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First case of pleural amyloidosis in systemic erythematosus: report and literature review

Introduction

Systemic lupus erythematosus (SLE) is a systemic autoimmune disease characterized by diverse multisystem involvement including nephritis, serositis, as well as respiratory system and central nervous system impairment [1]. Secondary amyloidosis (AA amyloidosis) can occur as a complication of chronic inflammatory disease such as rheumatic diseases, especially rheumatoid arthritis [2–5]. However, AA amyloidosis is rarely described in patients with SLE [6, 7]. To date, the literature shows that amyloidosis associated with SLE can occur in organs and tissues including the kidney, heart, lung, bone marrow, gastrointestinal tract, liver, spleen, and adrenal cortex [6, 7]. We report the first case of SLE with pleural amyloidosis, which is the real cause of massive pleural effusion.

Case report

A 44-year-old woman was admitted to our department for the third time because of bilateral massive pleural effusion. She previously underwent conization for cervical precancerous lesions in 2006. In 2013, she developed intermittent lower extremity edema without consulting doctors. In 2016, unclear chest pain appeared, especially after deep breathing, along with polyarthralgia, dry mouth, oral ulcer, and alopecia. She presented to our hospital and underwent a systemic medical examination. Her antinuclear antibody (ANA) titer was 1:1000 (indirect immunofluorescence assay, IIF), anti-double stranded DNA antibody (anti-dsDNA) was 1:10 (IIF), and anti-Ro52, anti-SSA, anti-histone, and anti-ANuA antibodies were positive. C-reactive protein (CRP) was 1.32 mg/l, erythrocyte sedimentation rate (ESR) was 54 mm/h, serum IgG was 15.8 g/l,and complement C3 and C4 were 0.51 g/l (normal range from 0.79 to 1.52 g/l) and 0.05 g/l (normal range from 0.16 to 0.38 g/l), respectively. There was protein in her urine protein and the 24-h urinary protein was 0.16 g. Computed tomography (CT) scan of the chest demonstrated massive pleural effusion on both sides and the lungs were partially compressed. The patient met the 1997 American College of Rheumatology revised criteria for the classification of SLE [8]. A diagnosis of SLE was supported by the following laboratory parameters: positive ANA (1:1000), positive antibodies to dsDNA (1:10), histones, Ro and La, and diminished serum complement. Subsequently, intravenous methylprednisolone (80 mg/day) combined with intravenous cyclophosphamide (200 mg every other day) therapy was given and she was discharged in better condition.

In March 2017, she suffered from exertional dyspnea and fatigue again. In August of the same year she underwent a repeat chest CT scan at our hospital, which detected similar bilateral massive pleural effusion (**Fig. 1**). A physical examination revealed diminished breath sounds throughout both lungs, but without lower-extremity edema. Her temperature was normal. There was no hepatosplenomegaly or lymphadenopathy. A series of tests pertaining to SLE disease activity, tumor, and infection were performed and we found that CRP, ESR, serum ferritin, lactate dehydrogenase (231 U/l), serum immunoglobulin, serum complement, and anti-dsDNA antibodies were normal. NT-proBNP was also normal. Thoracentesis revealed exudative pleural effusion and no tumor cells were found (**Table 1**). In addition, interferon-gamma release assay (IGRA) was negative. Initially, intravenous dexamethasone (20 mg/day) was given for 5 days, followed by intravenous methylprednisolone at a dosage of 40 mg/day. Mycophenolate mofetil was administered at a dosage of 1500 mg/day, as well as hydroxychloroquine. Additionally, we also administered diuretic treatment. However, a chest CT scan after 2 weeks of treatment did not show a reduction in pleural effusion. In view of this, we

Table 1 Results of pleural effusion

Total protein	46.6 g/l
Albumin	31.2 g/l
Glucose	5.55 mmol/l
Lactate dehydrogenase	566 U/l
CEA	3.1 U/ml
CA 125	62.32 U/ml
Adenosine deaminase	6 U/l
Rivalta test	Positive
Cell count	4,830/μl
Neutrophil	80%
Lymphocyte	20%
Acid-fast staining	Negative
Microbe culture	Negative
Tumor cells	Negative

CEA carcinoembryonic antigen, *CA 125* cancer antigen 125

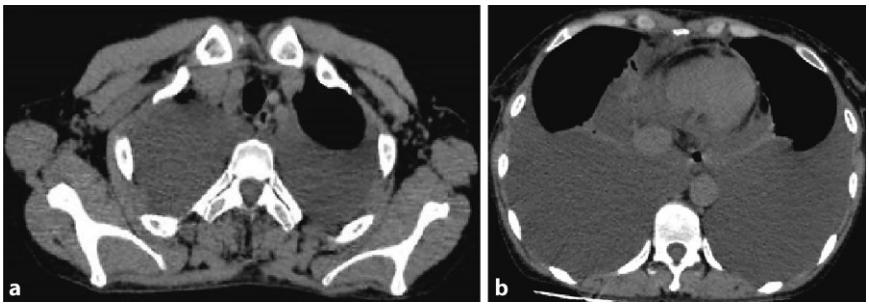

Fig. 1 ▲ Chest computed tomography scan showing bilateral massive pleural effusion from the upper (**a**) to the lower chest (**b**)

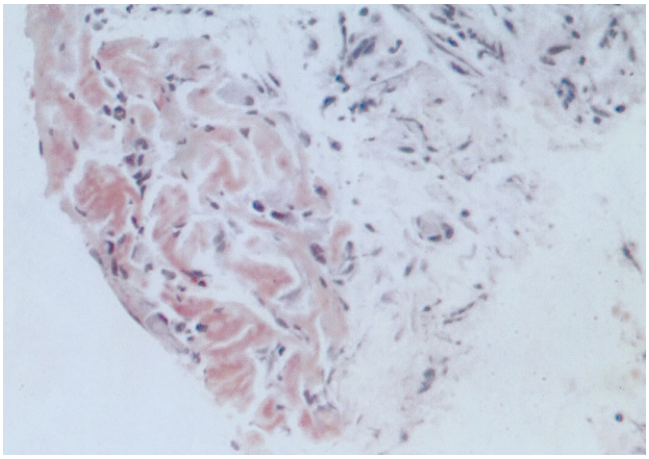

Fig. 2 ◀ Congo red staining demonstrating amyloid deposition in pleural biopsy specimen [Hematoxylin and Eosin (H&E) staining plus Congo red staining, ×40]. The immunohistochemical staining: CK (+), CK5/6 (+), CR (+), D2-40 (+), Ki-67 (+), TTF-1(–), κ(+/–), λ(–)

hypothesized that tuberculous pleurisy could be the reason that IGRA was negative with the use of glucocorticoids and immunosuppressive agents [9]. Thus, she was discharged with anti-tuberculosis treatment and oral prednisone tapered to 40 mg/day.

After 1 month of anti-tuberculosis treatment, we performed another chest CT scan, which still showed no difference compared with the last scan. She was admitted to our department for the third time and a more thorough examination was undertaken. Pleural effusion was still exudative, culturing was negative, and no tumor cells were found. IGRA and polymerase chain reaction (PCR) of mycobacterium were both negative. No space-occupying lesions were found via abdominal CT scan and Budd–Chiari syndrome was excluded by ultrasonography of the portal vein, hepatic veins, and inferior vena cava. On the basis that no evidence of infection and tumor was found contributing to exudative pleural effusion, we gave her intravenous dexamethasone (40 mg/day) for 3 days, followed by intravenous methylprednisolone at a maintaining dosage of 80 mg/day. Moreover, we placed a chest tube for drainage to relieve the dyspnea. Finally, we decided to perform thoracoscopic biopsy of the pleura on account of the fact that the drainage volume of pleural effusion did not decrease. Amyloid A deposition was detected and confirmed by pretreatment of potassium permanganate in pleural biopsy specimen (**Fig. 2**). She was referred to another hospital for treatment.

Discussion

AA amyloidosis is secondary to chronic inflammatory disease including chronic sepsis, rheumatic diseases, and malignancy [2–5]. Among rheumatic diseases, there are very few reports of SLE complicated with AA amyloidosis in the literature [3, 6, 7]. This may be underestimated because the symptoms resulting from amyloidosis often overlap with SLE and can be relieved by treating SLE. The current literature shows that numerous organs can be involved including the kidney, heart, lung, bone marrow, gastrointestinal tract, liver, spleen, and adrenal cortex [6, 7]. Furthermore, the kidney is the most common organ involved with amyloidosis; therefore, renal amyloidosis may be mistaken for lupus nephritis. In the case of our patient, amyloid was deposited in the pleura, which led to pleural effusion.

Generally, the common causes of bilateral pleural effusion in SLE are pleurisy and hypoproteinemia, both of which are secondary to lupus flare and can be improved with an aggressive treatment of SLE [10–12]. If the response is not good, we should make a careful differential diagnosis and screen other causes such as congestive heart failure, malignancy, and pleural infection, employing thoracentesis and even pleural biopsy. In the present case, the initial pleural effusion of our patient responded well to glucocorticoids, suggesting that pleural effusion might have been due to pleurisy at the very beginning. The recurrent pleural effusion resistant to glucocorticoids and immunosuppressive agents revealed that the pathogenesis of pleural effusion might change. The aforementioned causes were carefully ruled out and finally pleural biopsy provided the answer.

Pleural amyloidosis is usually accompanied by pleural effusion, which is either exudate or transudate [13]. Although the exact mechanism of the production of pleural effusion is not clear, amyloid deposited in parietal pleura could play a pathogenic role in inhibiting the absorption of pleural fluid. Moreover, pleural thickening can be detected in pleural amyloidosis, which may mimic pleural malignancy [14, 15]. There have been only a small number of reports in regard to pleural amyloidosis and most of the cases are of multiple myeloma [13, 16, 17]. Herein, we present the first case of pleural amyloidosis in SLE.

Conclusion

Amyloidosis is rarely described in SLE patients but should not be underestimated. Pleural amyloidosis should be taken into account when no other cause is found

as an explanation for pleural effusion resisting treatment.

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Compliance with ethical guidelines

Conflict of interest. J. Xiong, Y. Ren, H. Li, B. Fu, and R. Wu declare that they have no competing interests.

Written informed consent was obtained from all patients included in the study prior to submission of the case report. Additional informed consent was obtained from all patients for whom identifying information is included in this article.

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Fachnachrichten

Arthrose: Wann brauche ich ein künstliches Kniegelenk?

Neue Patientenleitlinie „Indikation Knieendoprothese"

Eine neue Patientenleitlinie, die von Betroffenen mitgestaltet wurde, beschreibt die Kriterien, die vor einem Gelenkersatz berücksichtigt werden sollten.

Obwohl der Gelenkersatz zu den erfolgreichsten Eingriffen in Orthopädie und Unfallchirurgie gehört, sind 10 bis 20 Prozent der Patienten unzufrieden mit dem Ergebnis. „Umso wichtiger ist es, dass Patienten bei der Entscheidung für oder gegen einen Gelenkersatz ein Mitspracherecht haben", betont Professorin Dr. med. Erika Gromnica-Ihle von der Deutschen Rheuma-Liga. „Es ist bekannt, dass sich die Erwartungen an eine Op. von Ärzten und Patienten unterscheiden", sagt die Expertin. Deshalb wurden bei der Erstellung der neuen Leitlinie „Indikation Knieendoprothese" auch Patientenvertreter miteinbezogen.

Die Leitlinie bietet wissenschaftlich gesicherte Empfehlungen, die den Patienten über die Kriterien für eine Gelenkoperation aufklären und bei der Entscheidung unterstützen sollen.

Die **Patientenleitlinie „Indikation Knieendoprothese"** ist online kostenlos verfügbar, unter: www.awmf.org/leitlinien/detail/ll/033-052.html

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