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[Case Report]

A case of dermatomyositis complicated with pleural effusion and massive ascites

Naoki Matsuoka[1)], Tomoyuki Asano[1)], Shuzo Sato[1)], Tomomi Sasajima[2)], Yuya Fujita[1)], Jumpei Temmoku[1)], Makiko Yashiro Furuya[1)], Haruki Matsumoto[1)], Eiji Suzuki[1)], Hiroko Kobayashi[1)], Hiroshi Watanabe[1)] and Kiyoshi Migita[1)]

[1)]*Department of Rheumatology, Fukushima Medical University School of Medicine, Fukushima, Japan,*
[2)]*Department of Rheumatology, Fukushima Rosai Hospital, Fukushima, Japan*

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Abstract

We report a patient with dermatomyositis (DM) complicated with progressive pleural effusion and ascites. A 40-year-old woman was hospitalized in our department because of severe myalgia and dysphagia, complicated with pleural effusion and massive ascites. Elevated muscle enzymes, Gottron's papules, and electromyography (EMG) confirmed the diagnosis of DM. Combined immunosuppressive treatment consisting of intravenous immunoglobulin (IV-IG), intravenous-cyclophosphamide (IV-CY) and tacrolimus resolved her myopathy and dysphagia as well as pleural effusion and massive ascites. Her clinical course and the absence of other factors that cause pleural effusion and ascites suggest that these symptoms were related to the pathophysiology of DM.

Key words : ascites, dermatomyositis, immunosuppressive treatment, pulmonary effusion

Introduction

Polymyositis-dermatomyositis (PM-DM) is a chronic inflammatory disorder that involves muscle and skin[1)]. Many cases of PM-DM are associated with internal malignancies and interstitial lung disease[2)]. In contrast to the frequent association of interstitial lung disease (ILD) in patients with DM, the development of pleural effusion and ascites in DM is regarded as rare and there is little information regarding their incidence, etiology, course, and prognosis[3,4)]. Therefore, it could be difficult to differentiate these cases due to DM from those due to other cases, including infections and malignancies. We herein report a female with DM complicated by pleural effusion and massive ascites. These conditions appear to be signs of her severe primary autoimmune disorder, DM. We hypothesize on the mechanisms behind the accumulating effusion and the therapeutic effect of immunosuppression in this unusual subset of DM.

Case report

A 40-year-old Japanese female was transferred to our hospital with severe myalgia and dysphagia. Previously admitted to a local hospital for elevated levels of muscle enzyme, she developed dysphagia and muscle weakness and transferred to our care for further evaluation. She had never smoked and had no significant past medical history. Computed tomography (CT) showed pleural effusion and massive ascites without evidence of internal malignancy or interstitial lung disease. The patient had skin lesions characteristic of dermatomyositis, which included facial erythema and Gottron's papules (Figure 1). Laboratory tests (Table 1) revealed a white blood cell (WBC) count of 6,000/μL (neutrophils 79%, lymphocytes 10%, and monocytes 10%), total protein 5.3 g/dL, albumin 2.7 g/dL, creatine kinase (CK) 2,613 U/L, lactate dehydrogenase (LDH) 543 U/L, C-reactive protein 0.05 mg/dL, ferritin 297 ng/mL, KL-6 567 U/mL, TSH 1.41 μU/mL, Free T4 (FT4) 0.86 ng/dL, Free T3 (FT3) 0.94 pg/mL. FT4

Corresponding author : Kiyoshi Migita MD E-mail : migita@fmu.ac.jp
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Table 1. Laboratory Findings on Admission

Peripheral blood		ANA	1 : 80 (<×160)
Red blood cells	537×10⁴/μL	Anti-ds-DNA Ab	(−) (<9.9)
Hemoglobin	15.8 g/dL	Anti-sm Ab	(−) (<6.9)
Hematocrit	48.0%	Anti-U1RNP Ab	(−) (<4.9)
Platelet	17.0×10⁴/μL	Anti-SSA Ab	(−) (<6.9)
White blood cells	6,000/μL	Anti-SSB Ab	(−) (<6.9)
Neutrophil	79.0%	Anti-Jo-1 Ab	(−) (<6.9)
Eosinophil	0.0%	Anti-MDA5 Ab	(−) (<32)
Monocyte	10.0%	Anti-ARS Ab	(−) (<24.9)
Lymphocyte	10.0%	Anti-TIF1-γ Ab	(−) (<32)
Basophil	1.0%	Anti-Mi-2 Ab	(−) (<53)
Blood chemistry		HBs-Ag	(−)
Total protein	5.3 g/dL (6.6-8.1)	HCV-Ab	(−)
Total bilirubin	0.6 mg/dL (0.4-1.5)	HIV-AgAb	(−)
Albumin	2.7 g/dL (4.1-5.1)	Tuberclosis specific interferon γ	(−)
Aspartate transaminase	150 U/L (13-33)	sIL-2R	725 U/ml (121-613)
Alanine transaminase	76 U/L (8-42)	CEA	1.3 ng/ml (0.0-5)
Lactate dehydrogenase	543 U/L (260-119)	CA19-9	13.9 U/ml (0.0-37)
Alkaline phosphatase	150 U/L (80-250)	CA-125	57 U/ml (0.0-35)
Creatine kinase	2,613 U/L (62-287)	CA15-3	26 U/ml (0.0-31)
Aldolase	19.8 U/L (2.7-7.5)	**Urinalysis**	
Myoglobin	676 ng/mL (0.0-60)	pH	6.5
Blood urea nitrogen	13.0 mg/dL (8-20)	S.G.	1.026
Creatinine	0.43 mg/dL (0.46-0.79)	U-protein	(1+)
Na	128 mEq/L (138-145)	U-bacterium	(1+)
K	4.0 mEq/L (3.6-4.8)	U-red blood cells	0-1/HPF
Cl	96 mEq/L (101-108)	U-white blood cells	1-4/HPF
Serological tests		hyalin cast	0-1/HPF
C-reactive protein	0.05 mg/dL (<0.30)	**Ascites**	
Erythrocyte sedimentation rate	4 mm/hr (<15)	Total protein	2.9 g/dL
Ferritin	297 ng/ml (12-60)	Albumin	1.8 g/dL
IL-6	43.9 pg/ml (0.1-1.9)	Lactate dehydrogenase	307 U/L
VEGF	39 pg/ml (11.4-270)	Glucose	159 mg/dL
KL-6	567 U/ml (0.0-499)	Cytology	class I
IgG	763 mg/dL (870-1,700)	Culture	negative
IgA	141 mg/dL (110-410)		
IgM	162 mg/dL (35-220)		
C3	83 mg/dL (65-135)		
C4	33 mg/dL (13-35)		
TSH	1.41 μU/mL (0.5-5.0)		
FT4	0.86 ng/dL (0.90-1.70)		
FT3	0.94 pg/mL (2.30-4.00)		

Abbreviation : IL-6 ; Interleukin-6, VEGF ; Vascular Endothelial Growth Factor, sIL-2R ; soluble interleukin-2 receptor, TSH ; thyroid stimulating hormone, FT3 ; free thyroid 3, FT4 ; free thyroid 4, ANA ; antinuclear antibodies, Ab ; antibody, MDA5 ; melanoma differentiation-associated gene 5, ARS ; aminoacyl-tRNA synthetase, TIF1-γ ; transcriptional intermediary factor 1-γ, HIV AgAb ; Human Immunodeficiency Virus antigen antibody, HBsAg ; hepatitis B virus surface antigen, HCVAb ; hepatitis C virus antibody, CEA ; carcinoembryonic antigen, CA19-9 ; carbohydrate antigen 19-9, CA125 ; carbohydrate antigen 125, CA15-3 ; carbohydrate antigen 15-3, S.G. ; Spacific Gravity

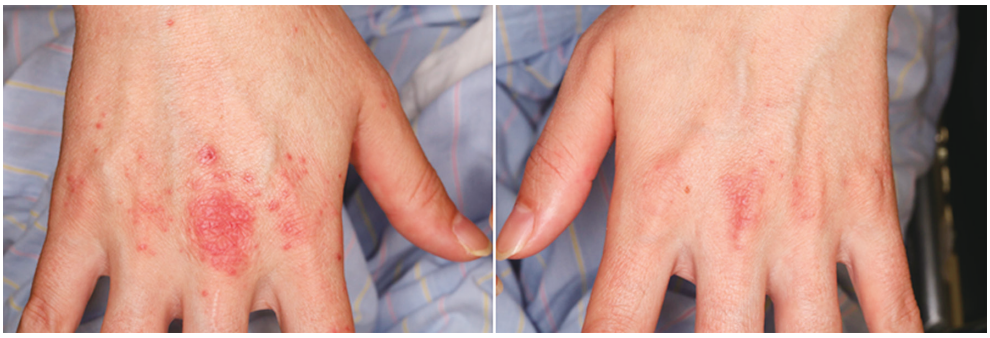

Fig. 1. Cutaneous findings on admission.
Gottoron's papules on the back of both hands were observed.

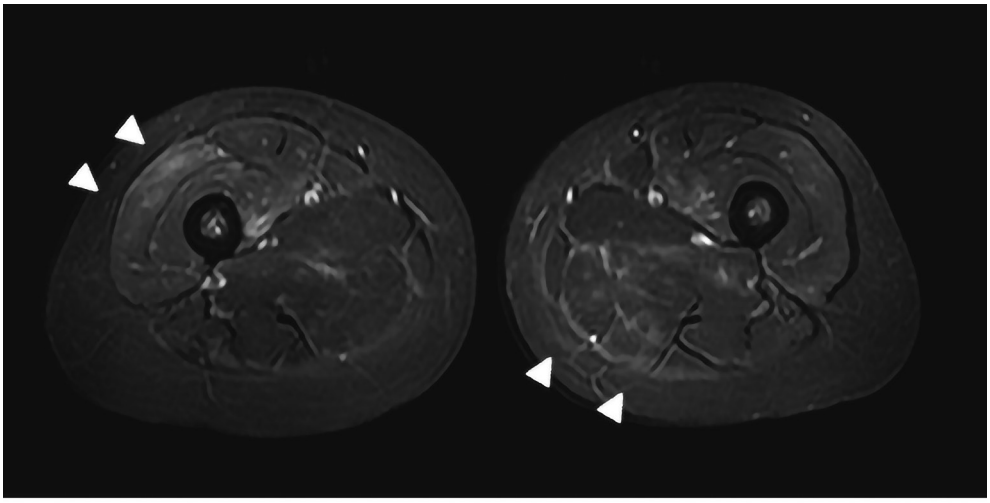

Fig. 2. Magnetic resonance imaging (MRI) of the lower limbs on admission.
Axial short TI inversion recovery (STIR) images showed high signal density in the affected proximal lower limbs (white arrow).

and FT3 were slightly low, consistent with euthyroid sick syndrome. The patient was negative for the presence of anti-nuclear antibody (ANA ; titer 1 : 80) and other autoantibodies, including anti-double-stranded DNA (anti-dsDNA) antibody, anti-Jo-1 antibody, anti-ARS antibody, anti-MDA5 antibody, and anti-TIF1-γ antibody. The panel of autoantibodies was examined using immunoblotting (Euroline autoimmune inflammatory myopathies 16Ag, Euroimmun, Luebeck, Germany), with only anti-PM/Scl-75 antibodies being weakly positive. However, no scleroderma symptoms were evident in this patient, who was negative for anti-Scl-70 antibody.

In addition, negative results were obtained for the presence of tumor markers, including carcinoembryonic antigen (CEA), carbohydrate antigen 19-9 (CA19-9), carbohydrate antigen 125 (CA125) and carbohydrate antigen 15-3 (CA15-3). Abdominocentesis revealed exudative ascites with no evidence of infections or malignancy. Biochemical analysis revealed the following results : TP 2.9 g/dL, LDH 307 U/mL, glucose 159 mg/dL, and culture was negative. An echocardiogram demonstrated normal left ventricular ejection fraction, normal left ventricular wall thickness without pericardial effusion, and normal right heart function. Electromyography revealed typical myopathic patterns : polyphasic and low-amplitude motor unit action potential. MRI showed an increased signal on axial short TI inversion recovery (STIR) images, most prominent in the proximal lower limbs (Figure 2).

The patient fulfilled the diagnostic criteria for DM articulated by Bohan and Peter[5,6] in the presence of typical skin manifestations, elevated muscle enzymes, muscle weakness, and myogenic pattern of electromyography (EMG) ; therefore, muscle bi-

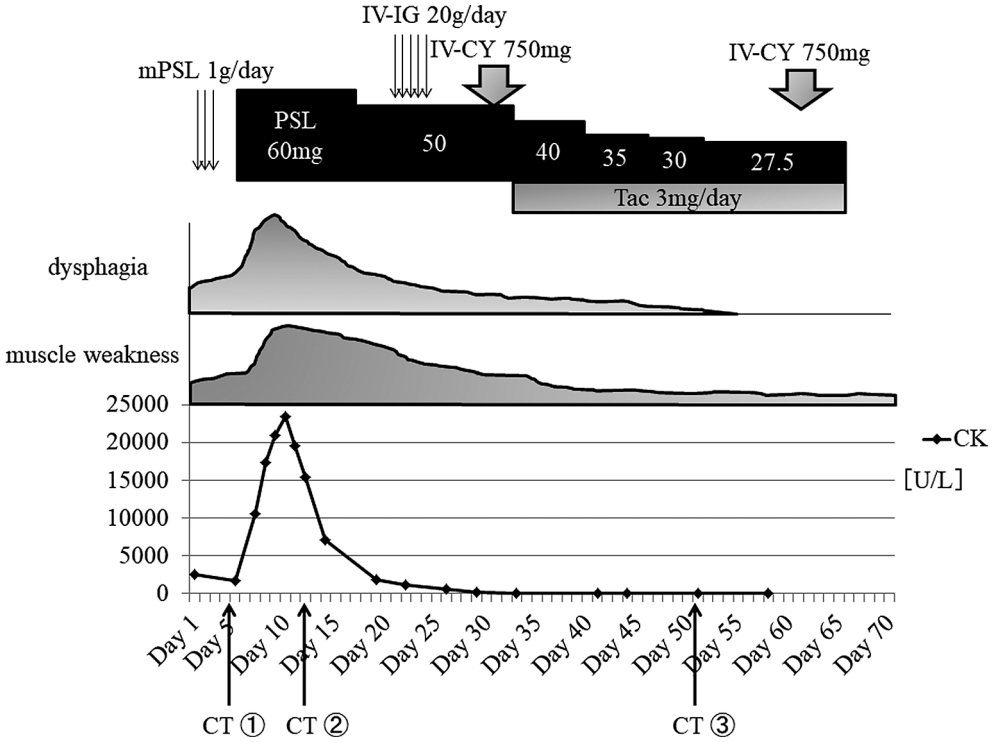

Fig. 3. Clinical course of the patient.
mPSL : methyl prednisolone, PSL : prednisolone, Tac : tacrolimus, IV-CY: high-dose intravenous cyclophosphamide, IV-IG : high-dose intravenous immunoglobulin, CK : creatine kinase, CT : computed tomography

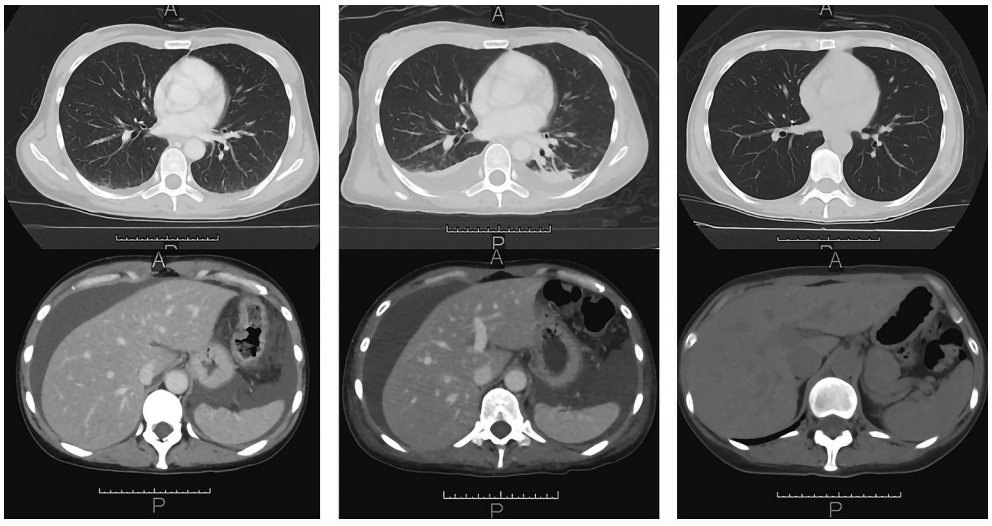

Fig. 4. Changes of ascites and pleural effusions detected by computed tomography (CT) during the clinical course (Day 4, Day 12, Day 54).
With immunosuppressive therapy, ascites and pleural effusions disappeared by Day 54.

opsy was omitted. The clinical course is shown in Figure 3. Our patient received intravenous methyl prednisolone pulse therapy (1,000 mg/day, 3 days). The treatment was followed by oral prednisolone (60 mg/day), without significant improvement in the myositis, muscle weakness, pleural effusion and ascites. Therefore, she was given intravenous immunoglobulin (IV-IG, 400 mg/kg, 5 consecutive days), followed by IV-CY (cyclophosphamide 750 mg), which resulted in remission of the myositis and improvement of the muscle weakness and dysphagia. This was followed by oral prednisolone (40

mg/day) and tacrolimus (3 mg/day). With these treatments, the pleural effusion and massive ascites resolved and the clinical manifestations including myositis and skin lesions improved. During treatment with PSL intermittent IV-CY therapy, creatine kinase (CK) decreased to within the reference interval, and remained there as. PSL was gradually tapered. There was no recurrence of pleural effusions or ascites (Figure 4) and the patient was discharged at Day 70.

Discussion

Pleural effusion associated with connective tissue disease (CTD) is common in patients with rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE)[7], whereas overt pleural effusion and ascites are rarely reported in patients with PM-DM[8]. The lung is the most commonly affected extra-muscular organ in DM[9], whereas pleural complications are rare and the pathology of these complications has not been extensively investigated. Our case report is of a patient with DM in whom pleural effusion and ascites were resolved by combination therapy consisting of corticosteroid and immunosuppressive agents.

Owing to the fact that DM is often associated with malignancies[10], it is necessary to perform thoracentesis or peritoneal tap in DM patients with pleural effusion or ascites. In the present case, cytological analysis for malignancy was negative. Other causes, such as congestive heart failure, hypothyroidism, malignancy, and renal insufficiency, were ruled out in our case. With the frequency of aspiration pneumonia due to respiratory muscle weakness[9], it is difficult to determine the etiology of pleural effusion in DM.

In the present case, analyses for infectious causes were negative. Although we could not completely rule out the possibility of infection, we concluded that this was unlikely since our patient responded well to steroid and immunosuppressant without antibiotics. In parallel with the clinical improvement of the myositis, the patient's pleural effusion and ascites also resolved rapidly.

Clinically important pleural effusion or ascites have rarely been reported in patients with DM.

An immune mechanism appears to have been an important cause of the pleural effusion and ascites in the current case, since there was a prompt response to immunosuppressive treatment after meticulous workup for other etiologies.

Pleural effusion in PM-DM has not been reported as an isolated finding, but only in association with ILD[11]. In the present case, serum KL-6 was slightly high, but CT findings didn't suggest presence of ILD. Others have reported that KL-6 is not only a serum marker for ILD but also has a putative role in the development of ILD onset[12] ; therefore, we should pay attention to the development of ILD.

Lakhanpal *et al.* reported that none of 65 patients with PM ($n=24$) or DM ($n=41$) had pleural effusions clinically or at autopsy, although histological evidence of fibrinous pleuritis was occasionally seen[13], but the mechanisms underlying dermatomyositis with effusion are still unclear.

We conclude that dermatomyositis caused the pleural effusion and ascites because other cases of exudative ascites were ruled out clinically, and there was an obvious response to immunosuppressive therapy.

Previous reports suggested that autoimmunity associated with underlying inflammatory myopathy was potentially an important cause of pleural effusion[14]. In patients with RA or SLE, circulating immune complexes localized in the serosal capillaries appear to activate the complement system, which induces endothelial injury and subsequent capillary permeability[15]. An important feature of the pleural affectation in rheumatic disease is high capillary permeability[15]. The observation of elevated vascular endothelial growth factor (VEGF), which contributes to the increased vascular permeability in some cases of seronegative symmetrical synovitis with edema (RS3PE) or TAFRO syndrome[16,17], prompted us to investigate VEGF in our case of DM, with a negative result. An immune mechanism appears to have been an important cause of the effusion in this case, given the good response to immunosuppressive treatments. The role of autoimmunity associated with underlying ILD or DM has been postulated to be an important cause of pleural effusion in DM[18]. The presence of anti-nuclear antibody is described in edema or pleural effusion[19], whereas myositis-specific autoantibodies have not been investigated. In our case, neither anti-nuclear antibody nor myositis-specific autoantibodies were detected. Therefore, the clinical phenotype of DM with pleural effusion and massive ascites could not be clarified. Further studies are warranted in order to gain a better understanding of the pathophysiology and to develop a therapeutic approach for pleural effusion and ascites, which seems to be a rare complication of DM.

In conclusion, the presentation of DM with pleural effusion and ascites is a rare clinical phenotype that is noteworthy because such cases are associated with significant morbidity. We need to be aware that pleural effusion and ascites may be the first presenting features of DM. Although there was a significant response to steroid and immunosuppressive treatments in our case, further information is needed to clarify the optimal treatment of these patients and elucidate the underlying pathogenesis of these conditions.

Conflict of interest

KM has received research grants from Chugai, Pfizer, and AbbVie. The rest of the authors declare that they have no competing interests

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