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Clinical characteristics of systemic lupus erythematosus with chylothorax and/or chylous ascites

An analysis of 15 cases in China

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Abstract

This analysis of clinical data from systemic lupus erythematosus (SLE) patients with chylothorax and/or chylous ascites was conducted to guide further clinical work.

From June 2008 to June 2019, 15 SLE patients (14 females and 1 male) with chylothorax and/or chylous ascites were hospitalized at the Beijing Shijitan Hospital. Sixty SLE patients without chylothorax and chylous ascites were randomly selected as controls. Patients'' clinical data was investigated.

The mean age of onset of chylothorax and/or chylous ascites in patients with SLE was 35.7 ± 3.7 years (range, 15–69 years). The mean disease duration of chylothorax and/or chylous ascites in patients with SLE was 13.7 ± 3.4 months (range, 1–48 months). Patients with chylothorax and/or chylous ascites were always diagnosed at later stages of SLE compared with the controls. Among cases, glomerulonephritis and hematologic system involvement were the most common complications. Anti-Sjogren's syndrome antigen A antibody was positive in 7 cases (46.7%). Among cases, direct lymphangiography was performed in 13 patients, indicating thoracic duct outlet obstruction or a poor backflow at the terminal of the thoracic duct. Subsequently, 13 patients were treated with corticosteroids, combined with immunosuppressants in 11 patients and thoracic duct surgery in 6 patients. Eleven patients were followed up for 0.5 to 7.0 years. One patient died of infection. Eight patients (53.3%) achieved remission.

Chylothorax and/or chylous ascites are rare complications of SLE. An early diagnosis and timely initiation of glucocorticoids, immunosuppressants, and surgery are critical to relieve symptoms and to improve prognosis.

Abbreviations: C3 = complement factor3, C4 = complement factor4, dsDNA = double-stranded DNA, ESR = erythrocyte sedimentation rate, CR = complete remission, PR = partial remission, RNP = ribonucleoprotein, rRNP = ribosomal RNPSLE = systemic lupus erythematousus, SLEDAI = systemic lupus erythematosus disease activity index, Sm = Smith, SSA = Sjogren syndrome antigen A, SSB = Sjogren syndrome antigen B.

Keywords: chylothorax, chylous ascites, systemic lupus erythematosus

1. Introduction

Chylothorax and chylous ascites are caused by the accumulation of chyle in the pleural and peritoneal cavities. The etiologies of chylothorax and chylous ascites can be classified as traumatic or nontraumatic. Obstruction or disruption of lymphatic channels resulting from the infiltration of malignancies is the most common nontraumatic cause, of which lymphomas account for 70% of all cases.[1] Other nontraumatic causes include tuberculosis, sarcoidosis, lymphangioleiomyomatosis, cirrhosis, and autoimmune diseases,[1–4] such as Behçet disease and systemic lupus erythematosus (SLE).[5,6]

SLE is a chronic inflammatory autoimmune disease that involves multiple organs and systems, including the skin, serous membrane, kidneys, and the hematological and nervous systems. Different studies have reported variable rates of serous membrane involvement in SLE including pleural, ascitic, and pericardial effusion in different regions with a range of 12% to 56%.[7,8] Patients with SLE may present or develop chylothorax and/or chylous ascites concomitant with the primary disease.[6,9–15] To the best of our knowledge, fewer than 15 cases of chylothorax and/or chylous ascites secondary to SLE have been reported in English-language literature, and clinical data have been limited to case reports or small cohorts.[6,9–15] Because the clinical characteristics of SLE-related chylothorax and/or chylous ascites remain largely unknown, additional studies are required to improve our understanding of this rare disorder.

The aim of this study was to identify the clinical features of chylothorax and/or chylous ascites in SLE. We reviewed the

Editor: Kuang-Ming Liao.

G-HZ, Y-HW, L-LZ, and W-BS designed research. G-HZ collected, analyzed, and wrote the paper.

The authors have no conflicts of interest to disclose.

All data generated or analyzed during this study are included in this published article [and its supplementary information files].

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How to cite this article: Zhang GH, Zhang LL, Wang YH, Shen WB. Clinical characteristics of systemic lupus erythematosus with chylothorax and/or chylous ascites: an analysis of 15 cases in China. Medicine 2020;99:51(e23661).

Received: 28 July 2020 / Received in final form: 6 October 2020 / Accepted: 7 November 2020

http://dx.doi.org/10.1097/MD.0000000000023661

medical records of 15 SLE patients with chylothorax and/or chylous ascites and 60 control patients who were admitted to the Beijing Shijitan Hospital during the last 11 years.

2. Methods

2.1. Patients

From June 2008 to June 2019, 683 cases of SLE patients were hospitalized at the Beijing Shijitan Hospital, 15 of which were SLE patients with chylothorax and/or chylous ascites. SLE patients admitted to the Beijing Shijitan Hospital during the same period were matched with controls at a 1:4 ratio on the basis of sex and age. Sixty SLE patients were randomly selected as the control group. Systemic lupus erythematosus patients fulfilled the 1997 version of American College of Rheumatology Classification Criteria for SLE.[16] The diagnosis of SLE patients with chylothorax and/or chylous ascites was based on at least one of the following criteria: a positive chyle test of effusion; triglyceride level in pleural; and abdominal effusion >110 mg/dL (1 mmol/L = 88.6 mg/dL); lymphoscintigraphy indicating radioactivity uptake in the pleural and abdominal cavity; and direct lymphangiography revealing that a contrast agent has entered the pleural and abdominal cavity.[17,18] Patients were excluded when their symptoms resulted from trauma, infection, or tumor. The disease activity of SLE was evaluated using the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) score. This study was approved by the ethics committee of the Beijing Shijitan Hospital, Capital Medical University. All patients provided written informed consent to participate in this study.

2.2. Clinical and laboratory data

Medical records were reviewed for the following clinical factors: age, gender, the duration from diagnosis of SLE to chylothorax and/or chylous ascites, clinical symptoms, and laboratory data of hematological abnormalities (leukocytopenia $< 4.0 \times 10^9$/L or lymphocytopenia $<1.0 \times 10^9$/L; thrombocytopenia $<100 \times 10^9$/L), elevated Erythrocyte sedimentation rate (ESR) level (>20 mm/h), hypocomplementemia (decrease in CH50, complement factor 3 [C3], or 4[C4] below the lower limit of normal for testing laboratory), hypoalbuminemia (serum albuminemia <35 g/L), antinuclear antibody, anti-double-stranded DNA (dsDNA) antibody, anti-extractable nuclear antigen antibodies (including anti-Smith [Sm] antibody, anti-Sjogren syndrome antigen A [SSA] antibody, anti-Sjogren syndrome antigen B [SSB] antibody, anti-Ribonucleoprotein [RNP] antibody, and anti-ribosomal RNP [rRNP] antibody). The SLEDAI was determined directly or calculated from medical records and laboratory data.

2.3. Statistical analysis

All data processing and statistical analyses were performed using SPSS software (version 21.0, IBM, Armonk, NY). The mean ± standard error (SE) was calculated for continuous variables, and the Student *t* test or Wilcoxon signed-rank test were used to analyze the differences between the 2 study groups. Categorical variables were expressed as percentages and compared using the χ^2 test or Fisher exact test when appropriate. Associations between baseline variables and risk of chylothorax and/or chylous ascites were estimated by computing the OR and 95% CI after performing univariate logistic regression analyses. All statistical tests were 2-tailed and a *P* value of <.05 was considered statistically significant.

Table 1

Clinical characteristics of cases and controls.

Variable	Cases, n = 15	Control, n = 60	*P*
Demographics			
Female	14 (93.3)	56 (93.3)	1.000
Age, yrs	36.9 ± 3.7	36.9 ± 1.8	.998
Clinical manifestations			
SLE onset age, yrs	32.0 ± 3.7	35.1 ± 1.8	.847
Disease duration, mos	**56.7 ± 17.0**	**23.1 ± 3.6**	**.012**
Fever	**1 (6.7)**	**31 (51.7)**	**.000**
Mucocutaneous involvement	**4 (26.7)**	**38 (63.3)**	**.018**
Arthritis	4 (26.7)	27 (45.0)	.249
Lupus Nephritis	6 (40.0)	25 (41.7)	1.000
Laboratory tests			
Hematological disturbance	6 (40.0)	40 (66.7)	.077
Leukocytopenia	5 (33.3)	32 (53.3)	.249
Thrombocytopenia	3 (20.0)	17 (28.3)	.746
Elevated ESR	**8 (53.3)**	**48 (80.0)**	**.048**
Hypoalbuminemia	6 (40.0)	32 (53.3)	.399
Hypocomplementemia	6 (40.0)	41 (68.3)	.071
Anti-dsDNA antibody positivity	4 (26.7)	26 (43.3)	.377
Anti-Sm antibody positivity	1 (6.7)	18 (30.0)	.096
Anti-SSA antibody positivity	7 (46.7)	38 (63.3)	.255
Anti-SSB antibody positivity	1 (6.7)	13 (21.7)	.276
Anti- RNP antibody positivity	3 (20.0)	20 (33.3)	.369
Anti- rRNP antibody positivity	2 (13.3)	21 (35.0)	.128
SLEDAI	**6.4 ± 2.1**	**11.9 ± 4.8**	**.005**

Values are mean ± standard error or n (%) unless otherwise specified. Statistically significant values ($P < .05$) are in bold face.

dsDNA = double-stranded DNA, ESR = erythrocyte sedimentation rate, RNP = ribonucleoprotein, rRNP = ribosomal RNP, SLE = systemic lupus erythematosus, SLEDAI = systemic lupus erythematosus disease activity index, Sm = Smith, SSA = Sjogren syndrome antigen A, SSB = Sjogren syndrome antigen B.

3. Results

3.1. Demographic factors

Overall, 15 patients (14 females and 1 male) were diagnosed with SLE complicated with chylothorax and/or chylous ascites at the Beijing Shijitan Hospital between June 2008 and June 2019. The age of onset of SLE was 32.0 ± 3.7 years (range, 4–69 years, Table 1). The disease duration of SLE was 56.7 ± 17.0 months (range, 0.5–240 months, Table 1). The age of onset of chylothorax and/or chylous ascites was 35.7 ± 3.7 years (range, 15–69 years, Table 2). The disease duration of chylothorax and/or chylous ascites in patients with SLE was 13.7 ± 3.4 months (range, 1–48 months, Table 2). Two patients (2/15, 13.3%) presented with chylothorax as the initial symptom of SLE, while 13 patients (13/15, 86.7%) presented with chylothorax and/or chylous ascites as a complication during the course of SLE. Of 13 patients, 6 (6/13, 46.2%) presented with pleural effusion as the initial symptom of SLE, followed by chylothorax, combined with or without chylous ascites. One patient (1/13, 7.6%) presented with ascites as the initial symptom of SLE, followed by chylous ascites and chythorax.

3.2. Clinical and laboratory features

Of the 15 patients, 6 (40.0%) had lupus nephritis, 6 (40.0%) had hematological involvement, 4 (26.7%) had arthritis, 4 (26.7%) had mucocutaneous involvement, and 1 (6.7%) had fever. Of the 6 cases with hematological involvement, leukocytopenia was the most common symptom (5/15, 33.3%), followed by thrombocy-

Table 2

Clinical characteristics, therapy, and prognosis of SLE patients with chylothorax and/or chylous ascites.

Patient/age (years)/sex	Duration of chylous effusion mos	Clinical symptoms Chylous effusion Site	Clinical symptoms Other symptoms Symptom	ESRmm/h	C3 g/L	ANA	Anti-ENA	Effusion TG mg/dL	Effusion CHOL mmol/L	Effusion Chyle test	SLEDAI	Therapy	Surgery	Prognosis
1/15/F	3	T	Dyspnea Rash LN	20	1.25	S1:100	Negative	66	1.93	+	6	MP HCQ MMF	Adhesion loosen operation of thoracic duct terminus	CR
2/20/F	1	T	Dyspnea LN	—	0.86	S1:80	SSA	—	—	+	8	Pred HCQ	NO	Lost to follow-up
3/24/F	12	T	Dyspnea Leukocytopenia thrombocytopenia hemolytic anemia	13	1.27	S1:1000	RNP	75	2.00	+	6	Pred HCQ TAC	Outlet expansion suture operation of thoracic duct	PR
4/26/M	24	A	Distension LN protein-losing enteropathy arthritis	108	0.56	S1:1000	SSA	113	1.68	+	10	Pred HCQ CTX	Adhesion loosen operation of thoracic duct terminus	CR
5/29/F	15	T A	Dyspnea Leukocytopenia thrombocytopenia	5	1.05	S1:100	Negative	52	1.60	+	4	Pred HCQ CsA	Adhesion loosen operation of thoracic duct terminus	PR
6/31/F	6	T A	Dyspnea distension LN	61	1.21	HS1:640	dsDNA	357	1.79	+	8	MP CTX	NO	PR
7/32/F	3	T A	Dyspnea Thrombocytopenia	55	1.24	HS1:320	dsDNA SSA	823	1.43	+	5	MP CsA	NO	Invalid
8/33/F	7	T	Dyspnea NO	5	0.95	HS 1:100	SSA	130	2.87	+	4	MP pulse Pred HCQ	NO	Lost to follow-up
9/35/F	48	T	NO Leukocytopenia arthritis	34	1.11	HS 1:1000	SSA SSB	272	2.33	+	7	HCQ	NO	Invalid
10/42/F	12	T	Dyspnea Leukocytopenia fever rash	55	0.67	S1:320	dsDNA	112	1.97	+	7	MP	NO	Lost to follow-up
11/47/F	5	T A	Distension Leukocytopenia	32	0.86	S1:160	rRNP	—	1.69	+	5	Diuresis	NO	Lost to follow-up
12/48/ F	36	T	Dyspnea Rash alopecia	15	0.93	HS1:320	SSA RNP rRNP	60	2.3	+	4	Pred HCQ AZA	Compression band loosen operation of thoracic duct terminus	PR
13/50/F	9	A	Distension Arthritis Raynaud's phenomenon LN	17	0.99	S1:320	Sm RNP	—	—	+	10	Pred HCQ	NO	PR
14/52/F	12	T A	Dyspnea LN arthritis protein-losing enteropathy	32	0.65	H1:320	SSA	144	1.81	+	8	MP pulse Pred HCQ	Compression band loosen operation of thoracic duct terminus	PR
15/69/F	12	T A	Dyspnea distension Protein-losing enteropathy	26	0.84	H1:1000	dsDNA	—	—	+	4	Pred	NO	Died

A = abdominal cavity, ANA = antinuclear antibodies, AZA = azathioprine, C3 = complement 3, CHOL = cholesterol, + = positive, CR = complete remission, CsA = cyclosporin A, CTX = cyclophosphamide, dsDNA = double-stranded DNA, ENA = extractable nuclear antigen, ESR = erythrocyte sedimentation rate, — = unknown, F = female, H = homogeneity, HCQ = hydroxychloroquine, LN = lupus nephritis, M = male, MMF = mycophenolatemofetil, MP = methylprednisolone, PR = partial remission, Pred = prednisolone, RNP = ribonucleoprotein, rRNP = ribosomal RNP, S = spot, SLEDAI = systemic lupus erythematosus disease activity index, Sm = Smith, SSA = Sjogren syndrome antigen A, SSB = Sjogren syndrome antigen B, T = thorax, TAC = tacrolimus, TG = triglyceride.

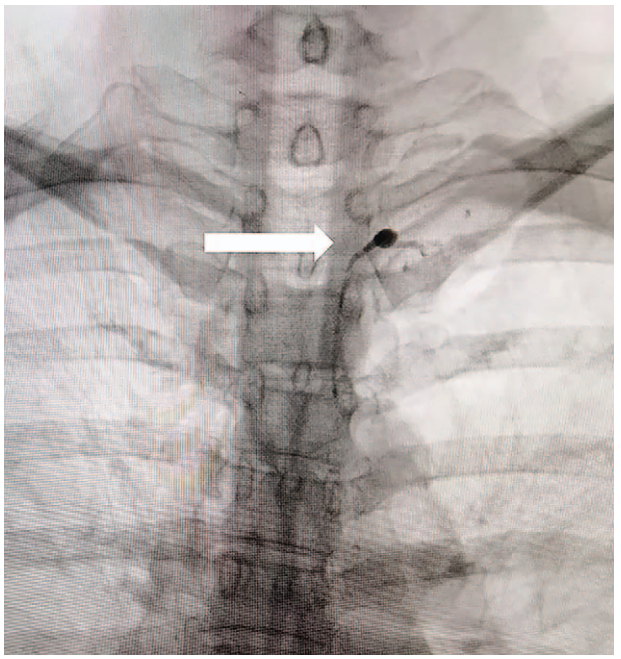

Figure 1. Lymphangiography shows thoracic duct outlet obstruction in our patients (white arrow).

topenia (3/15, 20.0%) and autoimmune hemolytic anemia (1/15, 6.7%). Six (6/15, 40%) cases developed hypoalbuminemia and 6 with hypocomplementemia. An elevated ESR level was observed in 8 cases (8/15, 53.3%). Antinuclear antibody was positive in all patients (100%). Anti-dsDNA antibody, anti-SSA antibody, anti-SSB antibody, anti-RNP antibody, anti-rRNP antibody, and anti-Sm antibody was positive in 4 (26.7%), 7 (46.7%), 1 (6.7%), 3 (20.0%), 2 (13.3%), and 1 (6.7%) cases, respectively. The mean SLEDAI score was 6.4 ± 2.1 (range, 4–10 [5–10 in 73.3% of cases and <5 in 26.7% of cases]). Pleural or abdominal effusion presented as chylomicron or was milky colored and a positive Chyle test was reported for all patients. Lymphoscintigraphy was performed in 15 patients. Chylothorax and chylous ascites were found in 6 patients simultaneously, chylothorax alone was present in 7 patients, and chylous ascites alone was present in 2 patients. Protein-losing enteropathy was diagnosed in 3 patients by ^{99m}Tc-labeled human serum albumin scintigraphy. Direct lymphangiography was performed in 13 patients. Eight patients showed thoracic duct outlet obstruction (Fig. 1), and 5 patients showed a poor backflow at the terminal of the thoracic duct.

3.3. SLE features of the case group

The incidence of fever in SLE patients with chylothorax and/or chylous ascites was significantly lower than in the control group ($P < .01$, Table 1). The SLE patients with chylothorax and/or chylous ascites had a lower incidence of mucocutaneous involvement ($P < .05$, Table 1) and a lower disease activity based on the SLEDAI score compared with controls (6.4 ± 2.1 vs 11.9 ± 4.8, respectively, $P < .01$, Table 1). The incidence of elevated ESR was significantly lower in cases than in controls ($P < .05$, Table 1). Comparisons of laboratory findings showed that hypoalbuminemia, hypocomplementemia, positive anti-SSA, anti-SSB, anti-Sm, anti-RNP, or anti-rRNP antibodies were more common in controls than in the case group (Table 1).

Table 3

Univariate logistic regression analyses of SLE with chylothorax and/or chylous ascites.

Variables	OR	95% CI	P
SLEDAI	0.688	0.551–0.859	.001
Disease duration of SLE	1.019	1.003–1.034	.016

SLE = systemic lupus erythematosus, SLEDAI = systemic lupus erythematosus disease activity index.

3.4. Univariate logistic regression analyses of SLE with chylothorax and/or chylous ascites

The presence or absence of chylothorax and/or chylous ascites in SLE patients (0 = without, 1 =with) was used as a binary dependent variable. General data, clinical indicators, and laboratory indicators were included as independent variables. Univariate logistic regression analyses were used to screen the influencing factors for chylothorax and/or chylous ascites in patients with SLE. The results suggest that SLE disease duration and SLEDAI score are statistically significant (all $P < .05$) (Table 3).

3.5. Treatment and prognosis

Of 15 patients, 13 (86.7%) were treated with corticosteroids. Among these 13 patients, 8 were initially treated with a high-dose steroid (prednisone-equivalent dose of 1.0–1.5 mg/kg/d); 2 received intravenous methylprednisolone pulse therapy (0.5 g/d for 3 days) followed by prednisone (1 mg/kg/d) or equivalent doses of methylprednisolone; and 3 were treated with a low-dose prednisone (<0.5 mg/kg/d). Immunosuppressants were administered to 11 patients (73.3%), including hydroxychloroquine (10 cases), intravenous cyclophosphamide (2 cases), combined with corticosteroids, cyclosporin A (2 cases), mycophenolate mofetil (1 case), tacrolimus (1 case), and azathioprine (1 case). Six patients underwent thoracic duct surgery. Three received surgery to release adhesion of the terminus of the thoracic duct, 2 received surgery to decompress the compression band of the thoracic duct, and 1 underwent thoracic duct export expansion suture. Conservative therapies for chylous fluid included low-fat diet and fasting in all patients. Four patients were lost to follow-up. Eleven patients were followed up for 0.5–7.0 years. One patient (6.7%) died of infection. Prognosis included complete remission (CR) defined by chylous effusion being completely absorbed; partial remission (PR) defined by chylous effusion absorbed by more than 50%; and invalid defined by chylous effusion absorbed by less than 50%. Remission included CR and PR. Eight patients (53.3%) achieved remission. Two patients (13.4%) who did not achieve remission had chylothorax and chylous ascites reduced by less than 50% (Table 2).

4. Discussion

Pleural and pericardial effusions are common clinical manifestations in SLE. Nevertheless, chylothorax and/or chylous ascites are extremely rare complications of SLE and only 12 cases of chylothorax and/or chylous ascites secondary to SLE have been reported in English-language literature. Table 4 summarizes clinical presentations and outcomes of these cases. To improve our understanding of these complications, we reviewed a large sample size of SLE-related chylothorax and/or chylous ascites. In our study, the age of onset of chylothorax and/or chylous ascites

Table 4

Literature review of chylous effusion in systemic lupus erythematosus.

Author	Age (years)/ sex	Country of patient	Duration of SLE mos		Clinical symptoms: Chylous effusion site symptom	Clinical symptoms: Other symptoms	ESR mm/h	C3 g/L	ANA	Anti-ENA	Effusion: TG mg/dl	Effusion: CHOL mmol/L	Therapy m (month); d (day)	Prognosis
Lee et al[10]	47/F	Korea	9	TA	Abdominal distension	Protein-losing enteropathy malar rash leukopenia	107	↓	SN1:320	SSA	106	0.3	MP 1mg/kg/d×1m pulse CTX×3 m	Chylothorax, chylous ascites completely resolved
	68/M	Korea	7	TA	Increased abdominal girth	LN (class II) protein-losing enteropathy	76	↓	HS1:1280	SSA	880	2.2	MP 1 mg/kg/d×5 d then 60 mg×1 m	Chylous effusion decreased significantly, Died of acute respiratory failure after 2 mo
Lin et al[12]	43/F	Taiwan	2	T	Dry cough	Lymphopenia	—	—	S1:1280	Sm RNP dsDNA SSA SSB	857	2.3	Pred 20 mg/d HCQ 400 mg/d Now AZA 50 mg/d	Chylothorax cleared rapidly no recurrence with a follow-up of 4 yr.
Chen et al[13]	93/F	Taiwan	Over 2 d	A	Abdominal fullness	Discoid rash, oral ulcers, proteinuria	—	↓	1:1280	negative	303	–	MP 250 mg ×3 d	Abdominal distention sub-sided obviously. Died of GI bleed 2 wk later
Song et al[11]	29/F	China	24	T	Chest congestion	NO	90	↓	1:1000	Sm	159	1.9	MP1g×3 d→Pred 60 mg/d CsA 100 mg bid	No recurrence follow-up period of 4 yr
	21/F	China	36	T	Chest congestion	Arthralgia, fever	70	↓	1:80	SSA Sm dsDNA	346	1.7	Pred 60 mg/d CTX 0.4 g/wk	No recurrence follow-up period of 2.5 y
	33/F	China	20	T	Chest congestion	Arthralgia,	Normal	↓	1:80	SSA dsDNA	478	3.5	MP 1 g×3d→80 mg/d CsA 100 mg bid	No recurrence follow-up period of 1.5 yr
	32/M	China	120	T	Chest congestion	Butterfly erythema	Normal	Normal	1:640	RNP dsDNA	248	2.2	MP 80 mg/d CTX 0.4 g/w +MTX12.5 mg/w +TAC 10 mg bid	No recurrence follow-up period of 10 mo
Kakar et al[15]	38/F	India	1½	T A	Abdominal distension	Arthralgia cytopenia	70	Normal	S1:100	SSA RNP dsDNA,	568	–	MP 250 mg/d×5 d MMF 1.5 g	Minimal left pleural effusion on 6 mo
Soysal et al[6]	61/F	Turkey	120	TA	Abdominal distension	NG	6	↓	H1:1000	Negative	542	–	MP1mg/kg/d * 15d HCQ 400mg/d	Fluids regressed No recurrence on 10 wks
Manzella et al[9]	36/F	Argentina	180	TA	Abdominal distension	Malar rash, discoid rash, lymphopenia	17	Normal	HS1:320	SSA dsDNA Sm RNP	270	–	MP 1g×3 d Perd 60 mg/d AZA 100 mg/d	Significant reduction of ascites and pleural effusion on 6 mo
Hasan et al[14]	52/F	African-American	4	T	Abdominal distension	LN (class V) fever, rash, joint pains	118	↓	Positive	Sm dsDNA	1732	–	MP intravenous monthly CTX	Resolution of ascites

A = abdominal cavity, ANA = antinuclear antibodies, AZA = azathioprine, C3 = complement 3, CHOL = cholesterol, CsA = cyclosporin A, CTX = cyclophosphamide, dsDNA = double-stranded DNA, ESR = erythrocyte sedimentation rate, — = unknown, F = female, H = homogeneity, HCQ = hydroxychloroquine, LN = lupus nephritis, M = male, MMF = mycophenolatemofetil, MP = methylprednisolone, MTX = methotrexate, N = nuclear, pred = Prednisolone, RNP = ribonucleoprotein, S = spot, Sm = Smith, SSA = Sjogren syndrome antigen A, SSB = Sjogren syndrome antigen B, T = thorax, TAC = tacrolimus, TG = triglyceride.

in SLE patients was 35.7±3.7 years. The disease duration of chylothorax and/or chylous ascites was 13.7±3.4 months. In addition, 86.7% of patients presented with chylothorax and/or chylous ascites as a complication during the course of SLE.

The underlying mechanisms of chylothorax and/or chylous ascites in SLE are poorly understood. There are a number of potential factors in this process. In addition to the skin, kidneys and hematological system being commonly involved in SLE, chronic inflammation of lymphatic vessels results in lymphatic stenosis or obstruction, an increase in endoluminal pressure and permeability of vascular walls, and finally chyle effusion. In our study, 13 patients with SLE underwent direct lymphangiography, which indicated thoracic duct outlet obstruction or a poor backflow at the terminal of the thoracic duct. Hypoproteinemia can cause mucosal edema of the intestinal wall, leading to increased permeability of the intestinal lymphatics and chyle overflow. In our study, hypoalbuminemia was observed in 6 cases, and protein-losing enteropathy was diagnosed in 3 patients. A pathological feature of SLE is the activation of complement by immune complexes deposited in blood vessel walls resulting in inflammation and increased capillary permeability. Thus, chylomicron can directly enter the pleural or abdominal cavity through the blood circulation. In our study, the mean SLEDAI score in SLE patients with chylothorax and/or chylous ascites was 6.4±2.1 (73.3%, range, 5–10), which indicated the SLE patients with chylothorax and/or chylous ascites occurred with low disease activity. Our study supports this point. However, the exact mechanism requires further study.

In our study, the mean duration of SLE with chylothorax and/or chylous ascites was significantly longer than that without this complication. Similar to our finding, a previous study reported a patient developed chylothorax and chylous ascites associated with SLE after 10 years of disease.[6] In another report, 4 patients developed this complication after a disease duration of between 20 and 120 months.[11] SLE patients with chylothorax and/or chylous ascites had a lower incidence of fever, mucocutaneous involvement, hypoalbuminemia, hypocomplementemia, positive anti-SSA, anti-SSB, anti-Sm, anti-RNP, or anti-rRNP antibody, and a lower SLEDAI score compared with the controls. Moreover, we found that the disease durations of SLE and SLEDAI score were the influencing factors for chylothorax and/or chylous ascites occurred in patients with SLE. However, due to the limited number of cases, it is still necessary to expand the sample size for multivariate logistic regression analysis to further explore whether the associated factors are risk factors or protective factors for chylous effusion in SLE in future study.

The Chyle test of effusion was positive for all patients, which supports the diagnosis of chylous effusion. A diagnosis was determined when a triglyceride concentration greater than 110 mg/dL was measured in the fluid. Table 4 showed triglyceride levels >110 mg/dL in all patients. In our study, triglyceride levels >110 mg/dL were reported in 7 patients, were unknown in 4 patients, and were between 50 and 110 mg/dL in 4 patients. A triglyceride level <110 mg/dL or unknown was nondiagnostic, requiring further evaluation for chylomicrons. Imaging such as lymphoscintigraphy or direct lymphangiography might help in these cases. Lymphoscintigraphy is used to image radioactivity in tissues. After subcutaneous injection, radioactive particles are transported by the lymphatic system and accumulate in the pleural or abdominal cavity, which confirms the existence of chylous effusion. In our study, 15 patients underwent lymphoscintigraphy, and both chylothorax and chylous ascites were identified in 6 cases, chylothorax alone in 7, and chylous ascites alone in 2. Unlike lymphoscintigraphy, direct lymphangiography is the gold standard for the diagnosis of lymphatic abnormalities because it can be used to image sites of lymphatic leakage or obstruction[19] and indicate the shape of the thoracic duct dynamically. In our study, 13 cases underwent lymphangiography, which showed thoracic duct outlet obstruction or a poor backflow at the terminal of the thoracic duct. Therefore, once chyle cannot be diagnosed by effusion triglyceride levels, timely imaging examination including lymphoscintigraphy and lymphangiography can be helpful for diagnosis. Furthermore, lymphangiography can aid identifying the cause of chylous effusion and to guide the next treatment.

The prognosis for patients with chylothorax and chylous ascites depends on the treatment of the underlying disease. SLE patients were treated with corticosteroids combined with immunosuppressants, including cyclophosphamide, cyclosporine, and tacrolimus. Conservative therapies for chylous fluid include low-fat diet and medium chain fatty acids, which are directly absorbed in the intestine and transported by the portal vein, not lymphatic vessels. In our study, 13 patients were treated with corticosteroids, and 11 of these also received immunosuppressants for SLE. Conservative therapies were given to all patients. Of 11 patients who could be followed, 8 patients achieved remission, of which 2 with a duration of chylous effusion <12 months responded well to glucocorticoid and immunosuppressive agents, in accord with previous studies.[6,9,11] Of the other 6 patients with remission, the duration of chylous effusion in 5 was ≥12 months, the duration in 1 patient was 3 months. These patients were treated with glucocorticoids and immunosuppressants, but chylous effusion did not decrease with SLE. Surgery was also performed in these patients. Three patients received surgery to release adhesion of the terminus of the thoracic duct, 2 received surgery to decompress the compression band of the thoracic duct, and 1 underwent thoracic duct export expansion suture. Chylous effusion was significantly decreased after surgery. The 5 patients with the duration of chylous effusion ≥12 months in our study is similar to the literature which Song et al[11] reported that the effect of conservative treatment with glucocorticoids and immunosuppressants was limited for SLE of long duration. Surgery should be performed to release the mechanical obstruction of the thoracic duct. In contrast, 1 patient with chylous effusion at 3 months did not respond well to glucocorticoid and immunosuppressive agents, the surgery is performed with effusion completely absorpted. The exact reason is unknown. More cases are needed to study these differences and determine which is the right timepoint for surgery. One patient died of infection caused by a loss of electrolytes and immunoglobulins.

This study had several limitations. Our study was performed at a single institution with a small sample size. Therefore, selection bias cannot be excluded. Our study was restricted to Chinese individuals. And a more systemic review should be performed to summarize the features between Chinese and Western cases. But the Western cases[14,15] were only 2 cases according to the English literature review.[6,9–15] We needed to collect cases to make further research in the future. The number of cases that underwent surgery is small and therefore further research is required to confirm the results of the present study, the choice of surgery timing, and the appropriate surgical method.

In summary, SLE can involve serous membranes, resulting in pleural, peritoneal, or pericardial effusion. Chylothorax and

chylous ascites are rarely described; however, they can present as the first symptom. In addition to blood samples, effusion of the serous membrane should be studied to define its nature, amount, and features. When multiple organs are involved, infections and neoplastic diseases should be excluded, while the possibility of SLE should be considered, so that timely medical treatment can be provided to control the disease and to improve the prognosis.

Acknowledgments

The authors thank all patients who participated in their study. The authors thank Edanz Group China (www.liwenbianji.cn/ac), for editing the English text of a draft of this manuscript.

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