

Pseudo-pseudo Meigs syndrome: an uncommon onset of Systemic Lupus Erythematosus

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Abstract

Serositis is seen in approximately 12% of patients with systemic lupus erythematosus (SLE), usually in the form of pleuritis or pericarditis. Peritoneal serositis with ascites is an extremely rare manifestation of SLE and ascites as initial manifestation of SLE is even rarer. Here, we describe a previously healthy 48-year-old female with periumbilical abdominal pain, constitutional symptoms, ascites, pleural effusions and raised CA-125 level as an initial manifestation of SLE, which led up to the diagnosis of pseudo-pseudo Meigs syndrome. PPMS is a rare manifestation of SLE and awareness of this entity among clinicians is crucial to ensure an early recognition and prompt treatment.

Keywords: Systemic lupus erythematosus; Autoimmunity.

Introduction

Serositis is seen in approximately 12% of patients with systemic lupus erythematosus (SLE), usually in the form of pleuritis and/or pericarditis¹. Peritoneal serositis with ascites is an extremely rare manifestation of SLE¹ and ascites as initial manifestation of SLE is even rarer. It is usually described in patients with established SLE and presents as mild to moderate painless ascites with gradual onset. Massive (Grade III/IV) ascites has been rarely reported^{2,3}. Here, we describe a patient with ascites and abdominal pain as an initial manifestation of SLE, which led up to the diagnosis of pseudo-pseudo Meigs syndrome (PPMS). PPMS is a newly emerging manifestation of SLE and only a few cases have been published

Case report

A 48-year-old female with no significant past medical history presented to the emergency department with periumbilical abdominal pain in the last month, history of increasing abdominal girth and constitutional symptoms (fatigue, weight loss of 15 kg in the last 2 months and anorexia). She, also, complained of polyarthralgia for the past four months involving the wrists, proximal interphalangeal joints and knees. She described morning stiffness of the hands lasting for more than an hour. She had no cardiac or respiratory symptoms.

On physical examination, her vital signs were normal, she looked older than she was, underweight and pale. Abdominal examination revealed distension with diffuse tenderness and dull note on percussion of the flanks. No abdominal masses or organomegaly were noticed. Cardiac and respiratory examination was normal. No peripheral edema, cutaneous lesions or stigmata of chronic liver disease were found. Mild tenderness at the proximal interphalangeal (PIP) joints without swelling or deformities was found during the musculoskeletal examination. The initial laboratory workup showed hemoglobin 8.8 grams/deciliter, total white blood cells 2050/ μ L, platelet 141 000/ μ L, erythrocyte sedimentation rate (ESR) 30 mm/hr, C-reactive protein (CRP) 47.6 mg/L, total protein 64 g/L, albumin 26 g/L and ferritin 857 ng/mL. Renal, liver and thyroid function tests were normal. Urine analysis showed leukocyturia, proteinuria and hematuria. Spot urine protein-to-creatinine ratio was 765 mg/g. A urine culture identified an *Escherichia coli*. Suitable antibiotic, according to the antimicrobial susceptibility testing, was started.

Since the patient had a history of weight loss, abdominal pain and distension, a study was carried out to look for underlying malignancy. Contrast-enhanced computed tomography (CT) of chest, abdomen and pelvis showed moderate ascites, mild bilateral pleural effusion and very small pericardial effusion. No other alterations were found. Cancer antigen 125 (CA-125) level was 60 U/ml (N 0-35). Carcinoembryonic antigen and cancer antigen 19-9 levels were normal.

A transthoracic echocardiogram showed a very small pericardial effusion, mild mitral and tricuspid valve regurgitation, normal ventricular systolic function and normal contractility.

Ascitic fluid workup showed characteristics of exudate with a serum-ascites albumin gradient (SAAG) of 0.9 (<1.1). Ascitic fluid culture was negative and no acid-fast bacilli or malignant cells were visualized. Mycobacterium tuberculosis polymerase chain reaction performed on ascitic fluid was also negative.

Since the patient had polyserositis, pancytopenia and arthralgia an autoimmune workup was done. Immunofluorescent antinuclear antibody (ANA) test showed homogenous pattern with a titer of 1:1280. Anti-double stranded DNA antibody (anti-dsDNA) level was markedly elevated (> 800 IU/mL) and anti-nucleosome antibodies were positive. Complement levels were low, C3 level of 54 mg/ dL (N 79-152) and C4 level of 17 mg/dL (N 18-55). SLE associated with PPMS has been diagnosed and the patient started oral prednisolone (20 mg daily) and hydroxychloroquine (200 mg daily).

During hospitalization, the patient had a progressive worsening of the pancytopenia and a blood transfusion was required. Also, an increase in spot urine protein-to-creatinine ratio was noticed.

A 24-hour urine protein test revealed 3080 mg/day. A renal biopsy was performed and showed class III lupus nephritis.

Intravenous methylprednisolone pulse (1 g daily for 3 days), followed by 0.5 mg/kg daily of oral prednisolone, bolus intravenous cyclophosphamide (1 g per month for a total of six months), angiotensin-converting-enzyme (ACE) inhibitor, calcium and vitamin D supplementation were also started.

The patient was discharged after 3 weeks. Steroid was tapered gradually and she started mycophenolate mofetil 2 g daily after monthly intravenous cyclophosphamide for six months. At 3 months follow-up, a significant clinical and laboratory improvement was noticed with recovery of her usual weight and a complete resolution of pancytopenia, proteinuria and polyserositis.

Discussion

Our patient presented with abdominal pain, ascites and constitutional symptoms with significant weight loss, which led us to the suspicion of malignancy. CA-125 was high but the CT scan didn't show any mass or tumor. Nonetheless, pleural and pericardial effusions, in addition to ascites, were observed.

The presence of polyserositis, pancytopenia, polyarthralgia and proteinuria raised the suspicion of SLE and immunological profile and renal biopsy confirmed this suspicion which led to the diagnosis of new-onset SLE associated with PPMS.

PPMS is a newly emerging manifestation of SLE, characterized by the presence of ascites, pleural effusions and raised CA-125 level. It was first described by Tjalma et al. in 2005, and after seven months, Schmitt et al. presented a similar case and named this entity as PPMS. Since then, thirteen cases have been published, as presented in Table 1⁴⁻¹⁷.

PPMS must be differentiated from Meigs Syndrome and Pseudo-Meigs syndrome. In Meigs syndrome, ascites and pleural effusions occur associated with a benign ovarian mass and in Pseudo-Meigs Syndrome occur the same clinical features but in association with any other abdominal or pelvic tumors. Both Meigs syndrome and Pseudo-Meigs Syndrome resolve after tumor resection. PPMS has no association with abdominal or pelvic tumors.

Due to the rarity of this condition, the pathophysiology underlying the ascites of PPMS is still not completely understood. The ascites in PPMS presented in this case and in all previously reported cases is low SAAG ascites (<1.1 g/dL). The leading hypotheses suggest that the underlying basis of this syndrome is severe, uncontrolled inflammation involving the serosa. This may be the result of lymphoaggregation of plasma cells, deposition of immune complexes on the peritoneum triggering a local inflammatory reaction or vasculitis of peritoneal vessels¹⁸. This inflammatory theory is supported by the finding of high serum ferritin and IL-6 levels in the ascitic fluid from another patients with PPMS^{9, 17, 19}.

The pleural effusion may develop by mechanical passive transfer of ascitic fluid through diaphragmatic apertures, intracellular gaps or across lymphatic vessels.

CA-125 is a widely used tumor marker for screening of adnexal malignancies but lacks sensitivity and specificity. CA-125 is constitutionally expressed by the omentum and mesovarium²⁰. In inflammatory conditions, such as SLE, there is an increase in proinflammatory cytokines such as IL-1b, vascular endothelial growth factor (VEGF), and fibroblast growth factor that will stimulate these cells to produce CA-125²¹. A previous cross-sectional study revealed that serositis is independently associated with serum CA-125 and CA-125 levels decrease and return to normal with the improvement of serositis²². CA-125 may therefore be an independent marker for serositis in SLE.

Renal involvement in PPMS is not frequently seen. In the previously reported cases, proteinuria and/or lupus nephritis was identified in a total of 6 patients (46.2%), the majority of which in a sub-nephrotic range. Our patient had a normal renal function and the proteinuria level reached nephrotic range. We performed a renal biopsy that showed class III lupus nephritis.

In our opinion the ascites is closely related to PPMS, since the patient had no generalized edema or other signs of nephrotic syndrome and the ascites appeared prior to the proteinuria increase. However, we can't completely exclude the influence of proteinuria and hypoalbuminemia in the maintenance of the ascites.

The general treatment approach to PPMS is to treat the underlying SLE. Steroids are considered the cornerstone of the treatment and the majority of reported patients were treated with oral or intravenous steroids⁴⁻¹⁷. Some patients needed more potent immunosuppression to control symptoms, being the most frequently used azathioprine (AZA), cyclophosphamide (CYC) and mycophenolate mofetil (MMF)^{4, 5, 7, 9, 11-17}. Rituximab and Belimumab can be of potential use in the future. In our case, we chose CYC over other immunosuppressants because of the clinical presentation severity and because the patient didn't want to get pregnant again.

In conclusion, PPMS is a diagnosis of exclusion and should be considered in the differential diagnosis of a patient presenting with ascites, pleural effusions, and an elevated CA-125 level. PPMS is a rare manifestation of SLE, but could be the initial manifestation, as our case demonstrates. Awareness of this entity among clinicians is crucial to ensure an early recognition and prompt treatment.

Tables and Figures

Table I. Literature review of the reported cases of Pseudo-Pseudo Meigs syndrome.

Article	Demographic features	Prior SLE diagnosis	Presenting symptoms	Initial treatment	Maintenance treatment	Outcome
Tjalma 2005 (4)	F, 38 y	Yes	Dyspnea, abdominal tenderness	PDN, AZA	-	Complete resolution of ascites in 10 weeks
Schmitt et al. 2005 (5)	F, 33 y	No	Dyspnea, abdominal distention, peripheral edema, anorexia	PDN, MMF, HCQ	-	Achieve remission
Ural et al. 2008 (6)	F, 38 y	No	Dyspnea, abdominal distention, rash, skin lesions, alopecia	PDN, HCQ	-	Recovered in 8 weeks
Bes et al 2011 (7)	F, 47 y	No	Dyspnea, vomiting, diarrhea	PDN, CYC	AZA	Resolution of symptoms after 4 weeks
Dalvi et al. 2012 (8)	F, 56 y	Yes	Abdominal distention, anorexia, weight loss, cachexia	PDN	MMF	Recurrence of ascites on PDN. Resolution after adding MMF.
Lee et al. 2013 (9) (2 cases)	(a) F, 29 y (b) F, 54 y	(a) No (b) Yes	(a) Dyspnea, abdominal distention, vomiting (b) Abdominal distention, anorexia, weight loss, cachexia	(a) MP, HCQ (b) MP, CYC	(a) HCQ (b) MMF	(a) Improvement of ascites in 4 weeks (b) Improvement
McVorrán et al. 2016 (10)	F, 40 y	No	Dyspnea, abdominal distention, Raynaud's phenomenon, arthralgia, photosensitivity	MP	-	Improvement
Zampeli et al. 2018 (11)	F, 40 y	Yes	Abdominal distention, dyspnea, hand swelling, Raynaud phenomenon, livedo reticularis, arthralgias/arthritis of hand joints, lymphadenopathy	MP, MMF	-	Recurrence after 2 months. CYC was started and remission was achieved.
Awad et al. 2019 (12)	F, 43 y	Yes	Recurrent abdominal distention	MP, RTX	-	Mild improvement of ascites.

Ahmed et al. 2019 (13)	F, 44 y	Yes	Abdominal distension, nausea	MP, AZA	AZA, PDN	Resolution of polyserositis in 2 months.
Tansir et al. 2019 (14)	F, 22 y	No	Abdominal distension	MP, HCQ, CYC	AZA	Resolution of ascites in 1 month.
Gao et al. 2019 (15)	F, 44 y	No	Abdominal distension, diarrhea, dyspnea, fatigue, weight loss, peripheral edema	MP, LFN, HCQ	-	Significant improvement in 2 months.
Li et al. 2019 (16)	F, 22 y	Yes	Abdominal distension, peripheral edema, fatigue	PDN, MMF	-	Significant improvement in 3 months.
Meena et al. 2021 (17)	F, 23 y	Yes	Abdominal distension, dyspnea, anorexia, peripheral edema	MP, HCQ, AZA	-	Decreased ascites in 2 weeks
Current case	F, 48 y	No	Abdominal pain and distention, weight loss, anorexia, arthralgia	MP, CYC, HCQ	MMF	Complete recovery in 3 months

Table I. Demographic features, presenting symptoms, treatment and outcome of reported cases of pseudo–pseudo Meigs' syndrome.

AZA: azathioprine; CYC: Cyclophosphamide; F: female; HCQ: hydroxychloroquine; LFN: leflunomide; MMF: mycophenolate mofetil; MP: methylprednisolone; PDN: Prednisolone; RTX: Rituximab; Y: year.

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