Geraldino-Pardilla et al. J Rheum Dis Treat 2015, 1:4
ISSN: 2469-5726

Journal of
Rheumatic Diseases and Treatment

Case Series: Open Access

Massive Serositis as the Initial Presentation of Systemic Lupus Erythematosus: A Report of Two Cases and Review of the Literature

Laura Geraldino-Pardilla[1] Yevgeniya Gartshteyn[1]* and Fabian Mendoza[2]

[1]*Department of Medicine, Columbia University, College of Physicians & Surgeons, USA*

[2]*Department of Medicine, Thomas Jefferson University, USA*

***Corresponding author:** *Yevgeniya Gartshteyn, MD, Department of Medicine, Columbia University, College of Physicians & Surgeons, 177 Fort Washington Ave 8SK 8-004 New York, NY 10032, USA, E-mail: yg2372@cumc.columbia.edu*

Abstract

Large volume effusions as a manifestation of active systemic lupus erythematous (SLE) is rare, and when it does occur, it is usually associated with complications of chronic lupus disease, such as nephrotic syndrome, constrictive pericarditis, heart failure or Budd-Chiari syndrome. Massive serositis as a presenting feature of SLE is rare. We de-scribe two adult cases of new onset SLE presenting with massive ascites in the first case, and large bilateral pleural effusions in the second case. The serositis in both patients responded well to high dose steroid therapy with signifi-cant improvement in symptoms. Only a small number of case reports describing massive ascites or large pleural effusions as initial manifestations of new onset SLE have been published. A literature review of these case reports and their treatment outcomes is described.

Keywords

Systemic lupus erythematosus, Lupus pleuritis, Lupus peritonitis, Lupus ascites, Pleural effusion

Introduction

Systemic lupus erythematosus (SLE) is an autoimmune disease with heterogeneous phenotypes. Although serosal inflammation is common in SLE, massive pleural ascites and large volume pleural effusions as presenting features are unusual. Unlike most cases of lupus serositis, patients with these large effusions tend to require aggressive management with high dose steroids and steroid-sparing agents [1].

Methods

Two case reports of SLE presenting as serositis with large volume effusions are described.

A literature review was performed using a Pubmed search (1964-2015) for all reported cases of large volume ascites or pleural effusions as the presenting features of new onset SLE. The following search terms were used: SLE/Lupus serositis, ascites, pleuritis, peritonitis, pleural effusion, peritoneal effusion. Only adult cases in the English language were reviewed.

Case Reports

Case 1

A 50-year-old immigrant from Central America, was admitted with rapidly increasing ascites. Medical problems included hypertension, chronic hepatitis C with cirrhosis and portal hypertension (treated with an 8 month course of PEG-IFN one year prior to admission), and end-stage renal disease (ESRD) status post cadaveric renal transplant 10 years prior but complicated by transplant rejection and new hemodialysis requirement over the last two years.

On presentation, the patient was febrile with cervical lymphadenopathy, accompanied by massive non-tender ascites with hemodynamic compromise requiring serial large-volume paracentesis (Figure 1). The serum-ascites albumin gradient (SAAG) was < 1.1, which was inconsistent with portal hypertension ascites or possible nephrotic syndrome given the end stage renal disease. Ascitic fluid WBC counts ranged from 77-675/mm^3 with a lymphocytic predominance. Peritoneal fluid bacterial, fungal,

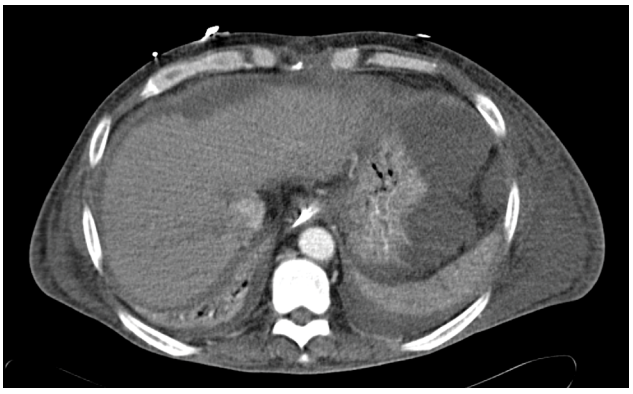

Figure 1: Axial, contrast enhanced computed tomography (CT) image of the abdomen showing ascites.

ClinMed International Library

Citation: Geraldino-Pardilla L, Gartshteyn Y, Mendoza F (2015) Massive Serositis as the Initial Presentation of Systemic Lupus Erythe-matosus: A Report of Two Cases and Review of the Literature. J Rheum Dis Treat 1:028

Received: November 26, 2015: **Accepted:** December 29, 2015: **Published:** December 31, 2015

and AFB cultures were negative and there were no malignant cells. Serum HIV, rheumatoid factor and cryoglobulins were negative. Tuberculin purified protein derivative (PPD) testing was negative as well. Hepatic or portal vascular thrombosis was ruled out with patent vessels seen on Doppler, and an echocardiogram noted preserved ventricular function. Serum ANA and anti-dsDNA antibodies were 1:2560 and 12,751 IU/mL, respectively (normal dsDNA is < 25 IU/ml). The patient was also leukopenic (WBC-2.7/mm^3) and had severe hypocomplementemia (C3 = 12 mg/dL, C4 = 4 mg/dL).

A diagnosis of SLE with lupus peritonitis was made and treatment initiated with intravenous methylprednisolone 500 mg/day for a week followed by prednisone 1 mg/Kg/day and hydroxychloroquine 400 mg daily. This resulted in hemodynamic stability, significant improvement of the ascites, rise in complement levels and lowering anti-DNA titers. The small volume ascites that remained revealed a SAAG >1.1 which was then attributed to the known portal hypertension.

Case 2

An 80-year-old patient with history of congestive heart failure (CHF) and breast cancer in remission after a left radical mastectomy, radiation and chemotherapy presented with dyspnea. On arrival the patient required emergent mechanical ventilation for respiratory failure due to massive bilateral pleural effusions and ascites. Pleural fluid analysis was exudative with negative cultures and cytology

Table 1: Case reports of ascites as the presenting feature of SLE.

Year/Author (reference)	Clinical Presentation	SAlb[a]	AsAlb[b]	ANA	anti-dsDNA	C3	C4	Treatment	Outcome
Mier [14]	24yo F with abdominal pain and distention x1 month	NR	3.9 g/dL	NR	13% binding (normal 0-2%)	30 mg/dL	4 mg/dL	Prednisone 60 mg/day	Resolution in 10 days
Ishiguro [10]	52yo F with fever, rash, abdominal distention x6 months	2.8 g/dL	2.2 g/dL	1:1280	36 U/mL (radio-immunoassay, normal < 10 U/mL)	< 20 mg/dL	< 5 mg/dL	Prednisolone 50 mg, Methylprednisolone 1 g/day × 3 days (repeated twice) followed by taper	Massive ascites resolved after pulse dose steroids
Hammoudeh [4]	27yo F with abdominal pain, n/v with new rash and joint pain	NR	Ascites Protein 4.8 g/dL	1:1280	1:20	51 mg/dL	10 mg/dL	Sulindac 400 mg/day, Chloroquine 500 mg/day	Discharged 1 week later with minimal symptoms
Weinstein [2]	33yo F with sharp peri-umbilical pain and increasing abdominal girth x1 week	2.7 g/dL	1.9 g/dL	pos	pos	23.7 mg/dL	7.9 mg/dL	Methyl-prednisolone + Cyclophosphamide	Discharged with minimal ascites and mild AKI
Ito [11]	77yo F with pancytopenia and worsening ascites and lower extremity edema x3 months	2.2 g/dL	2.3 g/dL	pos	71 U/mL	20.4 mg/dL	9.4 mg/dL	Prednisolone 60 mg/day, Methylprednisolone 0.5 g/day × 3 days (× 2) tapered to 15 mg over by 2 months	Complicated by pneumonia, death
Trock [15]	80yo F with increasing abdominal girth and extremity edema over 3 weeks, found to have massive ascites and pericarditis	NR	NR	1:640	37 (crithidia assay, normal < 25)	62 mg/dL	13 mg/dL	Methylprednisolone 60 mg followed by prednisone 20 mg bid, AZA 100 mg/day, Hydroxychloroquine 400 mg/day	Resolution without symptoms by 4 weeks, but recurred on 2 year follow up
Forouhar-Graff [7]	18yo F with n/v, diarrhea, abdominal distention x4 weeks	2.9 g/dL	1.9 g/dL	1:5120	1:80	53 mg/dL	4 mg/dL	Methylprednisolone 250 mg × 3 days, then 60 mg/day × 4 weeks	Over the course of 18 months, was still steroid dependent and AZA was started given 2 relapses
Prasad [8]	26yo F with 2.5 months of abdominal distention and fever postpartum	2.5 g/dL	1.72 g/dL	pos	115 U/mL	44.9 mg/dL	6.85 mg/dL	Prednisolone 1 mg/kg; hydroxychloroquine maintenance	Ascites resolved by 4 weeks; in remission at 3 months follow-up
Pott Junior [16]	47 yo F with increasing abdominal size x2 months and diffuse pain	2.5 g/dL	1.65 g/dL	1:160	neg	na	na	Prednisone 60 mg/day; chloroquine 250 mg/day	Ascites resolved and patient was asymptomatic at 3 months follow-up
Liu [18]	19yo M with abdominal pain/n/v x3 days	3.4 g/dL	NR	pos	pos	55 mg/dL	10 mg/dL	Prednisone 60 mg/day; chloroquine 250 mg/day	Symptoms resolved at 3 months follow-up
Zhou [1]	39yo F with abdominal distention and pain x20 days	3.2 g/dL	NR	1:800	neg anti-Sm pos	65 mg/dL	5 mg/dL	Methylprednisolone 40 mg/day, taper to 10 mg/day; 0.2 g/day hydroxychloroquine maintenance	Abdominal pain and distention improved by day 7, ascites resolved by 1 month

YO: Year Old; M: Male; F: Female; NR: Not Reported; n/v: Nausea and Vomiting; Neg: Negative; Pos: Positive; AZA: Azathioprine. aSalb,serum albumin; bAsAlb, ascites albumin

Table 2: Case reports ofmassive pleural effusions as the presenting feature of SLE.

Year/Author	Clinical Presentation	Pleural fluid WBC	ANA	anti-dsDNA	C3	C4	Treatment	Outcome
Bouros [3]	20yo M with dyspnea and fevers ×1 week	500 × 106 cells/L; 70% lymphocytes	1:350	pos	17.5 mg/dL	3.52 mg/dL	methylprednisolone 64 mg/day × 2 months then slowly tapered; cyclophosphamide 150 mg/day × 6 months, then 100 mg/day × 6 months	effusion resolved by 20 days, minimal pleural thickening remained
Mitra [12]	20yo F with dyspnea × 7 days	200-1970 × 106 cells/L; 20-40% lymphocytes, 60-80% neutrophils	1:160	98 ng/dL	NR	NR	prednisolone 1 mg/kg/day, maintained on chronic steroids	near complete resolution of pleural effusion at 4 weeks
Wan [5]	23yo F with cough and chest pain x1 week	NR	320X	1:620	35.5 mg/dL	< 10 mg/dL	prednisolone 2 mg/kg/day; methotrexate 7.5 mg/wk - subsequently maintained on prednisolone 10 mg/day	effusion decreased dramatically by 1 month
Chang [17]	66yo M with fever and dyspnea × 1-2 weeks despite levoquin for pneumonia.	340-2950 × 106 cells/L ; 3-16% lymphocytes and 48-92% neutrophils	1:1280	1:160	dcr	dcr	methylprednisolone 1 mg/kg/day	complete resolution of pleural effusion and symptoms

YO: Year Old; M: Male; F: Female; NR: Not Reported; Pos: Positive; DCR: Decreased Serum Complement Levels (taken from the original publication, actual serum level not reported).

negative for malignant cells. An echocardiogram showed preserved ventricular function and a small pericardial effusion. A CT scan of the chest confirmed large bilateral pleural effusions. V/Q scan was low probability for pulmonary embolism. Bronchoscopic lavage had no growth from cultures and was negative for malignant cells. A right-sided heart catheterization was normal. After diuresis, the patient was extubated but required emergent chest tube placement for pleural fluid drainage.

Serologies revealed a positive serum ANA (1:320), anti-ds-DNA (119), and borderline complement levels (C3 = 89, C4 = 14). Acute renal failure subsequently developed and a renal biopsy revealed Class IV/V lupus nephritis (LN). After no response to prednisone 60 mg/day, methylprednisolone 500 mg/day for 3 days was started followed by a steroid taper, hydroxychloroquine 400 mg daily and mycophenolate mofetil titrated to 2 g/day. The renal function improved over the subsequent days and the pleural and peritoneal effusions resolved.

Discussion

Although serositis is found in 63% of SLE patients on autopsy, [2] massive ascites and large pleural effusions are uncommon in the lifetime of lupus disease, and are even more rare as the initial manifestation [2-4]. Pleural effusions occur in up to 50% of patients with SLE, but it is the presenting feature in only 1-5% of patients, with effusions usually small to moderate in size [5]. Unlike pleural involvement, the true prevalence of lupus peritonitis is unknown but presumably low, although probably overlooked despite several cases being published since Metzger's initial case report in 1974 [6].

Large effusions are usually attributed to a complication from CHF, constrictive pericarditis, nephrotic syndrome, portal hypertension, Budd-Chiari, peritoneal carcinomatosis, infectious peritonitis or pneumonia. One of these etiologies is usually cited as the cause for the 8-11% of SLE patients that develop ascites during the lifetime of their disease [7,8]. It is nonetheless important to consider active SLE in the differential, as was the situation in the two cases described that had SLE-related massive ascites and/or large pleural effusions as the initial presentation of SLE. Our patients met the 1997 American College of Rheumatology classification criteria for SLE [9], given positive anti-ANA and anti-ds-DNA antibodies, serositis, as well as leukopenia in case No.1, and lupus nephritis in case No.2. For case No.1, although portal hypertension was present, the low SAAG in the absence of infection, malignancy, or acute portal thrombosis was inconsistent with portal hypertension ascites and suggested peritonitis of unknown etiology. Given the positive serum ANA and ds-DNA antibodies, low complement levels, and a significant clinical response to steroids, SLE remains the most likely diagnosis. Unfortunately, the etiology of the ESRD in this patient could not be determined since the renal biopsy had been performed many years prior in Central America. It is also debatable whether the discontinuation of the immunosuppressants, which the patient had in the past taken following the renal transplant, now unmasked the SLE, or whether the treatment with PEG-IFN, on the other hand, resulted in a drug-induced lupus-like illness. In the second case, although the patient had a history of a prior CHF episode, the echocardiogram and right heart catheterization were normal, arguing against CHF as the cause for the large effusions.

Serositis results from fluid and protein leak due to increased permeability of the microvascular circulation that occurs with inflammation of the pleural and peritoneal microvessels. The presumed vasculitis is caused by immune-complex deposition and complement activation, described since the 1970s and noted in biopsies of the pleural and peritoneal vessels [2,10-12]. Bitran et al. revealed granular depositions of IgG and complement along the mesothelial layer and blood vessels in SLE patients with serositis [13]. In massive ascites, marked serosal exudate in conjunction with a reduced peritoneal absorptive capacity facilitate rapid fluid accumulation.

A review of similar adult cases of massive ascites and severe pleuritis as the presenting features of SLE is summarized in table 1 and table 2, respectively [1-5,7,8,10-12,14-18]. Ascites fluid characteristics include a WBC range from 10-1630/mm^3 with lymphocytic predominance, [2,7] a SAAG < 1.1, and occasionally positive ANA, anti-dsDNA antibodies, and lupus erythematosus (LE) cells. Pleural fluid characteristics include a WBC 200-3000/mm^3 with either a neutrophilic or lymphocytic predominance, high protein and LDH counts, positive ANA, elevated anti-dsDNA titers and presence of LE cells [5,17]. For treatment, most patients required high dose steroids followed by a taper, with complete resolution of serositis noted in some and moderate reduction in others. Additional immunosuppression was administered in 4 of the 15 reported patients [2,3,5,15]. Chest tube drainage or pleurodesis were rarely required [5].

Conclusion

Since Dubois stated in 1964 that lupus serositis does not cause significant effusions [19], case reports have been published suggesting that massive lupus serositis does occur and can be the main initial manifestation of the disease. Our case reports and review of the literature emphasize how appropriate evaluation and aggressive immunosuppressive therapy is often required to assure a positive outcome in these cases.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not- for-profit sectors.

References

1. Zhou L, Ming Sun C, Li Chen W, Zhang H, Wang P, et al. (2014) Massive and painful ascites as a presenting manifestation of systemic lupus erythematosus flare: a case report and literature review. Rev Med Chil 142: 255-260.

2. Weinstein PJ, Noyer CM (2000) Rapid onset of massive ascites as the initial presentation of systemic lupus erythematosus. Am J Gastroenterol 95: 302-303.

3. Bouros D, Panagou P, Papandreou L, Kottakis I, Tegos C (1992) Massive bilateral pleural effusion as the only first presentation of systemic lupus erythematosus. Respiration 59: 173-175.

4. Hammoudeh M, Siam AR (1995) Recurrent peritonitis with ascites as the predominant manifestation of systemic lupus erythematosus. Clin Rheumatol 14: 352-354.

5. Wan KS (2008) Pleuritis and pleural effusion as the initial presentation of systemic lupus erythematous in a 23-year-old woman. Rheumatol Int 28: 1257-1260.

6. Metzger AL, Coyne M, Lee S, Kramer LS (1974) In vivo LE cell formation in peritonitis due to systemic lupus erythematosus. J Rheumatol 1: 130-133.

7. Forouhar-Graff H, Dennis-Yawingu K, Parke A (2011) Insidious onset of massive painless ascites as initial manifestation of systemic lupus erythematosus. Lupus 20: 754-757.

8. Prasad S, Abujam B, Lawrence A, Aggarwal A (2012) Massive ascites as a presenting feature of lupus. Int J Rheum Dis 15: e15-16.

9. Hochberg MC (1997) Updating the American College of Rheumatology revised criteria for the classification of systemic lupus erythematosus. Arthritis Rheum 40: 1725.

10. Ishiguro N, Tomino Y, Fujito K, Nakayama S, Koide H (1989) A case of massive ascites due to lupus peritonitis with a dramatic response to steroid pulse therapy. Jpn J Med 28: 608-611.

11. Ito H, Nanamiya W, Kuroda N, Inoue M, Sasaoka A, et al. (2002) Chronic lupus peritonitis with massive ascites at elderly onset: case report and review of the literature. Intern Med 41: 1056-1061.

12. Mitra B, Sengupta P, Saha K, Sarkar N, Pal J (2005) Systemic lupus erythematosus presenting with recurrent pleural effusion without any systemic manifestation. J Assoc Physicians India 53: 1073-1106.

13. Bitran J, McShane D, Ellman MH (1976) Arthritis Rounds: Ascites as the major manifestation of systemic lupus erythematosus. Arthritis Rheum 19: 782-785.

14. Mier A, Weir W (1985) Ascites in systemic lupus erythematosus. Ann Rheum Dis 44: 778-779.

15. Trock D, Voinea A, Wolk J, Majoros S (2005) New-onset lupus presenting as serositis in an 80-year-old woman: does a high-titer ANA in pleural, pericardial, or peritoneal fluid help confirm the diagnosis? J Clin Rheumatol 11: 292-293.

16. Pott Júnior H, Amate Neto A, Teixeira MA, Provenza JR (2012) Ascites due to lupus peritonitis: a rare form of onset of systemic lupus erythematosus. Rev Bras Reumatol 52: 116-119.

17. Chang WT, Hsieh TH, Liu MF. Systemic lupus erythematosus with initial presentation of empyematous pleural effusion in an elderly male patient: a diagnostic challenge. J Microbiol Immunol Infect 46: 139-142.

18. Liu R, Zhang L, Gao S, Chen L, Wang L, et al. (2014) Gastrointestinal symptom due to lupus peritonitis: a rare form of onset of SLE. Int J Clin Exp Med 7: 5917-5920.

19. Dubois EL, Tuffanelli DL (1964) Clinical Manifestations of Systemic Lupus Erythematosus. Computer Analysis of 520 Cases. JAMA 190: 104-111.