CASE REPORT

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Secondary Antiphospholipid Antibody Syndrome Due to Systemic Lupus Erythematosus: A Case Report with Superior Mesenteric Artery Involvement

Sistemik Lupus Eritematozusa Bağlı Sekonder Antifosfolipid Antikor Sendromu: Superior Mezenterik Arter Tutulumuyla Seyreden Olgu Sunumu

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ÖZ

Antifosfolipid antikor sendromu (AFAS); antifosfolipid protein antikor pozitifliği yanı sıra rekurren vasküler tromboz ve/veya gebelik kayıpları ile karakterize bir hastalıktır. Altta yatan bir hastalık saptanmadığında primer tip; altta yatan başka bir romatolojik hastalık varlığında sekonder tip olarak sınıflandırılır. Sekonder AFAS, en sık sistemik lupus eritematozusa (SLE) bağlı gelişir. Burada, AFAS'ta superior mezenterik arter tutulumuna bağlı iskemik kolit vakasını sunduk. 59 yaşında SLE tanısı bulunan kadın hastaya, ani gelişen hematokezya ve akut batın kliniği olması üzerine çekilen kontrastlı bilgisayarlı tomografi anjiografide (BT-anjiografi) superior mezenterik arterde tromboz saptandı. Bu olgu AFAS'a bağlı gastrointestinal sistemdeki farklı damar tutulumu ve tedavi stratejisi açısından ilginçti.

Anahtar Kelimeler: antifosfolipid antikor sendromu; iskemik kolit; sistemik lupus eritematozus

ABSTRACT

Antiphospholipid antibody syndrome (APS); is a disease characterized by anti-phospholipid protein antibody positivity as well as recurrent vascular thrombosis and/or pregnancy loss. When no underlying disease is detected, it is classified as primary type; when there is another underlying rheumatologic disease, it is classified as secondary type. Secondary APS, most commonly develops due to systemic lupus erythematosus (SLE). We present a case of ischemic colitis due to superior mesenteric artery involvement in APS. 59-year-old female patient diagnosed with SLE had sudden-onset hematochezia and acute abdomen. Therefore, the patient underwent contrast-enhanced computed tomography angiography (CT angiography). Thrombosis was detected in the superior mesenteric artery. This case was interesting in terms of different vascular involvement and treatment strategy in the gastrointestinal tract due to APS.

Keywords: anti-phospholipid antibody syndrome; ischemic colitis; systemic lupus erythematosus

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INTRODUCTION

APS is an autoimmune disease that develops due to pathogenic antiphospholipid antibody positivity, mostly accompanied by venous and less commonly arterial thrombosis and recurrent pregnancy loss.[1,2,3] It is classified as secondary type in the presence of another underlying rheumatological disease. Secondary APS, most commonly develops due to systemic lupus erythematosus (SLE). APS was first described by Graham RV Hughes in 1983.[1] For this reason, it is also known as "Hughes Syndrome". The approximate incidence of APS is 5 cases per 100.000 people, and the estimated prevalence is 40-50 cases per 100.000 people.[2,3] The clinical spectrum of APS includes hematologic, obstetric, neurological, cardiovascular, dermatological, renal and orthopedic findings.[3] The clinical findings it contains are shown in the Table 1 below.

Table 1. The clinical findings in APS.

Hematological	Thrombocytopenia, thrombosis, microangiopathic hemolysis
Obstetrics	Recurrent abortions
Neurological	İschemic attack, epileptic seizures, cognitive disorders, chorea, transverse myelitis, multiple sclerosis
Cardiovascular	Endocarditis, myocardial infarction
Dermatological	Livedo reticularis, skin necroses
Renal	Glomerulonefrit, renal thrombotic microangiopathy
Orthopedic	Avascular necrosis of bones, non-traumatic fractures

Serious thrombotic events are more common in patients with SLE-related APS.[2] Liver-related vascular pathologies are most common in gastrointestinal system involvement of APS. Budd-Chiari syndrome, hepatic-veno-occlusive disease, small hepatic vasculitides, hepatic infarction, portal hypertension-associated cirrhosis have been reported among hepatic manifestations. Spleen infarction, acute pancreatitis, acute intestinal infarction are seen less frequently.[4]

CASE REPORT

A 59-year-old female patient with a diagnosis of hypertension (HT) was admitted to our outpatient clinic with complaints of widespread body pain for 6 months, a butterfly-shaped rash on the face, alopecia without scarring, and aphthae in the mouth. The patient had previously abortions 3 times earlier than 10 weeks. Therefore, the Anti-nuclear antibody (ANA) and double-stranded DNA antibody (Anti-dsDNA) that we examined with the immunofluorescent essay (IFA) method were positive, the ANA titer was 1:320 in the nuclear pattern The patient was diagnosed with SLE with a total score of 10 according to the 2019 European Alliance of Associations for Rheumatology/American College of Rheumatology (EULAR/ACR) classification criteria. Organ involvement due to SLE was investigated and there was no evidence of involvement. Anti-cardiolipin immunoglobulin M and G and Beta2-glycoprotein values, which we did due to recurrent abortions and repeated at 12-week intervals, were negative. Lupus anticoagulant was repeated at 12-week and was positive. The patient's C reactive level was 12 mg/l and her erythrocyte sedimentation rate was normal. (Table 2) We prescribed hydroxychloroquine, acemethazine, pantoprazole, and acetylsalicylic acid treatments for the patient who had no history of thrombosis and was diagnosed with SLE and secondary APS. In the follow-up of the patient, sudden abdominal pain and hematochezia developed 4 months later. Since we detected rebound and defense in the abdominal examination, we decided to perform contrast-enhanced computed tomography angiography (CT angiography) for the acute abdomen. Since we detected an image compatible with ischemic colitis secondary to superior mesenteric artery (SMA) thrombosis in CT angiography, we decided to perform rectosigmoidoscopy and we detected ischemic colitis.(Figure 1) In our examination for the etiology, we did not detect cardiac arrhythmia of patient. No intracardiac thrombus was detected in echocardiography. We did not detect factor V Leiden mutation, prothrombin mutation, antithrombin and protein C and S deficiency, which are hematological causes that may predispose to thrombosis. Our patient was diagnosed with HT 1 year ago and was under control with antihypertensive medication. No hypertensive retinopathy was detected in retinal examination. We terminated the oral treatment and prescribed intravenous pantoprazole, high-dose methylprednisolone and cyclophosphamide for the patient with a diagnosis of SLE-related APS. In addition, metronidazole and ceftriaxone were given with the possible risk of perforation. The dose of methylprednisolone was gradually reduced to 1 mg/kg. After the bleeding stopped, subcutaneous enoxaparin every 12 hours and oral warfarin were given until the target INR was between 2-3. Since the patient responded to the treatment, it was planned to continue with

oral warfarin, oral methylprednisolone (MP) and 150 mg azathioprine (AZA) as maintenance after 6 cycles of cyclophosphamide-mesna treatment was completed. Written informed consent was obtained from the patient.

Table 2. Laboratory tests of the patient.

IFA-ANA *	1:320 (nuclear pattern) Positive
IFA Anti-dsDNA**	Positive
CRP †	12 mg/l
ESR‡	9 mm/h
Beta2-glycoprotein ††	Negative
Anti-cardiolipin immunoglobulin M and G ††	Negative
Lupus anticoagulant ††	Medium Titer Positive

*: Anti nuclear antibody
**: Double-stranded DNA antibody
†: C reactive protein
‡: Eryrocyte sedimentation rate
††: Tested twice, 12 weeks apart

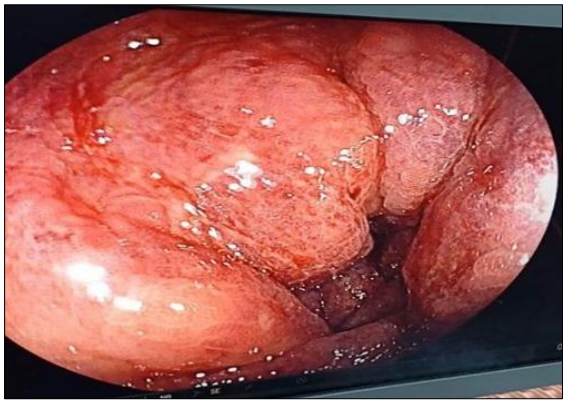

Figure 1. Colonoscopy images of the patient compatible with Ischemic colitis.

DISCUSSION

The patient's age, APS auto-antibodies and vascular involvement are among the features that make our case different.In the study conducted by Yayla et al. reported that 76% of 43 APS patients were women and the median age was 46 years.[5] Our case was a 59-year-old female and was compatible with the literature in terms of gender. However, she was older in terms of age. When this situation was analyzed, it was emphasized that the patient did not go to the doctor's control in terms of recurrent abortions, so the diagnosis might have been determined at an older age. However, the patient had rash, alopecia, oral aphthae and widespread body pain for 6 months. There was also no previous history of thrombosis. Bagger et al. reported that of 158 female patients with recurrent abortions showing moderately positive anticardiolipin antibodies have an increased risk of developing SLE in the future and that these patients should be followed up.[6] In line with this information, it is useful to monitor anticardiolipin antibodies of patients with recurrent abortions and to be careful in terms of the possibility of developing SLE and APS, even if there is no previous thrombotic event. Our case is significant in this respect.

Although the classical auto-antibodies involved in the pathogenesis of APS are anti-cardiolipin antibodies which are lupus anticoagulant, and β2-glycoproteins, it is accepted that new auto-antibodies and different subtypes also play a role in the pathogenesis.[3] Although anti-cardiolipin and β2-glycoprotein were negative in our patient, the lupus anticoagulant during 12 weeks, at least twice a week, was positive. This may be due to different subtype antibody positivity that has not yet been detected.

Superior mesenteric artery thrombosis is rare in APS. In one case report of England et al. expalined that mesenteric artery involvement is rare in APS because relatively more prostacyclin is secreted in this region.[7] The study of Kaushik et al. about intra-abdominal involvement in APS showed that abdominal thrombosis or ischemic event was reported in 42 (19.5%) of 215 patients. Major vascular thrombosis including inferior vena cava, portal and superior mesenteric veins, splenic vein and aorta was analyzed in 52% of 42 patients, and abdominal visceral ischemia resulting in renal infarction, intestinal ischemia, spleen infarction, pancreatitis, liver infarction was reported in 36 patients.[8] Our case progressed with superior mesenteric artery thrombosis.

Treatment of acute mesenteric ischemia includes open surgery or revascularization with endovascular approach. Bowel resection may be required in delayed and necrotic cases.[9] In our patient, general surgery consultation was performed after SMA thrombosis was seen in contrast-enhanced CT angiography. We predicted that this condition was not caused by atherosclerosis or embolism, but was due to immunity, so surgery or endovascular intervention may lead to re-thrombosis with endothelial damage. Therefore, immunosuppressive therapy was planned for the patient. In addition, antibiotherapy was started for the risk of bowel perforation.

According to the APS guideline published by EULAR (European Alliance of Associations for Rheumatology), it

is recommended to keep the INR target between 2-3 in patients with arterial thrombosis for the first time. Rituximab treatment comes to the fore in resistant cases where recurrent arterial thrombosis is observed despite an INR between 3-4.[10] Since SLE was accompanying in our case, pulse methylprednisolone treatment with cyclophosphamide was applied. When the bleeding caused by hematochezia was under control, subcutaneous enoxaparin was administered every 12 hours and oral warfarin treatment was given until the INR was between 2-3, in line with the recommendations of the cardiovascular surgeons. Since the patient responded to the treatment, it was planned to continue with oral warfarin, oral methylprednisolone (MP) and 150 mg azathioprine (AZA) as maintenance after 6 cycles of cyclophosphamide-mesna treatment was completed.

In conclusion, APS should be considered in cases with recurrent pregnancy loss, unexplained thrombosis in atypical regions, and underlying rheumatological disease. In this way, early diagnosis helps prevent serious complications. It should not be forgotten that immunosuppressive agents are also included in the treatment as well as anticoagulants.

Conflict of Interests

The authors declare that there is not any conflict of interest regarding the publication of this manuscript.

Ethics Committee Permission

Written informed consent was obtained from the patient.

Authors' Contributions

Concept/Design: BK. Data Collection and Processing: BK. Data analysis and interpretation: BK, İY, NCÇ, GP, HŞE, AŞ. Literature Search: BK, İY, NCÇ, GP, HŞE, AŞ. Drafting manuscript: BK, İY, NCÇ, GP, HŞE, AŞ. Critical revision of the manuscript: AŞ. Supervision: AŞ.

REFERENCES

1. Negrini S, Pappalardo F, Murdaca G, Indiveri F, Puppo F. The anti phospholipid syndrome: from pathophysiology to treatment. Clin Exp Med. 2017;17(3):257-267.
2. Pons-Estel GJ, Andreoli L, Scanzi F, Cervera R, Tincani A. The anti phospholipid syndrome in patients with systemic lupuserythematosus. J Autoimmün. 2017;76(1):10-20.
3. Uthman I, Noureldine MHA, Ruiz-Irastorza G, Khamashta M. Management of anti phospholipid syndrome. Ann Rheum Dis. 2019;78(2):155-161.
4. Uthman I, Khamashta M. The abdominal manifestations of the antiphospholipid syndrome. Rheumatology (Oxford). 2007;46(11):1641-1647.
5. Yayla ME, Yüksel M, Şahin D, et. al. Clinical Features of Patients with Anti phospholipid Syndrome and Differences of Patients with Recurrent Thrombosis, A Single Center Retrospective Study. J Ankara Univ Fac Med. 2021;74(1):52-59.
6. Bagger PV, Andersen V, Baslund B, et. al. Anti-cardiolipin Antibodies (IgG and IgA) in Women with Recurrent Fetal Loss Correlate to Clinical and Serological Characteristics of SLE. Acta Obstet Gynecol Scand. 1993;72(6):465-469.
7. England RJA, Woodcock B, Zeiderman MR. Superior Mesenteric Artery Thrombosis in a Patient with the Anti phospholipid Syndrome. Eur J Vasc Endovasc Surg. 1995;10(3):372-373.
8. Kaushik S, Federle MP, Schur PH, Krishnan M, Silverman SG, Ros PR. Abdominal Thrombotic and Ischemic Manifestations of the Anti phospholipid Antibody Syndrome: CT Findings in 42 Patients. Radiology. 2001;218(3):768-771.
9. Kerzmann A , Haumann A , Boesmans E , Detry O, Defraigne JO. Acute mesenteric ischemia. Rev Med Liege. 2018;73(5-6):300-303.
10. Tektonidou MG, Andreoli L, Limper M, et. al. EULAR recommendations for the management of anti phospholipid syndrome in adults. Ann Rheum Dis. 2019;78(10):1296-1304.