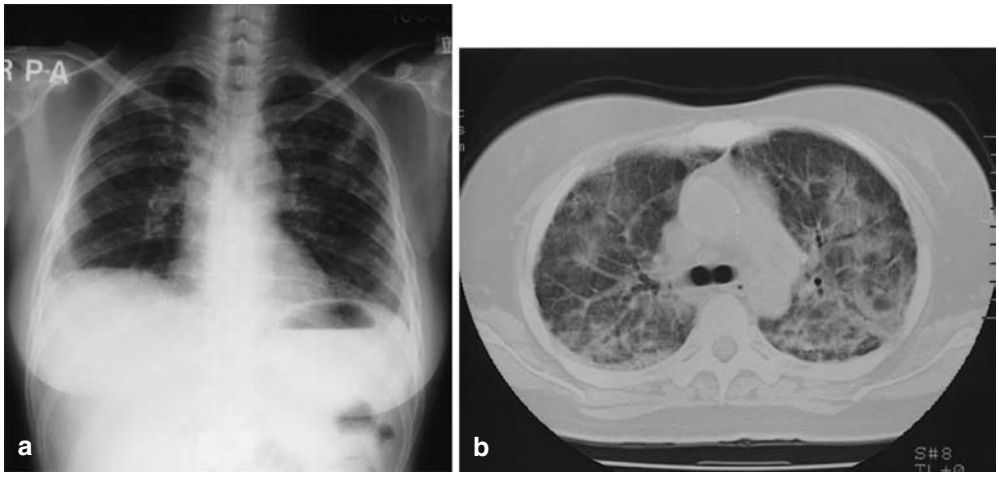


Fig. 2. Findings of chest X-ray (**a**) and CT on 16 June (**b**)

and perivascular infiltration of mononuclear cells. We thus diagnosed the patient with ADM rather than typical DM.

During the disease course, the chest X-ray findings showed exacerbations of the granular shadows. Blood gas analysis revealed marked hypoxemia: 46.5 mmHg PaO_2, 36.4 mmHg $PaCO_2$, and 84.2% SaO_2 with oxygenation 13 l/min 50%. We therefore initiated a pulse methylprednisolone therapy at 1000 mg for 3 successive days followed by 60 mg/day oral prednisolone beginning on 14 April. Despite such treatment, the chest X-ray findings failed to improve. We could not detect any signs of infection. In addition to such clinical features, pulmonary function testing revealed worsening of diffusion capacity, i.e., %DLCO was decreased to 48% on 25 April. We thus prescribed Cy-A at 200 mg/day beginning on 28 April. She initially responded well to this treatment (85.2 mmHg PaO_2 with oxygenation 4 l/min to 70.9 mmHg PaO_2 on room air). However, dyspnea recurred and the %DLCO was 50.2%. Because it is hard to differentiate exacerbated IP from an opportunistic infection such as PC, mycobacteria, fungi, and some viruses, we performed a bronchoscopy on 4 June. The bronchoalveolar lavage fluids (BALF) were prepared for microbiology, virology, and KL-6 to establish a diagnosis. The serum level of KL-6 was also measured at the same time. Using polymerase chain reaction (PCR) we detected DNA of PC in the BALF. Other microbiological studies of the BALF showed negative results, although β-D-glucan was elevated to 251 pg/μl in the sera on 11 June. The levels of KL-6 in the sera and the BALF were elevated to 2170 U/ml (normal <500) and 604 U/ml (normal <340), respectively. After the procedure, dyspnea and pyrexia exaggerated with a CRP elevation to 5 mg/dl on 10 June. We thus initiated antibiotic therapy and anti-fungi therapy on 11 June. Nevertheless, pyrexia persisted and CRP rose to 10 mg/dl on 15 June. In addition, a chest CT taken on 16 June revealed the newly developed shadows, ground grass opacity, suggesting PC pneumonia (Fig. 2a, b). Based on the BALF analysis, radiologic findings, and marked elevation of KL-6 in the serum, we diagnosed her as having PC pneumonia and exacerbated IP. We thus added sulfamethoxazole/trimethoprim on 16 June. As a result, her symptoms lessened, and chest X-ray findings improved. The subsequent clinical course was uneventful, and she was discharged on 25 July (Fig. 3a, b). She was placed on a regimen of Cy-A 225 mg/day with prednisolone 20 mg/day and was monitored carefully for serum levels of Cy-A. The serum levels of KL-6 gradually decreased after discharge, had lowered to 632 U/ml in December 1998, had almost normalized (580 U/ml) in August, and were normalized in October 1999. In July 2000, her chest X-ray findings and KL-6 levels

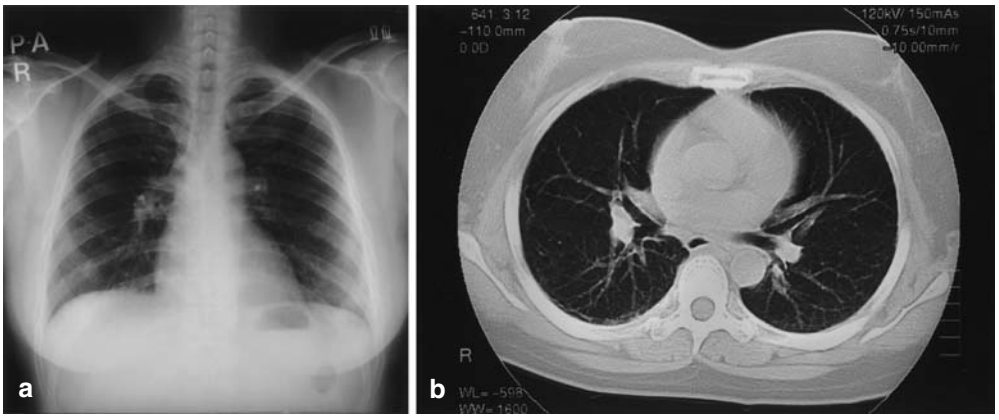


Fig. 3. Findings of chest X-ray (**a**) and CT on discharge (**b**)

were normal (268 U/ml), and she now takes prednisolone 10 mg/day.

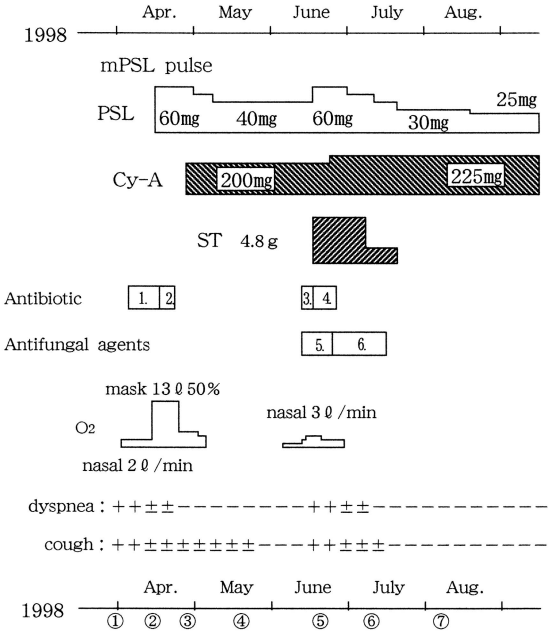
Discussion

ADM was first reported in 1975,[1] and the distinctive criteria were elucidated by Euwer and Sontheimer in 1993.[6] They consist of four clinical features: specific findings for DM such as Gottron's sign, heliotrope erythema, perinail erythema, and capillary dilatation; dermal biopsy findings compatible with DM; loss of myopathy on the girdle muscles; and no elevations of myogenic enzyme (CK and aldolase) in the sera. The latter two features require a 2-year observation.

Our patient apparently fulfilled two of the four criteria: the presence of Gottron's sign and the pathologic findings compatible with DM. Concerning myopathic signs, we could not verify myopathy and the elevation of myogenic enzymes in the sera after more than 2 years Cy-A treatment. In addition, the initial elevation of aldolase was faint and transient. Taking these observations into account, we diagnosed our patient as having ADM. Because her IP progressively worsened despite pulse methylprednisolone therapy, and Cy-A had been reported to be effective for ADM-related pneumonitis, we initiated Cy-A with successful results.[9,10]

For making the differential diagnosis and evaluating the efficacy of Cy-A against IP, we measured the levels of KL-6 in the sera whilst also monitoring chest X-rays, blood gas parameters, serum lactic dehydrogenase (LDH), and serum levels of Cy-A. In our patient, the serum LDH failed to correlate with the changes in X-ray findings or with clinical symptoms. Serum KL-6 levels appeared useful for evaluating IP activity after PC pneumonia had been cleared.

KL-6 is a glycoprotein in the MUC-1 mucin family and is strongly expressed on the surface of type II alveolar epithelium when alveolar damage causes a fibrosing process involving a mistaken attempt at repair; the usefulness of KL-6 in evaluating IP was reported by Kohno et al. in 1989.[11] An extended study was performed to verify its usefulness for the evaluation of IP activity in 1996.[12–14] Serum levels of KL-6 do not elevate in patients with common pneumonia except for PC; therefore, we can use KL-6 to make a differential diagnosis between IP exacerbation and common pneumonia caused by bacteria and fungi.[12–14] With the KL-6 results, we could continue to monitor Cy-A treatment to ameliorate IP in our patient after PC pneumonia had been controlled.[13,14]



	①	②	③	④	⑤	⑥	⑦
date	3.31#	4.14	4.28	5.18	6.18	7.9##	8.5
O_2	RA	13 ℓ 50%	4 ℓ	RA	3 ℓ	RA	RA
PaO_2 (mmHg)	80.4	46.5	85.2	70.9	81.4	88.7	ND
LDH (IU/ℓ)	388	394	308	260	646	345	327
CRP (mg/dℓ)	2.59	4.49	0.10	0.21	6.18	0.31	0.73

Fig. 4. Clinical course. Cy-A, Cyclosporin-A; mPSL, methylprednisolone; ST, sulfamethoxazole/trimethoprim; 1, cefactor (750 mg); 2, sulbactam sodium/ampicillin sodium (3 g), amikacin sulfate (600 mg); 3, sulbactam sodium/ampicillin sodium (3 g); 4, cefozopran hydrochloride (3 g); 5, amphotericin B (15 mg); 6, fluconazole (200 mg); #, admission; ##, discharge; *RA*, room air; *ND*, not done; *LDH*, lactic dehydrogenase; *CRP*, C-reactive protein

In conclusion, Cy-A may be useful against corticosteroid-resistant IP that develops in a patient with ADM.

References

1. Krain LS. Dermatomyositis in six patients without initial muscle involvement. Arch Dermatol 1975;111:241–5.
2. Person CM. Polymyositis and dermatomyositis. In: McCarty DJ, editor. Arthritis and allied conditions. 9th ed. Philadelphia: Lea and Ferbiger; 1979. p. 742–61.
3. Bohan A, Peter JB. Polymyositis and dermatomyositis. N Engl J Med 1975;292:344–7.
4. Nawata Y, Kurasawa K, Takabayashi K, Mike S, Watanabe N, Hiragiri M, et al. Corticosteroid resistant interstitial pneumonitis in dermatomyositis/polymyositis: prediction and treatment with cyclosporin. J Rheumatol 1999;26:1527–33.
5. Euwer RL, Sontheimer RD. Amyopathic dermatomyositis (dermatomyositis sine myositis): presentation of six new cases and review of the literature. J Am Acad Dermatol 1991;24:959–66.
6. Euwer RL, Sontheimer RD. Amyopathic dermatomyositis: a review. J Invest Dermatol 1993;100:S124–7.
7. Kobayashi J, Kitamura S. KL-6: a serum marker for interstitial pneumonia. Chest 1995;108:311–15.
8. Hamada H, Kohno N, Yokoyama A, Hirasawa Y, Hiwada K, Sakatani M, et al. KL-6 as a serologic indicator of *Pneumocystis carinii* pneumonia in immunocompromized hosts. Intern Med 1998;37:307–10.
9. Kavanagh GM, Ross JS, Black MM. Dermatomyositis treated with cyclosporin. J R Soc Med 1991;84:306.
10. Lueck CJ, Trend P, Swash M. Cyclosporin in the management of polymyositis and dermatomyositis. J Neurol Neurosurg Psychiatry 1991;54:1007–8.
11. Kohno N, Koizumi S, Awaya S. New serum indicator of interstitial pneumonitis activity: sialylated carbohydrate antigen KL-6. Chest 1989;96:68–73.
12. Kitamura S, Hiwada K, Kobayashi J, Kohno N, Kawai T, Satou A, et al. Use of the ED046 kit to analyze serum KL-6 in patients with pneumonitis (in Japanese, abstract English). Nihon Kyobu Shikkan Gakkai Zasshi 1996;34:639–45.
13. Kohno N, Awaya Y, Oyama T. KL-6, a mucin-like glycoprotein, in bronchoalveolar lavage fluid from patients with interstitial lung disease. Am Rev Respir Dis 1993;148:637–42.
14. Yokoyama A, Kohno N, Kondo K, Ueda S, Hirasawa Y, Watanabe K, et al. Comparative evaluation of sialylated carbohydrate antigen, KL-6, CA19–9, and SLX as serum markers for interstitial pneumonia. Respirology 1998;3:199–202.