Case report

Systemic lupus erythematosus with secondary Sjögren's syndrome mimicking hematologic malignancy

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Abstract:

A 43-year-old female experienced significant weight loss over a period of 6 months. The physical examination revealed mild anemia and lymphadenopathy in the left cervical region (0.5 cm) and left axillary region (2 cm). Mild splenomegaly was suggested by increased splenic dullness. The blood tests showed anemia and an elevation of the globulin level. The thoracic and abdominal CT scans showed ground glass opacities in both lower lung fields and generalized lymphadenopathies, suggesting lymphoma. The pathological reports from the bone marrow, axillary lymph node, and liver revealed no malignant involvement. The immunologic tests were compatible with systemic lupus erythematosus with secondary Sjögren's syndrome. After treating with corticosteroids, hydroxychloroquine, artificial tears, and saliva substitutes, the patient's symptoms improved, and her weight returned to normal. This case highlights the possibility of autoimmune diseases showing similar symptoms to hematologic malignancies. Therefore, physicians must be aware of autoimmune diseases to provide patients with accurate treatment and improve their overall well-being.

Keywords : ● *Autoimmune diseases* ● *Mimicking* ● *Hematologic malignancies*

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รายงานผู้ป่วย

โรคทางระบบภูมิคุ้มกัน แสดงอาการคล้ายกับมะเร็งทางโลหิตวิทยา

วรรณพร โรจนปัญญา
สาขาโลหิตวิทยา กลุ่มงานอายุรกรรม โรงพยาบาลเชียงรายประชานุเคราะห์

บทคัดย่อ

ผู้ป่วยหญิง 43 ปี มีน้ำหนักลดผิดปกติ ในระยะเวลา 6 เดือน ตรวจร่างกายพบต่อมน้ำเหลืองที่คอซ้ายขนาด 0.5 ซม. และที่รักแร้ซ้ายขนาด 2 ซม. ตรวจคลำพบม้ามโต จากการตรวจเลือดพบว่ามีฮีโมโกลบินลดลง โกลบูลินในเลือดสูง จากการทำเอกซเรย์คอมพิวเตอร์พบว่ามี ground glass opacities ที่ปอดส่วนล่างทั้งสองข้าง มีต่อมน้ำเหลืองโตหลายตำแหน่ง คิดถึงภาวะมะเร็งต่อมน้ำเหลือง ผลการตรวจเพิ่มเติมไม่พบมะเร็งต่อมน้ำเหลืองจากชิ้นเนื้อจากไขกระดูก ต่อมน้ำเหลืองบริเวณรักแร้ และชิ้นเนื้อตับ แม้ได้รับการสืบค้นอย่างเต็มที่แล้ว ผลทางห้องปฏิบัติการทางภูมิคุ้มกัน เข้าได้กับโรค SLE และ Sjögren's syndrome หลังให้การรักษาโดยยา corticosteroids hydroxychloroquine น้ำตาเทียม และน้ำลายเทียม อาการของผู้ป่วยดีขึ้น น้ำหนักเพิ่มขึ้นกลับมาเท่าเดิม จากผู้ป่วยรายนี้แสดงให้เห็นว่า โรคทางระบบภูมิคุ้มกันผิดปกติ อาจมีอาการและอาการแสดงคล้ายกับโรคมะเร็งทางโลหิตวิทยาอย่างมากได้ แพทย์จึงควรตระหนักและให้การสืบค้นให้ครอบคลุมเพื่อเป็นประโยชน์ในการวินิจฉัยและการรักษาต่อไป

คำสำคัญ : ● *โรคทางระบบภูมิคุ้มกัน* ● *คล้ายกับ* ● *มะเร็งทางโลหิตวิทยา*

วารสารโลหิตวิทยาและเวชศาสตร์บริการโลหิต. 2568;35:315-21.

Introduction

Lymphadenopathy is a frequent clinical finding and often poses a diagnostic challenge[1]. This symptom commonly appears in several diseases including malignancy, infection, and autoimmune diseases[2]. Persistent lymphadenopathy over two weeks indicates that further investigation should be carried out[3]. The etiology of lymphadenopathy can be divided in infection, self-limited disease, malignancy (lymphoma or metastatic cancer), autoimmune disease and other diseases[4]. Lymphoma is a common hematologic malignancy of the lymphatic system[5]. The common symptoms are lymphadenopathy, night sweats, fever, significant weight loss and fatigue[6]. The definite diagnosis of the lymphoma subtype is usually revealed from pathological diagnosis. Some diseases, for example, autoimmune diseases, can present atypically, mimicking the symptoms of hematologic malignancies. Similarly, malignancies could manifest as rheumatic diseases and can encompass the musculoskeletal system[7,8]. This case report highlights the patient's signs and symptoms, which were the most similar to lymphoma.

Case report

The patient in this case report was a 43-year-old female experiencing significant weight loss and intermittent coughing. Her body weight unintentionally decreased from 58 to 50 kg over a period of six months. She didn't have a history of fever, rashes, jaundice, abdominal pain or abnormal hair loss. She visited the hospital because she was concerned about losing weight, and she could perform normal physical activities in her daily life. No history of TB contact or congenital diseases was reported in her family. She had no underlying diseases, and no history of smoking, alcohol consumption or unsafe sex. The physical examination revealed mild anemia and lymphadenopathy in the left cervical region (0.5 cm) and the left axillary region (2 cm). Mild splenomegaly was noted. Equal breath sounds in both lungs and crepitation in the left lower lung were found. The complete blood count showed Hb 9.4 gm/dL, Hct 28.4%, WBC count 2,400 cells/cu.mm, neutrophil 56%, lymphocyte 33%, monocyte 7%, atypical lymphocyte 2%, MCV 86.8 fl and platelet count 221,000 cell/cu.mm. Her blood chemistry demonstrated total protein 10.2 gm/dL, albumin 3.2 gm/dL, globulin 7.0 gm/dL, total bilirubin 0.5 mg/dL, direct bilirubin 0.1 mg/dl, AST 65 U/L, ALT 45 U/L, alkaline phosphatase 81 U/L, calcium (corrected) 9.36 mg/dL, phosphorous 3.6 mg/dL, and uric acid 7.0 mg/dL. Urine analysis was negative for proteinuria and RBCs. The tests for anti-HIV, anti-HCV, and HBsAg were all negative. For the evaluation of anemia, a peripheral blood smear was examined, revealing microspherocytes without an increase in polychromasia. The absolute reticulocyte count was 42,300/μL. Direct coombs test was positive: IgG (3+), C3b/C3d (+) and LDH 397 U/L (0-247 U/L). At this point, the patient was considered to have secondary autoimmune hemolytic anemia.

Because the problems constituted significant weight loss, generalized lymphadenopathy, warm-type AIHA and an increase in the globulin level, the most likely differential diagnosis of secondary AIHA was hematologic malignancies, autoimmune diseases and infection-induced AIHA. On the same day, the thoracic and abdominal CT scans showed ground glass opacities (GOOs) in both lower lung fields and lymphadenopathies in the left perihilar, mediastinal, bilateral axillary, supraclavicular and intraabdominal paraaortic nodes, suggesting hematologic malignancies (Figure 1, A; abdominal CT scan and B; thoracic CT scan).

The patient did not have a fever and was not an immunocompromised host, so disseminated infection was less likely. However, because of intermittent coughing and ground glass opacities in both lower lung fields, the sputum AFB and gene-expert for TB were tested and found negative. The patient had already received antibiotic treatment during the initial phase without significant improvement. She did not have a rash, abnormal hair loss, arthralgia, or arthritis, so at that time, malignancy, especially lymphoma, was thought to be the most likely cause of the disease.

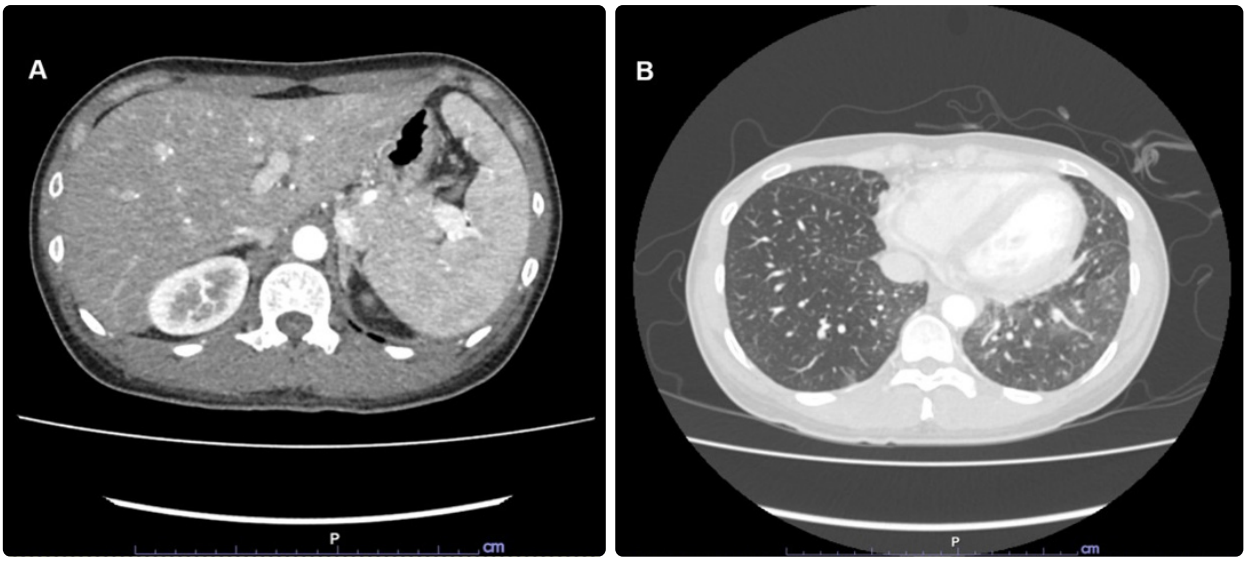

Figure 1 Thoracic and abdominal CT scans showed ground glass opacities in both lower lung fields and lymphadenopathies in the left perihilar, mediastinal, bilateral axillary, supraclavicular and intraabdominal paraaortic nodes, suggesting hematologic malignancies (A; abdominal CT scan and B; thoracic CT scan).

Because lymphoma was the most likely diagnosis, one week later, she was scheduled to undergo a lymph node biopsy. The lymph node core biopsy at the left axillary region was carried out and revealed reactive hyperplasia, CD3 and CD20 showing preserved lymphoid follicles, Bcl-2 (-), CD138 (-), IgG (-) and IgG4 (-). Further investigations involved bone marrow aspiration and biopsy. The results showed normocellular bone marrow, no evidence of lymphoma, no plasma cell myeloma, immunohistochemistry study; CD3 (-), CD20 (-), CD19 (-), PAX5 (-), CD5 (-), CD10 (-), CD30 (-) and CD138 (-). Having liver involvement in lymphoma is common; in this setting, a histopathologic diagnosis from a liver biopsy could help evaluate the pattern of abnormal cell infiltration[9]. In this case, the patient had a transaminitis profile. Subsequently, a liver core-needle biopsy was performed and revealed occasional steatosis, minimal portal infiltration by lymphocytes, no Kupffer cell hyperplasia, no hemophagocytosis, no cholestasis, no fibrotic change and was negative for tumor and granuloma.

Discussion

When treating lymphadenopathy, the persistence of lymphadenopathy for more than two weeks indicates that further investigations are necessary[3]. In this case, the patient had unexplained cervical and axillary lymphadenopathies. Most causes are of infectious origin or breast cancer. However, lymphoproliferative disorder remains in the differential diagnosis.

Following the investigation, lymphoma was ruled out for this patient. Therefore, alternative causes that mimic lymphoma should be considered. A summary of potential lymphoma mimics is presented in Table 1. In this case, the patient presented an increased globulin level, and the scope of the disease could have been IgG4-related lymphadenopathy. The serum protein electrophoresis and immunofixation showed polyclonal gammopathy (Figure 2). The immunoglobulin G level was 4,130 mg/dL (Reference value among adults 548 to 1,768 mg/dL), IgG subclass 4 level 0.242 g/L (Reference range 0.0392 to 0.864), and total IgE 54.39 kIU/L (Reference range < 150).

"IgG4-related disease (IgG4-RD) is characterized by elevated levels of the anti-inflammatory immunoglobulin IgG4 and is most commonly associated with symptoms such as lymphadenopathy, salivary gland enlargement, autoimmune pancreatitis, retroperitoneal fibrosis, sclerosing cholangitis, and tubulointerstitial nephritis.[10] In evaluating the hematologic findings–particularly lymphadenopathy and hyperglobulinemia–IgG4-related disease (IgG4-RD)

Table 1 Common lymphoma mimickers

Category	Condition	Key Features Mimicking Lymphoma
Autoimmune Diseases	Systemic Lupus Erythematosus[18]	Generalized lymphadenopathy, fever, cytopenia
	Sjögren's Syndrome[15]	Parotid gland enlargement, lymphadenopathy
	Rheumatoid Arthritis[1]	Reactive lymphadenopathy, systemic symptoms
Infectious Diseases	Tuberculosis[19]	Lymphadenopathy (especially cervical), weight loss, night sweats
	HIV/AIDS[20]	Persistent generalized lymphadenopathy, fever, weight loss
Granulomatous Diseases	Sarcoidosis[21]	Bilateral hilar lymphadenopathy, systemic symptoms (fever, weight loss)
	Kikuchi-Fujimoto Disease[22]	Fever, cervical lymphadenopathy, weight loss, night sweats
Benign Lymphoproliferative Disorders	Castleman Disease[19]	Lymphadenopathy, systemic symptoms
Fibroinflammatory Disease	IgG4-related Disease[11]	Lymphadenopathy, mass-like lesions in multiple organs

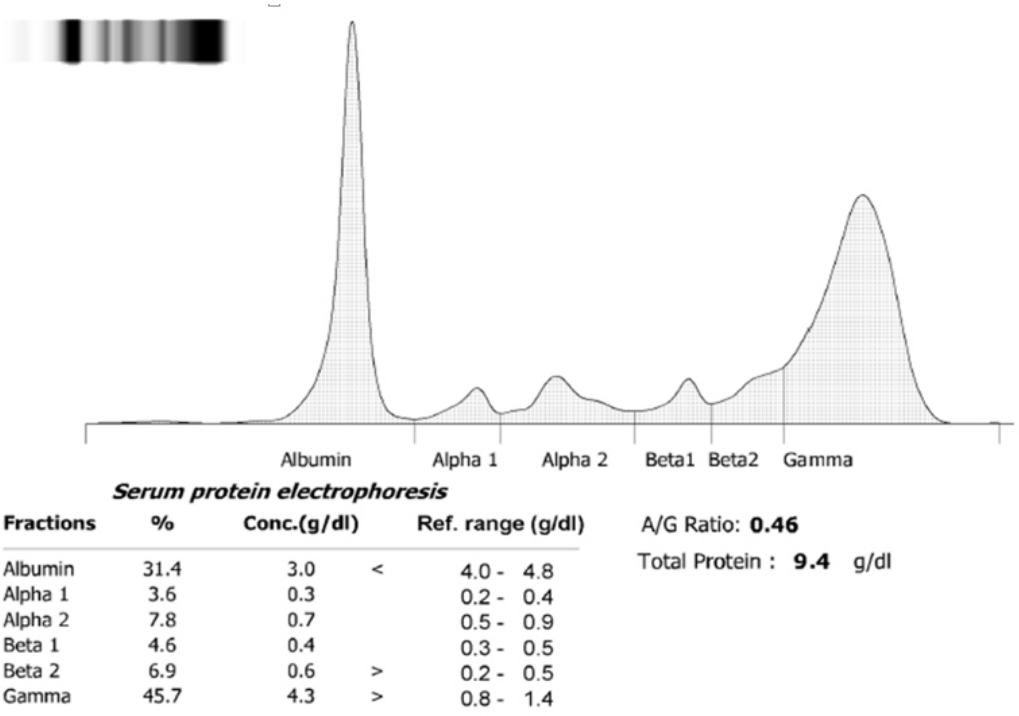

Figure 2 Serum protein electrophoresis showed polyclonal gammopathy.

should be considered in the differential diagnosis. In this case, however, the patient did not present with lesions in the salivary glands or pancreas. Furthermore, there was no histopathological evidence of IgG4-RD in the lymph node specimen. The diagnosis of IgG4-related lymphadenopathy typically requires an increased number of IgG4-positive plasma cells (> 400 cells/mm^3) and an IgG4/IgG ratio exceeding 40%, in conjunction with clinical features consistent with IgG4-RD. Based on these criteria, the likelihood of IgG4-RD in this patient was considered low.

However, the clinical differential diagnosis of this setting could also have been made for autoimmune-mediated diseases. In addition, GGOs in the lower lung fields in this patient could have been caused by various conditions including viral pneumonia and atypical bacterial pneumonia. However, the patient had already received treatment during the initial phase without significant improvement. The presence of GGOs should raise suspicion for interstitial lung disease, such as nonspecific interstitial pneumonia (NSIP), associated with autoimmune conditions, rather than suggesting lymphoma.

One case report indicated patients with symptoms of multisite adenopathy that appeared radiologically were suggestive of lymphoma. However, after re-evaluation, the final diagnosis was systemic lupus erythematosus (SLE)[12]. Finally, the patient reported she had experienced a dry mouth and eyes for two months. Immunologic testing was conducted as part of the differential diagnosis for autoimmune diseases. Laboratory workup for SLE was performed during the second week following her initial visit, and testing for Sjögren's syndrome was completed in the third week. Results revealed a strongly positive antinuclear antibody (ANA) by immunofluorescence assay (IFA) at a titer of ≥ 1:5120, showing a fine speckled, homogeneous, and nucleolar pattern. Additional findings included evidence of autoimmune hemolysis within the hematologic domain, as well as positive anti-dsDNA antibodies and decreased complement levels–C3 (0.50 g/L; reference: 0.90-1.80 g/L) and C4 (< 0.008 g/L; reference: 0.10-0.40 g/L–within the immunologic domain. These findings are consistent with SLE and meet the 2019 EULAR/ACR classification criteria, with a total score of 14[13,14].

The patient's history, after re-examination, indicated she had experienced dry mouth and eyes for two months, which was compatible with the symptoms of Sjögren's syndrome. The blood test showed a positive result for anti-SSA/Ro antibodies. Further evaluations by a dentist and an ophthalmologist confirmed the presence of severe dry mouth and eyes. These findings are consistent with a diagnosis of Sjögren's syndrome, meeting the 2016 ACR/EULAR classification criteria with a total score of 5[15,16]. The coexistence of Sjögren's syndrome and SLE is commonly observed in clinical practice, with Sjögren's syndrome frequently presenting as a secondary condition among patients with SLE[17]. Both diseases can cause symptoms such as dry mouth, dry eyes, joint pain and fatigue, and may contribute to lymphadenopathy that mimics lymphoma. This combination is not classified as an overlap syndrome. An overlap syndrome refers to the coexistence of two or more distinct systemic autoimmune diseases, each meeting full diagnostic or classification criteria and contributing equally to the clinical picture.

However, conducting a detailed history from the onset including questions about symptoms such as a dry mouth and eyes, is essential. A patient may not perceive these as issues and may not report them unless directly questioned. A comprehensive approach to history taking can facilitate earlier diagnosis and lead to improved patient outcomes.

In summary, the final diagnosis of this case was SLE with secondary Sjögren's syndrome due to the symptoms of significant weight loss, lymphadenopathy, hepatosplenomegaly, severe xeropthalmia, severe xerostomia, AIHA and NSIP. After treating with corticosteroids 50 mg/day and tapered to 5 mg/day at eight weeks, hydroxychloroquine 200 mg/day, artificial tears and saliva, her symptoms were relieved, and her weight returned to normal over three months.

Conclusion

This case highlights the possibility of autoimmune diseases, such as SLE and Sjögren's syndrome, showing signs and symptoms similar to hematologic malignancies. Therefore, physicians must be aware of and investigate autoimmune diseases to provide patients with accurate treatment and further improve their overall well-being.

Declarations

Ethics approval and consent

This case report was approved by the Chiangrai Hospital Ethical Committee.

Consent for publication

Informed consent was obtained from the patient for a case report publication.

Availability of data and materials

Not applicable

Competing interests

The author has declared that no conflicts of interest exist.

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