

A Case of Digital Autoamputation with Concurrent Sjogren's Syndrome, Antiphospholipid Syndrome, and Ovarian Cancer

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Abstract

Sjogren's syndrome (SS) is a chronic autoimmune disease that is characterized by focal lymphocytic infiltration of the exocrine glands. SS mostly affects middle-aged women, and results in an increased risk of developing malignant neoplasm, particularly hematologic malignancies. The concurrent occurrence of SS, ovarian cancer, and autoimmune disease is very rare. Here, we present a case with postoperative digital autoamputation in a young Sjogren's patient diagnosed with high-grade serous ovarian cancer. The patient was later also diagnosed with antiphospholipid syndrome. Clinicians should note that female genital tract malignancies might occur in autoimmune diseases. In addition, when planning for surgery, they should also be aware of the possibility of another autoimmune disease and different patterns of postoperative complications such as venous thromboembolism and thrombophlebitis. A multidisciplinary approach is required to achieve successful management. To the best of the authors' knowledge, this is the second case with concurrent SS and ovarian cancer and the first case with concurrent SS, antiphospholipid syndrome, and ovarian cancer.

Keywords: Antiphospholipid syndrome, autoimmune diseases, high-grade serous ovarian carcinoma, Sjogren's syndrome, venous thromboembolism

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INTRODUCTION

Sjogren's syndrome (SS) is a chronic autoimmune inflammatory disease characterized by lymphocytic infiltration of the exocrine glands. Its prevalence in the general population ranges between 1% and 3%,^[1] and it mostly affects middle-aged women.^[2] Patients with SS are at an increased risk for developing malignancies, especially lymphoproliferative diseases.^[3,4] However, the current data regarding SS and the risk of solid tumors are scarce.

Antiphospholipid syndrome (APS) is also a systemic autoimmune disorder with vascular manifestations associated with thrombotic and inflammatory mechanisms caused by antiphospholipid (aPL) antibodies.^[5] Venous thromboembolism (VTE) can lead to morbidity and mortality, especially in immune-mediated diseases, which contribute to the formation of thrombosis through chronic inflammatory mechanisms.^[6]

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Here, we present the case of a young patient with SS and high-grade serous ovarian cancer (HGSC) who postoperatively developed finger necrosis that led to autoamputation and a postoperative diagnosis of a second autoimmune disease. These associations may have clinical importance in understanding the relation between autoimmune diseases and ovarian cancer, and thus in managing these diseases, as malignancies are more commonly encountered in patients with autoimmune conditions.

CASE REPORT

A 35-year-old woman, 1 gravida and 1 para, was referred to our clinic with a complaint of abdominal pain. The patient had been diagnosed with SS when she was aged 30 years. In terms of family history, her father was diagnosed with lymphoma. The patient had been on hydroxychloroquine (Plaquenil® 400 mg tablet once daily) for the treatment of SS. She neither smoked nor consumed alcohol. On physical examination, the patient's body mass index was 19.6 kg/m². A multiloculated heterogeneous adnexal mass of 14 cm with massive ascites was detected on ultrasonography. She had elevated serum levels of cancer antigens (CAs; CA125: 6160.0 U/mL; CA15-3: 326.0 U/mL). Magnetic resonance imaging (MRI) was consistent with carcinomatosis peritonei. Chest computed tomography showed left-sided pleural effusion with bilateral views of ground-glass opacities. Colonoscopic and gastroscopic evaluations were normal. The patient underwent an exploratory laparotomy. The finding of the intraoperative frozen section examination was consistent with HGSC, and its diagnosis was confirmed with histopathologic examination after cytoreductive surgery.

Physical examination in the first postoperative hour revealed a loss of sensation, coldness, and bluish coloration in both forearms, especially in the fifth digit of the left hand. Bilateral radial and ulnar pulses were palpable. Bilateral upper extremities arterial and venous system doppler ultrasonography was consistent with acute thrombophlebitis. For treatment, elevation of upper extremities, pentoxifylline (20–40 cc/h), and low-molecular-weight heparin (enoxaparin sodium 40 mg/0.4 ml twice daily) were used. On the second day, bullous lesions were noted on the fingertip and drained to prevent ischemia. However, there was development of progressive ischemic necrosis of the finger [Figure 1]. The patient was commenced on iloprost infusion and oral steroid (methylprednisolone 32 mg once daily). When complete demarcation of the necrosis was developed, an autoamputation of the fifth finger without surgical

debridement was done, following which the patient's finger became thinner. The patient's rheumatologic clinical evaluation with a broad spectrum of immunologic markers demonstrated her second autoimmune disease: APS [Table 1]. The patient received six cycles of paclitaxel and carboplatin for the treatment of HGSC, which was well tolerated.

DISCUSSION

Sjogren's syndrome is a systemic autoimmune disease characterized by lymphocytic infiltration of mainly salivary and lacrimal glands in which B-cell hyperactivity plays a key role.^[7] Although in the literature there are contrasting findings regarding the association between SS and malignancies,^[8] there is strong evidence that primary severe SS increases the risk of cancer, especially non-Hodgkin lymphoma. The risk is higher in females. A recent retrospective study with primary SS showed that malignancy affected 28.3% of primary SS patients. In addition, vasculitis and the presence of glandular complications were found to be the strongest risk factors



Figure 1: Ischemic necrosis of the finger on the on the postoperative 11th day

Table 1: Laboratory results

Laboratory test	Result	Reference range
Antithrombin III activity (%)	63	79-112
Anti-SSA (immunoblotting)	3+++	Negative
ANA	2++	Negative
Lupus anticoagulant (with confirmatory test) (sec)	56	<44
C3 (mg/dL)	58	83-193
C4 (mg/dL)	7	15-57
Protein C (%)	50	70-130
Protein S (%)	52	70-150
APCR	82	≥120

Anti-SSA - Anti-Sjögren's syndrome-associated antigen A;

ANA - Antinuclear antibody; C3 - Complement component 3;

C4 - Complement component 4; APCR - Activated protein C resistance

for lymphoma. However, in the same study, only one patient with SS had concurrent ovarian cancer. The patient's age at diagnosis of SS and ovarian adenocarcinoma was 54 years and 71 years, respectively.^[9] To the best of the author's knowledge, here, we present the second such case of a young primary SS patient who developed HGSC at the age of 35 years.

SS is associated with an increased risk for thrombosis not only due to chronic inflammation but also the additional risk of the autoimmune disease itself. The interaction between autoimmune disease, inflammatory response, and coagulation system contributes to the development of VTE formation.^[10] Many studies have shown that the risk of VTE in patients with SS is three times higher than that in the general population.^[11] Although lower extremity thrombosis is more common, the risk of upper extremity thrombosis should also be considered in vasculitic diseases, in which inflammation-induced thromboembolic process is more prominent in the postoperative period.

Our patient had an acute onset of finger ischemia without preexisting Raynaud's phenomenon. Although our patient had been under prophylactic treatment of thromboembolism, she experienced the development of thrombosis. For primary SS, the presence of vasculitis is associated with increased mortality.^[12] SS with small vessel occlusions without the evidence of vasospasm is treated with cold, tobacco avoidance, and vasodilator drugs, and is healed over months without major tissue loss, as in our case.

Patients with primary SS may have systemic involvement and frequently demonstrate serologic findings such as antinuclear antibody (ANA), anti-Ro/SS-A, anti-La/SS-B antibodies, and RF.^[13] Our patient had ANA and anti SS-A positivity. Our patient also had low serum C3 and C4 levels, both of which are associated with a higher risk of mortality.^[12] Low C4 levels strongly suggest immune-complex disease, and are associated with a high prevalence of systemic primary SS involvement, including vasculitis.^[12]

When planning for surgery, a multidisciplinary team, including rheumatology, internal medicine, vascular medicine, anesthesiology and reanimation, and gynecologic oncology, is required to prevent complications related to vasculitis and thromboembolism.

APS has vascular manifestations that are associated with thrombotic and inflammatory mechanisms caused by aPL antibodies. According to the current laboratory criteria for APS, aPL antibodies can be one of the three types:

lupus anticoagulant, anticardiolipin antibodies, or anti-beta 2-glycoprotein I antibodies. For a definite diagnosis of APS, fulfilling at least one clinical and one laboratory criteria of the updated Sapporo Classification criteria is recommended. APS can also occur in association with other autoimmune diseases.^[5] Our patient met the Sapporo classification to have a definite diagnosis of APS given that she had vascular thrombosis and lupus anticoagulant positivity (on ≥ 2 occasions at least 12 weeks apart).

CONCLUSION

The risk of malignancy accompanying rheumatic diseases should be considered. Certain clinical and serological factors can identify patients with SS at high risk of mortality and requiring close monitoring and aggressive treatment. In addition, a patient with an autoimmune disease could also have a second autoimmune disease. Multidisciplinary management is important. These newly described associations may have clinical importance and contribute to our understanding of both autoimmunity and cancer.

Declaration of patient consent

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

Peer review

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Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Cornec D, Chiche L. Is primary Sjögren's syndrome an orphan disease? A critical appraisal of prevalence studies in Europe. *Ann Rheum Dis* 2015;74:e25.
2. Qin B, Wang J, Yang Z, Yang M, Ma N, Huang F, *et al.* Epidemiology of primary Sjögren's syndrome: A systematic review and meta-analysis. *Ann Rheum Dis* 2014;74:1983-9.
3. Weng MY, Huang YT, Liu MF, Lu TH. Incidence of cancer in a nationwide population cohort of 7852 patients with primary Sjögren's syndrome in Taiwan. *Ann Rheum Dis* 2012;71:524-7.
4. Brito-Zerón P, Kostov B, Fraile G, Caravia-Durán D, Maure B, Rascón FJ, *et al.* Characterization and risk estimate of cancer in patients with primary Sjögren syndrome. *J Hematol Oncol* 2017;10:90.

5. Tektonidou MG, Andreoli L, Limper M, Amoura Z, Cervera R, Costedoat-Chalumeau N, *et al.* EULAR recommendations for the management of antiphospholipid syndrome in adults. *Ann Rheum Dis* 2019;78:1296-304.
6. Zöller B, Li X, Sundquist J, Sundquist K. Risk of pulmonary embolism in patients with autoimmune disorders: A nationwide follow-up study from Sweden. *Lancet* 2012;379:244-9.
7. Mavragani C, Moutsopoulos H. Sjögren syndrome. *Can Med Assoc J* 2014;186:E579-86.
8. Liang Y, Yang Z, Qin B, Zhong R. Primary Sjögren's syndrome and malignancy risk: A systematic review and meta-analysis. *Ann Rheum Dis* 2014;73:1151-6.
9. Lazarus M, Robinson D, Mak V, Møller H, Isenberg D. A incidence of cancer in a cohort of patients with primary Sjögren's syndrome. *Rheumatology* 2006;45:1012-5.
10. Lee JJ, Pope JE. A meta-analysis of the risk of venous thromboembolism in inflammatory rheumatic diseases. *Arthritis Res Ther* 2014;16:435.
11. Abrol E, González-Pulido C, Praena-Fernández JM, Isenberg DA. A retrospective study of long-term outcomes in 152 patients with primary Sjögren's syndrome: 25-year experience. *Clin Med (Lond)* 2014;14:157-64.
12. Singh AG, Singh S, Matteson EL. Rate, risk factors and causes of mortality in patients with Sjögren's syndrome: A systematic review and meta-analysis of cohort studies. *Rheumatology (Oxford)* 2016;55:450-60.
13. Kassan SS, Moutsopoulos HM. Clinical manifestations and early diagnosis of Sjögren syndrome. *Arch Intern Med* 2004;164:1275-84.