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CASE REPORT

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A case of very-late-onset systemic lupus erythematosus

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Abstract A 93-year-old woman was admitted to our hospital because of fever. Radiographic findings revealed accumulation of pleural fluid. Moreover, blood tests revealed inflammation, lymphopenia, hypocomplementemia, positive for anti-nuclear antibody, and elevated anti-DNA antibody level. Therefore, the patient was diagnosed with pleuritis associated with systemic lupus erythematosus (SLE). Administration of prednisolone 20 mg/day resulted in a marked improvement in fever, pleuritis, and laboratory findings. We report a case of very-late-onset SLE that occurred at the age of 93.

Key words Systemic lupus erythematosus (SLE) · Very late onset · 93-year-old

Introduction

Systemic lupus erythematosus (SLE) is a systemic chronic inflammatory disorder with a predilection for juvenile and adult women. Autoimmunity is said to play a major part in the mechanism of onset and pathogenesis of SLE, but its etiology is still unknown. Onset is in early and adult life in approximately 80% of cases. The most common age at diagnosis is the 20s (33.2% of cases), followed by the 30s (26.6%) and teens (19.5%). In contrast, late onset in persons who are 50 and older is seen in markedly fewer cases (6.4%).[1] Moreover, reports of very late onset in persons over 80 years old are sparse. According to our search, the case of SLE that we encountered, the onset of which occurred at the age of 93 appears to be the oldest case in the literature. We report this case and review the literature.

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Case report

Patient: 93-year-old woman.

Chief complaint: Fever, impaired appetite.

Past history: Hypertension and hyperlipidemia beginning in 1992. Multiple cerebral infarctions in 1995.

Family history: Noncontributory.

Present illness: Fever appeared in early July 2002. She was diagnosed with a urinary tract infection at a nearby clinic and given antibiotics, but no improvement was seen. She was admitted to our hospital on July 24 for a thorough examination and treatment.

Present condition: Height 135.0 cm, weight 42.1 kg, blood pressure 96/60 mmHg, pulse rate 80/min, respiratory rate 24/min, body temperature 38.0°C, alert, palpebral conjunctival anemia absent, bulbar conjunctival jaundice absent, cyanosis absent. On chest auscultation, the first and second heart sounds were normal, no cardiac murmur was detected, and diminished lung sound in the lower lung field. No abdominal tenderness. Bowel sound was normal. No hepatic/splenic tumor. Edema in both lower legs was recognized.

Laboratory findings (Table 1): The leukocyte count was slightly high at 9600×10^6/l, and the lymphocyte count was slightly low at 1094×10^6/l. Activated partial thromboplastin time was normal. The erythrocyte sedimentation rate was elevated at 92 mm/h, and C-reactive protein (CRP) was elevated at 3.7 mg/dl. Serum total protein and serum albumin were low at 6.1 g/dl and 2.4 g/dl, respectively. Hepatic function, renal function, and electrolytes were normal. On immunological test, the patient was positive for anti-nuclear antibodies (ANA) at a titer of 1:1280 (homogeneous 1:1280, speckled 1:1280). Anti-DNA antibody (RIA) was 53 IU/ml, complement value (CH50) was ≤7.0 U/ml, C3 was 43 mg/dl, and C4 was 3 mg/dl, which were all low. The patient was negative for other autoantibodies such as anti-

Table 1. Laboratory findings on admission

WBC (10^6/l)	9600	Alb (g/dl)	2.4	CRP (mg/dl)	3.7	CEA (ng/ml)	2.4
Neutrophils (10^6/l)	7978	GOT (IU/l)	20	ANA (fold)	1280	CA19-9 (U/ml)	1.0
Lymphocytes (10^6/l)	1094	GPT (IU/l)	5	Homogeneous (fold)	1280	CYFRA (ng/ml)	1.4
RBC (10^{10}/l)	351	LDH (IU/l)	449	Speckled (fold)	1280	NSE (ng/ml)	<10
Hgb (g/dl)	11.4	CHE (IU/l)	381	α DNA ab (IU/ml) (RIA)	53		
Ht (%)	34.6	CPK (IU/l)	20	α U1-RNP ab (fold)	(–)	Urinalysis	
Plt (10^{10}/l)	18.0	BUN (mg/dl)	9	α Sm ab (fold)	(–)	Protein	(–)
Reticulocytes (%)	3.2	Cr (mg/dl)	0.55	CH50 (Unit)	<7	Sugar	(–)
ESR (mm/h)	92	Na (mM/l)	139	C3 (mg/dl)	43	Blood	(–)
APTT (s)	23.0/30.8	K (mM/l)	3.5	C4 (mg/dl)	3		
TP (g/dl)	6.1	Cl (mM/l)	102	β-D glucan (pg/ml)	<11		

WBC, white blood cell; RBC, red blood cell; Hgb, hemoglobin; Ht, hematocrit; PLT, platelet; ESR, erythrocyte sedimentation rate; APTT, activated partial thromboplastin time; TP, total protein; ALB, albumin; GOT, glutamic oxaloacetate transaminase; GPT, glutamic pyruvic transaminase; LDH, lactic dehydrogenase; CHE, cholinesterase; BUN, blood urea nitrogen; Cr, creatinine; Na, sodium; K, potassium; Cl, chloride; CRP, C-reactive protein; ANA, anti-nuclear antibodies; α DNA ab, anti-DNA antibodies; α U1-RNP ab, anti-RNP antibodies; α Sm ab, anti-Sm antibodies; CH50, 50% hemolytic complement activity; CEA, carcinoembryonic antigen; CA19-9, carbohydrate antigen 19-9; CYFRA, cytokeratin 19 fragment; NSE, neuron-specific enolase

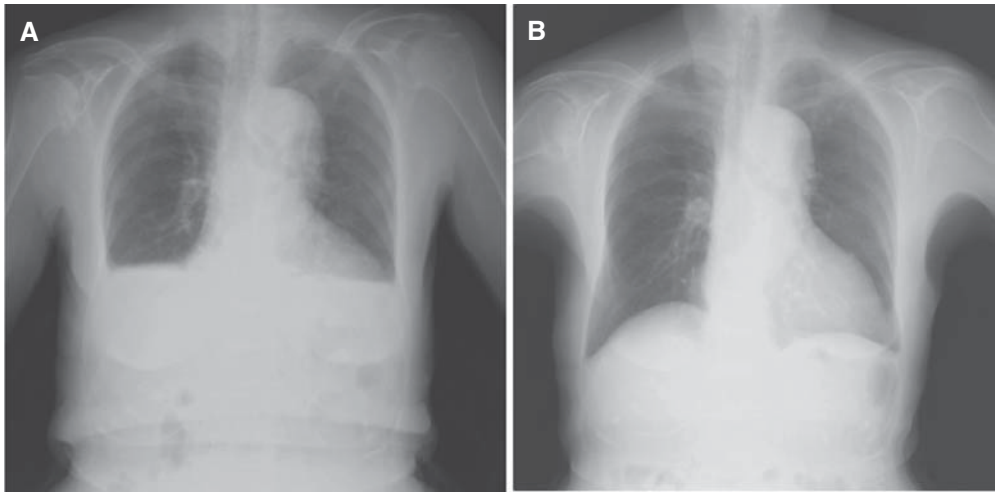

Fig. 1. Chest X-ray findings on admission (**A**). Chest X-ray showing decreased transparency on bilateral lower lung fields, which was caused by accumulation of pleural fluid. Chest X ray after admission of the prednisolone (October 10, 2002) (**B**). Pleural fluid markedly decreased after treatment with 20 mg/day of prednisolone

U1RNP antibodies, anti-Sm antibodies, anti-SS-A antibodies, and anti-SS-B antibodies. Anticardiolipic antibody IgG was mildly positive at 15 U/ml, but lupus anticoagulant was negative. Tumor markers such as CEA, CA19-9, CYFRA, and NSE were normal. No abnormality was seen on urinalysis. Cultivation tests of sputum, urine, stool, and blood were negative. Tuberculin skin test and acid-fast bacteria culture of gastric juice were negative. β-D-glucan was negative. Stool occult blood test was negative.

Chest X-ray findings showed decreased transparency on bilateral lower lung fields, which was caused by accumulation of pleural fluid (Fig. 1A). Findings of bilateral pleural fluid accumulation were also seen on chest computed tomography (CT; Fig. 2). No abnormality was seen on electrocardiogram. Cardiac ultrasound showed mild LVH, AR I°, MR I°, TR I°, and PR I°, but the ejection fraction was 67%. Head CT showed lacunar infarction and encephalatrophy. Ultrasonography and computed tomography showed no abdominal or pelvic abnormalities. Gastroscopy revealed chronic gastritis. Pleural puncture was not performed because the patient showed symptoms of dementia and refused to undergo the test.

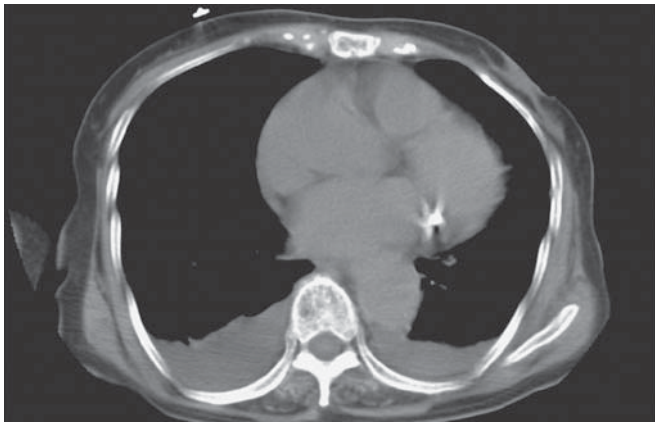

Fig. 2. Chest computed tomographic (CT) findings on admission. Findings of bilateral pleural fluid accumulation were also seen on chest CT

Course after being admitted (Fig. 3): Because the leukocyte count was slightly high and as CRP was elevated, we looked for an infection using cultivation tests and other methods, but an infection focus was not found. Because the

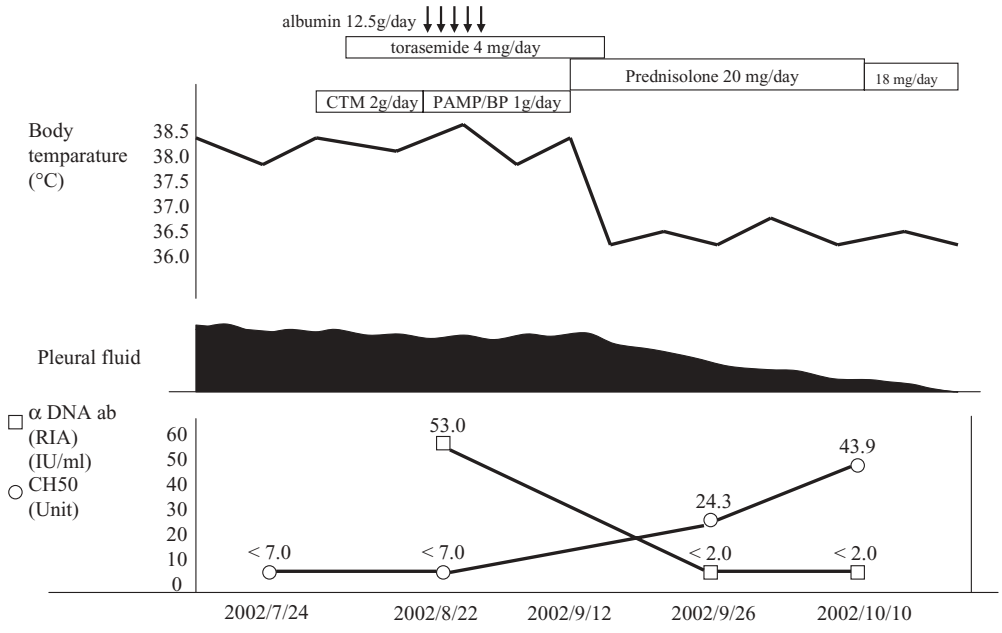

Fig. 3. Clinical course after being admitted. *CTM*, cefotiam hydrochloride; *PAMP/BP*, panipenem/betamipron; *α DNA ab*, anti-DNA antibodies; *RIA*, radioimmunoassay; *CH50*, 50% hemolytic complement activity

leukocyte count normalized and there was an improving tendency of the CRP level from 3.7 mg/dl to 1.9 mg/dl as a result of administration of various antibiotic agents, the patient may have had a concomitant infection, but her fever continued, and no decrease in the pleural fluid was seen. Therefore, we concluded that an infection was not likely the center of the pathologic condition causing the fever and accumulation of pleural fluid.

Edema of the lower extremities improved with administration of an albumin preparation and a diuretic, but there was no reduction in pleural fluid. We also looked for a malignant tumor, but no positive findings were found. Being unable to assess the properties of the pleural fluid, we were not able to identify the cause of the pleural fluid accumulation. However, we suspected pleuritis caused by SLE because the patient did not respond to administration of antibiotics, diuretics, or albumin preparations and no other clear cause for the fever and accumulation of pleural fluid could be found. Moreover, the patient had lymphopenia, was positive for ANA, had an elevated anti-DNA antibody level, and had hypocomplementemia. Prednisolone 20 mg/day, which is equivalent to 0.5 mg/day/kg body weight, was initiated on September 12, 2002, after which the fever rapidly broke and the pleural fluid markedly decreased (Fig. 1B). This was followed by a marked improvement in lymphopenia, hypocomplementemia, and elevated anti-DNA antibody level. The dosage of prednisolone was decreased gradually beginning October 10.

Discussion

The onset of collagen disease and other autoimmune disorders usually occurs before old age, after which the onset is rare. SLE is no exception. It occurs most commonly in those in their 20s, 30s, and 40s. In an investigation of 570 SLE patients conducted by our institution, the age of onset was 16–49 years in 87.9% of the cases, and a late onset in persons age 50 and above accounted for only 3.7% of cases.[2] In a national survey of 1614 SLE patients in Japan, the onset in persons age 50 and above was rare at 6.4%.[1] Moreover, according to reports in the United States and Europe, late onset was uncommon, ranging from 6.1%–20.1% of cases.[3–9] The onset in persons age 80 and above is even rarer, with only several reports worldwide. Overseas, Mirsattari et al.[10] reported a case of SLE with neuropsychiatric symptoms that occurred at the age of 88. In Japan, Takeda et al.[11] reported an 88-year-old patient with an overlap syndrome that comprised systemic sclerosis and SLE, the onset of which is thought to have occurred past the age of 80. The onset in our patient was at the age of 93. According to a search of the literature, this appears to be the oldest reported age of onset at present. It is a valuable case that we feel merits a case report.

The patient had symptoms of dementia and refused to undergo testing. Therefore, the nature of the pleural fluid could not be investigated by a pleural puncture test. However, no other clear cause was found after other tests were performed. A diagnosis of SLE with pleuritis was made because the patient's fever and accumulation of pleural fluid did not respond to administration of antibiotics, diuretics, or albumin preparations, and since blood tests revealed findings indicative of inflammation, lymphopenia, hypocomplementemia, and elevated anti-DNA antibody level. In terms of treatment, administration of prednisolone 20 mg/day, which is equivalent to about 0.5 mg/day/kg body weight, resulted in the fever rapidly breaking and a marked decrease in pleural fluid. Moreover, in terms of blood tests, hypocomplementemia, elevated anti-DNA antibody level, and other indicators of SLE activity improved markedly. The clinical course, in which corticosteroids were effective, corroborated the diagnosis.

There are fewer incidences of late-onset SLE than early-onset SLE and the epidemiology and clinical manifestations differ in several ways.

SLE is said to occur more often in women. The age of onset also influences the sex difference of SLE. The male-to-female ratio is reported to generally be 1:8–10.[12–14] The sex difference was more marked in Japan, where a national survey of 1614 cases showed the male-to-female ratio to be 1:12.7.[1] In an investigation by our institution, whereas the ratio was 1:7 in juvenile-onset cases age 15 and younger, and 1:13 in adult-onset cases age 16–49, it was 1:4 in late-onset cases 50 and above, which was less of a sex difference.[2]

According to published reports, the clinical course of late-onset SLE is mild in terms of clinical manifestations, and is characterized by a low incidence of lupus nephritis, CNS lupus, malar rash, etc., and a high incidence of serositis and thrombocytopenia.[6,7,13,15–17] The present patient also developed serositis at onset, which is consistent with the characteristics of late-onset SLE.

Various factors affect the immune system with increased age such as changes in immunocompetence, various infections, changes in the endocrine milieu including sex hormones, changes in the autonomic nervous system, extent of the effect of genetic markers, other disorders, eating habits, medications, and changes in activities of daily living and other environmental factors.[18–22] Those factors are believed to be involved in the pathogenesis of late-onset SLE.

SLE, which most commonly occurs before old age, rarely at an advanced age, but investigation of late-onset cases is important as aging of the population continues. This case, the onset of which occurred at the age of 93, is believed to be a valuable case because, as far as our search shows, it is the oldest age of onset of SLE in the literature.

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