A case report of pseudo–pseudo Meigs' syndrome

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To the Editor: A 24-year-old female patient was admitted to our department with complaints of fatigue and pedal edema. She was diagnosed with systemic lupus erythematosus (SLE) 4 years ago and thus the diagnostic criteria could not be traced. She had been treated with prednisolone, hydroxychloroquine, and cyclophosphamide for 2 years, and her disease was controlled in stable condition. Occasionally, pain on her lower extremity was her only complaint, which could be relieved by prednisolone. Eight months before admission to our hospital, she got progressive abdominal distension and edema of lower extremities. Abdominal ultrasonography at the local hospital showed ascites; so the patient was treated with diuretic, which made her feel much better. But the patient presented herself with shortness of breath to the local hospital 5 months later. Computed tomography (CT) scan of the thorax showed bilateral pleural effusion. Again, she took diuretic but no significant relief was achieved. In March 2017, the patient was admitted to our department. On physical examination, she had a normal temperature and blood pressure. She was identified with diminished breath sounds, ascites, and edema of the two legs. Her ankles were swollen and tender. Laboratory findings were as follows: white blood cell (WBC) was 1340/mm^3, but there was no anemia or thrombocytopenia. C-reactive protein was 14 mg/dL. The antinuclear antibody titer was 1:320 (granular type), whereas anti-double-stranded DNA antibody, anti-Sm antibody, anticardiolipin antibodies, and lupus anticoagulant were negative. Complement C3 was 45.1 mg/dL (normal range 78.5–152.0 mg/dL) and C4 was 4.84 mg/dL (normal range 14.5–36 mg/dL). Coombs test was positive. Proteinuria was quantified at 0.36 g/24 h and kidney function was normal. Albumin was 3.35 g/dL and ferritin was 42.49 ng/mL. CA125 was 949 IU/mL (normal range 0–35 IU/mL), whereas other tumor markers including alpha fetoprotein (AFP), carcino-embryonic antigen (CEA), and CA199 were normal. CT scan of the thorax showed pleuropericardial effusions, and abdominal ultrasonography showed massive ascites and splenomegaly. Vaginal ultrasound was done to exclude malignancies, which showed inhomogeneous echo of endometria but no mass was detected. Endoscopy, colonoscopy, and bone marrow biopsy were unrevealing. A diagnostic paracentesis was performed. Pleural fluid was exudative, and stains for acid-resistant bacilli and routine cultures were negative; no malignant cells were found. TB-Igra (interferon gamma release assay) was also negative. Dilatation and curettage revealed normal histology and no signs of atypia. A laparoscopy was suggested but the patient preferred a more conservative option; therefore, positron emission tomography/CT was applied as a second choice, which revealed pulmonary inflammation and polyserositis. The maximum standardized uptake value was 2.6 in the bilateral femoral head indicating femoral head necrosis, but still there was no sign of malignancy [Figure 1]. She was diagnosed with pseudo–pseudo Meigs' syndrome (PPMS) associated with SLE and her prednisolone was replaced by 80 mg/day intravenous methylprednisolone, whereas mycophenolate mofetil was added to her treatment. Her symptoms were gradually relieved. Three months later, CT scan of her thorax showed a decrease in pleuropericardial effusion and the abdominal distention alleviated remarkably.

The case we presented here is consistent with the phenomenon known as PPMS.[1] The concept of PPMS is defined by the presence of ascites, pleural effusions, and an elevated CA125 level in a patient with SLE. Although serous effusion is common in SLE, massive ascites as the initial presentation of SLE is rare, and accompanies either manifestations of active disease or results from nephrotic syndrome, protein-losing enteropathy, and constrictive pericarditis; a diagnosis of PPMS can be made when these diseases are excluded. It is supposed that pleural effusions develop secondary to communication with the peritoneal cavity and mechanical passive transfer of ascetic fluid through diaphragmatic apertures or intracellular gaps or across lymphatic vessels.[1] A literature search regarding PPMS could only identify nine articles [Supplementary Table 1; http://links.lww.com/CM9/A49], and our case makes the number to 10. As we can see in the previous cases, many patients experienced invasive

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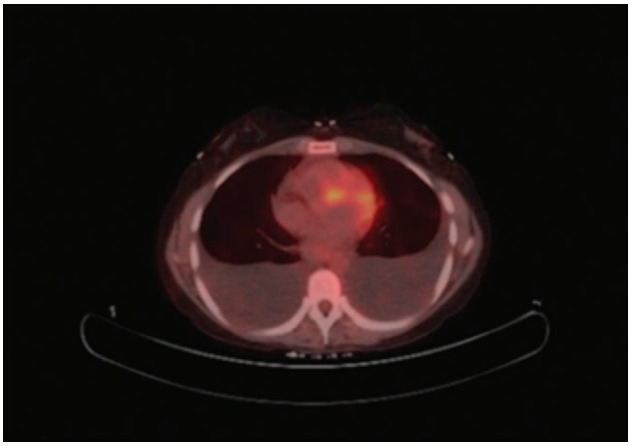

Figure 1: Positron emission tomography/computed tomography scan of the chest showing bilateral pleural effusions.

inspections to confirm the diagnosis. The term of PPMS is supposed to be a diagnostic dilemma to avoid unnecessary invasive inspections so that patients could get appropriate treatment strategy.

The pathophysiology underlying the ascites of PPMS is still under much debate. Ferritin levels were significantly high in the cases presented by Lee *et al*,[2] providing an evidence of severe uncontrolled inflammation in SLE with PPMS, whereas in another two cases, the results turned out differently. We prefer to consider PPMS as chronic serositis, for most of the patients showed a chronic course of disease without abdominal pain or chest pain. Meanwhile, in each reported case, ascites or hydrothorax were all exudates that indicate ongoing inflammation, and by adding corticosteroids or increasing dosage of corticosteroids, the disease progression can be prevented, which suggests a flare-up of SLE.

As a SLE patient with massive ascites is likely to be admitted by gynecologists, an elevation of CA125 will prompt an extensive search for an underlying malignancy as it is considered to be closely related to gynecological tumors. But a literature search revealed that CA125 is expressed by mesothelial cells of the serosal tissue, including peritoneum, and not by gynecological tumor cells.[3-5] It is considered that CA125 level increases as a result of the interaction between cytokines and human peritoneal mesothelial cells.[6-8] It is also supposed that the mechanical irritation from the ascites to peritoneal mesothelial cells could cause the rise of the CA125. A literature search revealed that when serous effusions exist, the serum CA125 level is elevated with statistical significance. A statistical analysis of 156 patients by Yang *et al*[9] revealed that serositis is independently associated with serum CA125 elevation. We suspect that when serositis exists, an elevation of CA125 level is much common than we thought whatever the underlying disease is, but large-scale data analysis is required to support the hypothesis. Therefore, when a known disease can explain the cause of serositis, an elevation of CA125 is not an imperative factor to prompt a search for malignancy.

As for the treatment of PPMS, all of the cases showed a good response to corticosteroids, but the dosage varied from prednisolone 40 mg/day to methylprednisolone 1 g/day.[6,7] Immunosuppression agents including azathioprine, mycophenolate mofetil, hydroxychloroquine, and cyclophosphamide were given to enhance curative effect. To avoid spreading of underlying tumor, we recommend adding moderate dose of corticosteroids first, if it works, and immunosuppression agents that should be added later.

Pseudo–pseudo Meigs' syndrome is a rare manifestation of SLE, which is less recognized by clinicians. The etiology is not yet clear, but chronic peritonitis and pleuritis may be the underlying mechanism. Elevated serum CA125 levels were reported in a variety of disease malignancies when serous effusions exist. As for PPMS, moderate dose of corticosteroids is effective to control symptom, and immunosuppressants should be added later if no progression of disease is observed after corticosteroids addition.

Declaration of patient consent

We certify that we have obtained all appropriate patient consent forms. In the form, the patient has her consent for her image and other clinical information to be reported in the journal. The patient understands that her name and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Conflicts of interest

None.

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