Letters to the Editor

Myocardial dysfunction in a patient with adult-onset Still's disease (AOSD)

Sirs,

Adult-onset Still's disease (AOSD) is a febrile disorder of unknown etiology. It is typically characterized by a spiking fever with salmon-pink evanescent rash and the involvement of various organs (1). However, myocardial dysfunction is a rare complication in AOSD. We report here a case of AOSD complicated with myocardial dysfunction that was diagnosed by electrocardiogram (ECG) and ^{201}Tl myocardial scintigram.

A 19-year-old woman was admitted to Aoyama Hospital, Tokyo Women's Medical University because of high-grade fever, polyarthralgia, myalgia, and a salmon-pink rash in October 2000. On admission, a salmon-pink rash on both lower and upper extremities was observed and a soft febrile lymph node with tenderness was palpable on her right neck. The laboratory findings were as follows: erythrocyte sedimentation rate (ESR) 60.4 mm/h; white blood cell counts (WBC) 28,500/μL (neutrophils 93%, lymphocytes 4.5%, monocytes 2%, and basophils 2%); hemoglobin 10.9 g/dL; platelet count 34. 3 x 10^4/μL; AST 92 IU/L; ALT 219 IU/L; LDH 390 IU/L; ALP 514 IU/L; ferritin 1000 ng/mL; C-reactive protein 10.7 mg/dL; RAHA< 40x; antinuclear antibody < 40x; and IL-18 8250 pg/mL.

She was diagnosed with AOSD according to the criteria for the classification of AOSD developed by Yamaguchi *et al*. (2). Other possible reasons for her fever, such as infection, malignancy, and connective tissue disease, were excluded by various examinations. Although there was no history of cardiac symptoms, electrocardiogram (ECG) on admission revealed a negative T wave of I, II, III, aV_F, V_5, and V_6. No abnormal findings were detected by echocardiogram. ^{201}Tl myocardial scintigram using dipyridamole showed reversible ischemic defects of the anterior, apical, and inferoseptal left ventricular walls. Cardiac catheterization revealed slightly diffuse hypokinesis of the left ventricle, but no significant stenosis of the coronary artery was observed on coronary angiography (CAG). We did not find any elevation in the serum markers for cardiac muscle. The spiking fever did not disappear using a low dose of prednisolone (PSL, 15 mg daily), started at the outpatient clinic. We concluded her disease activity was not being attenuated, and that it was necessary to increase the PSL dosage after an examination of cardiac function. Increasing the dosage of PSL to 30 mg daily gradually improved the symptoms and laboratory data, and finally the disease activity was completely inhibited. Follow-up ECG and ^{201}Tl myocardial scintigraphy, performed after treatment with 30 mg daily of PSL, revealed almost normal results. She is now on a maintenance dose of prednisolone (5 mg/day) in our outpatient clinic without recurrence.

It is worth noting that the present case was complicated with asymptomatic myocardial dysfunction in the initial state of AOSD. Since the efficacy of corticosteroid therapy for myocardiopathy was demonstrated by the results of the ECG and ^{201}Tl myocardial scintigraphy, we speculate that the inflammation of the vessels may be related to the myocardial dysfunction. However, no apparent abnormality was detected in either the echocardiography or the cardiac catheterization. We inferred from these observations that the abnormal findings on the ECG and ^{201}Tl myocardial scintigraphy might have been a reflection of the inflammation of small vessels that could not be detected by CAG. The complication of myocardial dysfunction in AOSD has previously been reported as rare. As far as we know, only 3 reports have been published concerning myocardial dysfunction with AOSD: two cases (3, 4) involved myocarditis, and one case (5) was due to microangiopathy (Table I). It is known that myocarditis generally results in STelevation on the ECG, as in the first two cases shown in Table I. In contrast, the case reported by Ueda *et al*. (5) was a symptomatic myocardial dysfunction induced by microangiopathy, with ST depression in the ECG. Myocardial dysfunction in that case was estimated using ECG, echocardiogram, and ^{201}Tl myocardial scintigraphy, while CAG indicated no abnormalities, consistent with our case. Interestingly, they demonstrated interstitial mononuclear cell infiltration around small vessels in the myocardium on pathological examination. They suggested that the immune system might play an important role in microangiopathy due to interstitial inflammation of the heart. Based on our case and theirs, we suggest that the small vessels might be responsible for myocardial dysfunction in AOSD.

It was previously reported that the IL-18 levels in AOSD patients were significantly higher than those in healthy donors (6). Moreover, IL-18 levels were related to the activity of the disease (7). In the present case, the level of serum IL-18 showed extreme improvement (8250 to 45 pg/mL) with steroid therapy. Recently, several reports have discussed the relationship between IL-18 and acute coronary syndrome (8-10). It can thus be speculated that IL-18 is a potent anti-angiogenic cytokine and may affect myocardial neoangiogenesis following ischemia. Since the level of IL-18 was also increased in our case, we suggest that IL-18 might have been a direct cause of the damage to coronary endothelial cells.

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Table I. Reports of myocardial dysfunction in patients with adult-onset Still's disease.

Cases	ECG	UCG	^{201}Tl-scintigraphy	Biopsy	Diagnosis
Bank *et al*., 1985 (3)	STelevation in $V_2 \sim V_4$	Pericardial effusion in $V_2 \sim V_4$	ND	Infiltration of diffuse interstitial mononuclear cells	Myocarditis
Sachs *et al*., 1990 (4)	Non-specific diffuse ST-Tchanges	Pericardial effusion, Mild alternation of left ventricular function	ND	Dense interstitial fibrosis, histiocyte and macrophage infiltration,myocardial myocardial vessel with fibrinoid necrosis	Myocarditis
Ueda *et al.*, 1997 (5)	STdepression in $V_4 \sim V_6$	Hypokinesis of septal and apical left ventricular wall	Ischemic defects of septal and apical left ventricular wall	Interstitial mononuclear infiltration with mild injury of the myocardium	Microangiopathy
Our case	Negative Twave of I, II, III, $_aV_F$,V_5 and V_6.	Within normal limits	Reversible ischemic defects of anterior, apical and anteroseptal left ventricular wall	ND	Microangiopathy

ECG: electrocardiography; UCG: ultrasonic cardiography; ND: not determined.

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Fatal pulmonary hypertension in primary Sjøgren's syndrome

Sirs,

Pulmonary hypertension (PH) is a rare finding in Sjøgren's syndrome (SS) (1, 2). One year after primary SS was diagnosed in a 55-year-old woman (keratoconjuctivitis sicca, wrist/finger arthralgias, leukocytopenia (2.2 x 10^9/l), polyclonal increased immunoglobulins, high ESR (83 mm/hr), RF Latex-test 62 IU/ml and negative ANA), the patient developed intermittent, non-radiating chest pain unrelated to exercise with normal treadmill testing. Two years later (after an ineffective trial with hydroxychloroquin 400 mg daily), dyspnoea developed gradually with normal chest X-ray findings. Again 2 years later she was referred because of increasing dyspnoea. There was central cyanosis, increased jugular venous pressure, slight non-tender hepatomegaly without ascites or peripheral oedema, bilateral basal crackles, regular tachycardia (104/min) and fixed splitting of the second heart sound, drumstick fingers with normal skin and joint findings (no Raynaud's phenomenon).

Other findings: Schirmer < 10 mm, sialometry 0.1 ml (15 min), labial biopsy focus score 4.5 (27 infiltrates in a 24 mm^2 specimen), hypergammaglobulinemia (IgG 18.7 g/l IgM 2.75 g/l and IgA1.73 g/l), negative results for ANA (ELISA-screen), anti-SSA and -SSB (ELISA), RF and anticardiolipin antibodies and lupus anticoagulant and normal TSH/T4. Transthoracic ultrasound revealed a hypertrophied right ventricle, displacement of the interventricular septum into the left ventricle, normal pericardium and estimated systolic pulmonary artery pressure 90 mm Hg. Perfusion scan, spiral- and high resolution CT were normal, with FVC and FEV1 80% and 79% of predicted and DLCO 73%. At catheterisation, the right atrial pressure was 15 mm Hg, systolic pulmonary artery pressure 100 mm Hg (increasing to 115 mm Hg with static exertion) and capillary wedge pressure 11 mm Hg. The procedure had to be terminated prematurely due to hypotension. Despite treatment with oxygen (2–4 l/min), calcium antagonists, ACE-inhibitors, diuretics and low weight molecular weight heparin, periods of hypotensive syncope became increasingly frequent and within days led to refractory circulatory shock. Autopsy confirmed the right ventricular hypertrophy (right ventricle weight 117 gr, left ventricle 142 gr) but no other structural heart disease. There was no evidence of interstitial or thromboembolic lung disease and pulmonary parenchyma was normal, essentially with markedly thickened arterioles and severe proliferation of smooth muscle (Fig. 1), without evidence for vasculitis or IgG, IgM or C3 deposition.

Pulmonary hypertension (PH) is known to complicate a number of connective tissue diseases (2). As there was no evidence of scleroderma, SLE or mixed connective tissue disease and as she fulfilled European classification criteria (3), we consider pSS the most likely cause for the fatal PH in this patient.

The English literature contains nine cases of PH in SS patients. Thromboembolic pulmonary occlusion associated with antiphospholipid antibodies and a pulmonary form of Raynaud's phenomena were described as causes for PH, but both were absent in this patient (4). The main symptom of PH is dyspnoea, but this is a rather unspecific finding in pSS patients (5). Unresolved chest pains were also considered to be a non-specific pSS symptom in this case, but proved to be early signs of PH, where chest pain is the next most common symptom (6).

The prognosis for PH patients in general is dismal with a median survival of 2.8 years (2,7). While some beneficial effect of immunosuppressive treatment is described in the literature (8), PH treatment with vasoactive drugs (prostacyclin, endothelin-receptor antagonist) (9, 10) shows promising results. With more effective therapy available, the early detection of PH with screening by non-invasive cardiac ultrasound becomes crucial, as illustrated also in pSS patients with unexplained dyspnoea and/or chest pains.

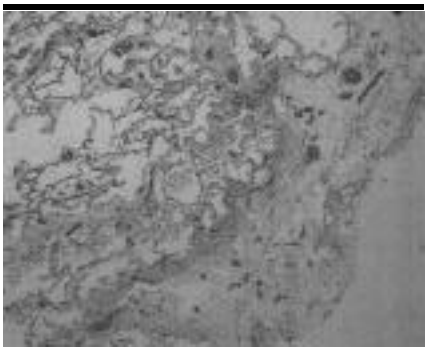

Fig. 1. Haematoxylin-eosin staining of pulmonary tissue showing largely intact lung parenchyma with spreaded lymphocyte infiltration, severe smooth muscle hypertrophy obliterating the vasculature without signs of vasculitis or trombi (**arrow**). (Courtesy of Dr. Tor Arne Hanssen, Dept. of Pathology, University Hospital North Norway).

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Myositis as a presenting feature of polyarteritis nodosa

Sirs,

Polyarteritis (PAN) is a vasculitis affecting predominantly the small and medium-size arteries (1); less commonly it may affect the muscles but this is not a frequent nor a main feature of the disease. We report a patient admitted to our hospital with a clinical pic-