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CASE REPORT

**Yoshito Yoshidome · Shinji Morimoto · Naoto Tamura
Shigeto Kobayashi · Hiroshi Tsuda · Hiroshi Hashimoto
Yoshinari Takasaki**

A case of primary antiphospholipid antibody syndrome presenting with dysfunctional uterine bleeding and cerebral infarction

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Abstract We report a 34-year-old woman who developed primary antiphospholipid antibody syndrome (APS) presenting with dysfunctional uterine bleeding and cerebral infarction. Antiphospholipid antibody syndrome presenting with bleeding manifestations is rare. We should recognize that APS may be associated with not only thrombosis but also bleeding.

Key words Cerebral infarction · Dysfunctional uterine bleeding · Primary antiphospholipid antibody syndrome

Introduction

Antiphospholipid antibody syndrome (APS) is characterized by recurrent arterial or venous thrombosis, or fetal loss, in association with antibodies against plasma proteins, which may be bound to anionic phospholipids. However, APS presenting with bleeding manifestations is rare. In this case report, we describe a patient with primary APS presenting with dysfunctional uterine bleeding and cerebral infarction.

Case report

A 34-year-old woman was admitted to our hospital on May 27, 2004 because of massive genital bleeding and right hemiparesis. She had been treated for primary APS diagnosed on the basis of Sapporo criteria with low-dose aspirin since sustaining a cerebral infarction 2 years earlier. Genital bleeding episodes other than menstruation had been repetitive since the beginning of 2004, and she was taking oral contraceptives.

On admission, her body temperature was 36.1°C, pulse rate 70 beats/min, blood pressure 96/60 mmHg, and respiration rate 24/min. Genital bleeding and anemia were apparent. Neurological examination found mild dysarthria and right hemiparesis. There were no abnormalities suggestive of systemic lupus erythematosus; specifically, there was no rash, no oral ulcer, and no arthritis. Laboratory studies showed the following values: white blood cell count, 4400/mm^3 (lymphocyte fraction = 39.0%); hemoglobin, 8.5 g/dl; platelets, $16.8 \times 10^4/mm^3$. Prothrombin time and activated partial thromboplastin time were normal. Platelet agglutination test demonstrated normal platelet function despite taking low-dose aspirin. C-reactive protein level was 0.1 mg/dl and erythrocyte sedimentation rate was 10 mm/h. Antinuclear antibody was positive at a titer of 1:20. Anti-dsDNA antibody, anti-Sm antibody, anti-U1-RNP antibody, anti-SS-A /Ro antibody, and anti-SS-B/La antibody were all negative. Diluted Russell viper venom test ratio was 1.38 (normal reference, <1.3). The serum level of anti-β2-glycoprotein I antibody was 125 U/ml (normal reference titer, <3.5), and that of anticardiolipin IgG antibody was 48 U/ml (normal reference titer, <10). Estradiol, progesterone, prolactin, luteinizing hormone, and follicle-stimulating hormone were normal. Histologically, the endometrium was normal. This suggested that the massive genital bleeding was due to dysfunctional uterine bleeding. Magnetic resonance imaging of the brain on admission showed high signal intensities in the subcortex of the left parietal lobe on diffusion weighted imaging, and magnetic resonance angiography demonstrated the stenosis of left middle cerebral artery (Fig. 1a,b). These were compatible with cerebral infarction relapse. Dilation and evacuation of the uterus was performed immediately after admission and the genital bleeding disappeared. She stopped taking oral contraceptives following cerebral infarction relapse and was administered anticoagulant therapy carefully. Right hemiparesis

Y. Yoshidome[1] (✉) · S. Morimoto · N. Tamura · S. Kobayashi · H. Tsuda · H. Hashimoto · Y. Takasaki
Department of Internal Medicine and Rheumatology, Juntendo University School of Medicine, 2-1-1 Hongo, Bunkyo-ku, Tokyo 113-8421, Japan

Present address:
[1]Department of Neurology and Geriatrics, Kagoshima University Graduate School of Medical and Dental Sciences, 8-35-1 Sakuragaoka, Kagoshima 890-8520, Japan
Tel. +81-99-275-5332; Fax +81-99-265-7164
e-mail: yoshidomey@mub.biglobe.ne.jp

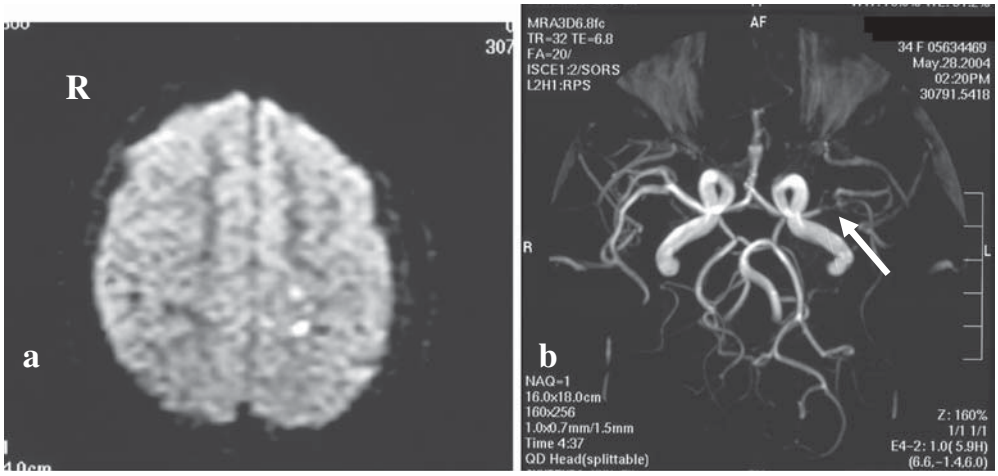

Fig. 1. **a** Magnetic resonance imaging of the brain on admission showed high-signal intensities in the subcortex of the left parietal lobe on diffusion weighted imaging. **b** magnetic resonance angiography demonstrated stenosis of the left middle cerebral artery (*arrow*)

and dysarthria improved gradually. She was discharged with slight neurologic sequelae.

Discussion

Antiphospholipid antibody syndrome is characterized by antibodies directed against either phospholipids or plasma proteins bound to anionic phospholipids. Patients with APS may display a constellation of clinical features including venous and arterial thrombosis, recurrent fetal losses, and thrombocytopenia. The reports of APS presenting with bleeding manifestations are rare. Adrenal insufficiency secondary to adrenal hemorrhage,[1] alveolar hemorrhage due to pulmonary capillaritis and microvascular thrombosis,[2] Lupus anticoagulant-hypoprothrombinemia syndrome associated with antiprothrombin antibody,[3] and complications of anticoagulant therapy[4] have been reported to show bleeding manifestations associated with APS.

In this case, a primary APS patient developed dysfunctional uterine bleeding and cerebral infarction at almost the same time. We considered that cerebral infarction was induced by APS, stenosis of left middle cerebral artery, hypovolemia due to massive bleeding, and oral contraceptive use.

The patient had taken low-dose aspirin, but platelet agglutination test demonstrated normal platelet function on admission. We considered the possibility of dysfunctional uterine bleeding associated with APS, because some cases showing bleeding manifestations associated with APS have been reported, although rarely.

In conclusion, we reported a case of primary APS presenting with dysfunctional uterine bleeding and cerebral infarction. It is suggested that APS may be associated with not only thrombosis but also bleeding. It is necessary to accumulate further cases to define the association characteristics of these diseases.

References

1. Caron P, Chabannier MH, Cambus JP, Fortenfant F, Otal P, Suc JM. Definitive adrenal insufficiency due to bilateral adrenal hemorrhage and primary antiphospholipid syndrome. J Clin Endocrinol Metab 1998;83:1437–9.
2. Gertner E. Diffuse alveolar hemorrhage in the antiphospholipid syndrome: spectrum of disease and treatment. J Rheumatol 1999;26:805–7.
3. Erkan D, Bateman H, Lockshin MD. Lupus anticoagulant-hypoprothrombinemia syndrome associated with systemic lupus erythematosus: report of 2 cases and review of literature. Lupus 1999;8: 560–4.
4. Ruiz-Irastorza G, Khamashta MA, Hunt BJ, Escudero A, Cuadrado MJ, Hughes GR. Bleeding and recurrent thrombosis in definite antiphospholipid syndrome: analysis of a series of 66 patients treated with oral anticoagulation to a target international normalized ratio of 3.5. Arch Intern Med 2002;162:1164–9.