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 factor 3, C4 = complement factor 4, dsDNA = double-stranded DNA, ESR = erythrocyte sedimentation rate, CR = complete remission, PR = partial remission, 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.

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. Other nontraumatic causes include tuberculosis, sarcoidosis, lymphangioleiomyomatosis, cirrhosis, and autoimmune diseases, such as Behçet disease and systemic lupus erythematosus (SLE).

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%. Patients with SLE may present or develop chylothorax and/or chylous ascites coexistent with the primary disease. 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. 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...
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 = 86.8 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 $\chi^2$ 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) | 1 (6.7) | .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 | | | |
| Leukocytopenia | 6 (40.0) | 40 (66.7) | .077 |
| Thrombocytopenia | 3 (20.0) | 17 (28.3) | .746 |
| Elevated ESR | 8 (53.3) | 48 (80.0) | .048 |
| Hypoaalbuminemia | 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- RNP 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 chylothorax.

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 thrombocytopenia,
| Patient/age (years)/sex | Duration of effusion mos | Clinical symptoms | Other Site Symptom symptoms | ESRmm/h | C3 g/L | ANA | Anti-ENA | TG CHOL Chyle mg/dL | mmol/L | test | SLEDAI | Therapy | Surgery | Prognosis |
|-------------------------|-------------------------|-------------------|-----------------------------|---------|-------|-----|---------|---------------------|--------|------|--------|---------|---------|-----------|
| 1/15/F                  | 3                       | 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                       | Dyspnea           | LN                           | —       | 0.86  | S1:80 | SSA      | —                  | —      | +    | 8      | Pred    | HCQ     | NO        | Lost to follow-up | PR |
| 3/24/F                  | 12                      | 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 terminus | PR |
| 4/26/M                  | 24                      | Distension        | LN protein-losing enteropathy arthritis | 108     | 0.56  | S1:1000 | SSA      | 113                  | 1.68   | +    | 10     | Pred    | HCQ CTX | Partial remission | CR |
| 5/29/F                  | 15                      | 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                       | Dyspnea distension | LN                           | 61      | 1.21  | HS1:640 | dsDNA    | 357                  | 1.79   | +    | 8      | MP CTX  | NO     | PR        | Lost to follow-up | PR |
| 7/32/F                  | 3                       | Dyspnea           | Thrombocytopenia             | 55      | 1.24  | HS1:320 | dsDNA SSA  | 823                  | 1.43   | +    | 5      | MP      | CsA     | NO        | Inailed | Inailed|
| 8/33/F                  | 7                       | Dyspnea           | NO                           | 5       | 0.95  | HS 1:100 | SSA      | 130                  | 2.87   | +    | 4      | MP pulse | Pred HCQ | NO        | Lost to follow-up | PR |
| 9/35/F                  | 48                      | NO                | Leukocytopenia arthritis     | 34      | 1.11  | HS   | SSA SSB  | 272                  | 2.33   | +    | 7      | HCQ     | NO     | Inailed | Lost to follow-up | PR |
| 10/42/F                 | 12                      | Dyspnea           | Leukocytopenia fever rash    | 55      | 0.67  | S1:320 | dsDNA    | 112                  | 1.97   | +    | 7      | MP      | NO     | Partial remission | PR |
| 11/47/F                 | 5                       | Distension        | Leukocytopenia               | 32      | 0.86  | S1:160 | rRNP     | 169                  | 1.69   | +    | 5      | Diuresis | NO     | NO        | Lost to follow-up | PR |
| 12/48/F                 | 36                      | Distension        | Rash alopecia               | 15      | 0.93  | HS1:320 | SSA RNP | 60                  | 2.3    | +    | 4      | Pred    | HCQ AZA | Compression band loosen operation of thoracic duct terminus | PR |
| 13/50/F                 | 9                       | Distension        | Arthritis Raynaud's phenomenon LN | 17      | 0.99  | S1:320 | Sm RNP  | —                  | —      | +    | 10     | Pred HCQ | NO     | PR        | Died   |
| 14/52/F                 | 12                      | 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                      | Dyspnea distension | Protein-losing enteropathy  | 26      | 0.84  | H1:1000 | dsDNA    | —                  | —      | +    | 4      | Pred    | NO     | Died      | 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, HCO = hydroxychloroquine, LN = lupus nephritis, M = male, MMF = mycophenolate mofetil, 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.
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 7 patients, and chylous ascites alone was present in 2 patients. Protein-losing enteropathy was diagnosed in 3 patients by 99mTc-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).

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

![Figure 1](image_url) Lymphangiography shows thoracic duct outlet obstruction in our patients (white arrow).
## 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 | Other symptoms | Other symptoms details | ESR mm/h | C3 g/L | ANA | Anti-ENA | CHOL mmol/L | Therapy m (month); d (day) | Prognosis                                                                 |
|-------------------|-----------------|--------------------|---------------------|-------------------|------------------------------|----------------|------------------------|-----------|--------|-----|----------|-------------|-----------------------------|------------------------------------------------------------------------------|
| Lee et al[10]     | 47/F            | Korea              | 9 TA                | Abdominal distension | Abdominal distension        | Malar rash, pleuritis | LN class II, pleuritis | 107       | 1.07   | S1:320 | SSA       | 106          | 0.3; Pred 60 mg/d; 1mg pulse CTX×3 m | Chylous effusion completely resolved                                             |
| Lin et al[17]     | 68/M            | Korea              | 7 TA                | Increased abdominal girth | Increased abdominal girth | Protein-losing enteropathy | Malar rash, pleuritis | 76        | 1.07   | HS1:1280 | SSA       | 880          | 2.2; Pred 20 mg/d HCO 400 mg/d | Died of acute respiratory failure after 2 mo Cytolyx cleared rapidly with no recurrence after a follow-up of 4 yr. |
| Chen et al[13]    | 93/F            | Taiwan             | Over 2 d A         | Abdominal fullness   | Abdominal fullness          | Discoid rash, oral ulcers, proteinuria | Malar rash, pleuritis | —         | 1.07   | —     | —       | 303          | 20 mg/d | Abdominal distension subsided obviously. Died of GI bleed 2 wk later |
| Song et al[11]    | 23/F            | China              | 24 T                | Chest congestion     | Chest congestion            | NO                        | Malar rash, pleuritis | 90        | 1.07   | 1:1000 | Sm       | 159          | 1.9; Pred 60 mg/d; 1mg pulse CTX×3 m | No recurrence follow-up period of 4 yr |
| Kang et al[18]    | 21/F            | China              | 36 T                | Chest congestion     | Chest congestion            | SSA Sm dsDNA             | SSA Sm dsDNA          | 70        | 1.07   | 1:30   | SSA Sm dsDNA | 346          | 1.7; Pred 60 mg/d; 1mg pulse CTX×3 m | No recurrence follow-up period of 2.5 yr |
| Han et al[20]     | 33/F            | China              | 20 T                | Chest congestion     | Chest congestion            | SSA Sm dsDNA             | SSA Sm dsDNA          | 70        | 1.07   | 1:30   | SSA Sm dsDNA | 478          | 3.5; Pred 60 mg/d; 1mg pulse CTX×3 m | No recurrence follow-up period of 1.5 yr |
| Zhang et al[8]    | 32/M            | China              | 120 T               | Chest congestion     | Chest congestion            | SSA Sm dsDNA             | SSA Sm dsDNA          | 90        | 1.07   | 1:1000 | SSA Sm dsDNA | 248          | 2.2; Pred 60 mg/d; 1mg pulse CTX×3 m | No recurrence follow-up period of 10 mo |
| Kakar et al[21]   | 38/F            | India              | 1½ T                | Abdominal distension | Abdominal distension        | SSA Sm dsDNA             | SSA Sm dsDNA          | 70        | 1.07   | 1:1000 | SSA Sm dsDNA | 568          | —; Pred 60 mg/d; 1mg pulse MMF 1.5 g | Minimal left pleural effusion on 6 mo Fluids resolved with no recurrence on 10 wks |
| Soyzeal et al[22] | 61/F            | Turkey             | 120 TA              | Abdominal distension | Abdominal distension        | SSA Sm dsDNA             | SSA Sm dsDNA          | 6         | 1.07   | H1:1000 | Negative   | 542          | —; Pred 60 mg/d; 1mg pulse MMF 1.5 g | Significant reduction of ascites and pleural effusion on 6 mo |
| Manzella et al[23]| 36/F            | Argentina          | 180 T               | Abdominal distension | Abdominal distension        | SSA Sm dsDNA             | SSA Sm dsDNA          | 17        | 1.07   | 1:30   | SSA Sm dsDNA | 270          | —; Pred 60 mg/d; 1mg pulse MMF 1.5 g | Resolution of ascites |
| Hasan et al[24]   | 52/F            | African-American   | 4 T                 | Abdominal distension | Abdominal distension        | SSA Sm dsDNA             | SSA Sm dsDNA          | 118       | 1.07   | —     | —       | 1732         | —; Pred 60 mg/d; 1mg pulse MMF 1.5 g | —; Pred 60 mg/d; 1mg pulse MMF 1.5 g |

_A=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, F=female, H=homogeneity, HCO=hydroxychloroquine, L= lupus nephritis, M=male, MMF=mycophenolatemofetil, MPG=methylprednisolone, MTX=methotrexate, N=nuclear, pred=prednisolone, RNP=ribonucleoprotein, 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. In another report, 4 patients developed this complication after a disease duration of between 20 and 120 months. SLE patients with chylothorax and/or chylous ascites had a lower incidence of fever, mucocutaneous involvement, hypoalbuminemia, hypocomplementemia, positive anti-SSA, anti-SSB, 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 chyleous effusion in SLE in future study.

The chyle test of effusion was positive for all patients, which supports the diagnosis of chyleous 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 chyleous 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 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 chyleous 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 chyleous 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 chyleous effusion <12 months responded well to glucocorticoid and immunosuppressive agents, in accord with previous studies. Of the other 6 patients with remission, the duration of chyleous effusion in 5 was ≥12 months, the duration in 1 patient was 3 months. These patients were treated with glucocorticoids and immunosuppressants, but chyleous 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. Chyleous effusion was significantly decreased after surgery. The 5 patients with the duration of chyleous effusion ≥12 months in our study is similar to the literature which Song et al. 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 absorbed. 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 were only 2 cases according to the English literature review. 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
chyloous 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.

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References
[1] Nair SK, Perko M, Hayward MP. Aetiology and management of chylothorax in adults. Eur J Cardiothorac Surg 2007;32:362–9.
[2] Hooper C, Lee YC, Maskell N. BTS Pleural Guideline Group-Investigation of a unilateral pleural effusion in adults: British Thoracic Society Pleural Disease Guideline 2010. Thorax 2010;65: i4–17.
[3] Chen YS, Memon P. Lymphangioleiomyomatosis manifesting as refractory chylothorax and chyloperitoneum. BMJ Case Rep 2019;12: e229958.
[4] Bhattacharji B, Schmidt F, Devkota A, et al. A case of chylothorax in a patient with sarcoidosis: a rare and potentially fatal complication. J Community Hosp Intern Med Perspect 2015;5:28300.
[5] Demirbas E, Atulgan K, Er ZC, et al. Treatment of chylothorax with pleurodesis (a lesser known complication of behcet’s disease): a case report. J Tehran Heart Cent 2018;13:180–2.
[6] Sosyal DE, Hazar Turan S, Ozmen M, et al. A rare case of systemic lupus erythematosus with chyloous ascites and chylothorax. Case Rep Rheumatol 2013;2013:797696.
[7] Liang Y, Leng RX, Pan HF, et al. The prevalence and risk factors for serositis in patients with systemic lupus erythematosus: a cross-sectional study. Rheumatol Int 2017;37:305–11.
[8] Man BL, Mok CC. Serositis related to systemic lupus erythematosus: prevalence and outcome. Lupus 2005;14:822–6.
[9] Manzella DJ, Dettori PN, Hertimian ML, et al. Chyloous ascites and chylothorax as presentation of a systemic progression of discoid lupus. J Clin Rheumatol 2013;19:87–9.
[10] Lee CK, Han JM, Lee KN, et al. Concurrent occurrence of chylothorax, chyloous ascites, and protein-losing enteropathy in systemic lupus erythematosus. J Rheumatol 2002;29:1330–3.
[11] Song P, Zhang J, Shang C, et al. Refractory chyloous pleural effusion with systemic lupus erythematosus: surgical treatment when steroid/immuno-suppressant resistant. Z Rheumatol 2019;78:797–802.
[12] Lin YJ, Chen DY, Lan JL, et al. Chylothorax as the initial presentation of systemic lupus erythematosus: a case report. Clin Rheumatol 2007;26:1373–4.
[13] Chen GL, Yang DH, Hsu WH. Chyloous ascites and pleural transudate: rare presentations in systemic lupus erythematosus in old age. Case Rep Immunol 2012;2012:390831.
[14] Hasan B, Asif T, Hasan M, et al. Chyloous ascites in systemic lupus erythematosus: a diagnostic challenge. Cureus 2017;9:e1226.
[15] Kakar A, Pipaliya K, Goga A. A rare combination: chylous polyserositis and autoimmune myelofibrosis as a presentation of systemic lupus erythematosus. Int J Rheum Dis 2019;22:516–20.
[16] Hochberg MC. Updating the American College of Rheumatology revised criteria for the classification of systemic lupus erythematosus. Arthritis Rheum 1997;40:1723.
[17] Doerr CH, Allen MS, Nichols FC, et al. Etiology of chylothorax in 203 patients. Mayo Clin Proc 2005;80:867–70.
[18] Soto-martinez M, Massie J. Chylothorax: diagnosis and management in children. Pediatr Respir Rev 2009;10:199–207.
[19] Ngan H, Fok M, Wong J. The role of lymphography in chylothorax following thoracic surgery. Br J Radiol 1988;61:1032–6.