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Abstract

A 34-year-old woman was admitted to our emergency room with a high fever, abdominal pain, dyspnea and confusion. High fever and abdominal pain had first occured after a cystocele operation 5 months earlier. Later, congestive heart failure with mural thrombus formation, peripheral polyneuropathy and ischemic cerebrovascular accident were identified in clinical follow-ups, and multiple arterial and venous thromboses were seen on cranial and abdominal magnetic resonance imaging angiography. The patient's symptoms improved with anticoagulant treatment. Antiphospholipid syndrome with elevated serum anticardiolipin IgG levels was diagnosed, and ischemic peripheral polyneuropathy with axonal degeneration was determined by sural nerve biopsy. In antiphospholipid syndrome, elevated anticardiolipin antibodies appear to be the most common acquired blood protein defect causing thrombosis. Disseminated vascular thrombosis in catastrophic antiphospholipid syndrome can result in multiorgan failure with increased morbidity and mortality. It rarely occurs secondary to various infections as in the case of our patient, who suffered postoperative intraabdominal infection. It is important to note that peripheral nervous system involvement is rare in antiphospholipid syndrome.

KEYWORDS: secondary antiphospholipid syndrome, peripheral neuropathy

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Case Report

Catastrophic Secondary Antiphospholipid Syndrome with Peripheral Nervous System Involvement: A Case Report

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A 34-year-old woman was admitted to our emergency room with a high fever, abdominal pain, dyspnea and confusion. High fever and abdominal pain had first occured after a cystocele operation 5 months earlier. Later, congestive heart failure with mural thrombus formation, peripheral polyneuropathy and ischemic cerebrovascular accident were identified in clinical follow-ups, and multiple arterial and venous thromboses were seen on cranial and abdominal magnetic resonance imaging angiography. The patient's symptoms improved with anticoagulant treatment. Antiphospholipid syndrome with elevated serum anticardiolipin IgG levels was diagnosed, and ischemic peripheral polyneuropathy with axonal degeneration was determined by sural nerve biopsy. In antiphospholipid syndrome, elevated anticardiolipin antibodies appear to be the most common acquired blood protein defect causing thrombosis. Disseminated vascular thrombosis in catastrophic antiphospholipid syndrome can result in multiorgan failure with increased morbidity and mortality. It rarely occurs secondary to various infections as in the case of our patient, who suffered postoperative intraabdominal infection. It is important to note that peripheral nervous system involvement is rare in antiphospholipid syndrome.

Key words: secondary antiphospholipid syndrome, peripheral neuropathy

In order for thrombus formation to occur, multiple preliminary factors first mentioned by Virchow at the beginning of the last century must be present [1]. Today it is defined as the end-point of several pathologic processes rather than as a disease, and it is known to occur secondary to other systemic diseases or prethrombotic events. Antiphospholipid syndrome, a systemic disorder characterized by arterial and venous thrombosis, can be either primary or secondary to connective tissue diseases, vasculitis or infections, or may be triggered by the use of any of several drugs. In the present report, we discuss the case of a patient with antiphospholipid syndrome which occured secondary to intraabdominal surgery and/or postoperative infection and which was complicated by multiorgan failure due to disseminated arterial and venous thrombosis.

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Case Report

A 34-year-old woman was admitted to our emergency room with a high fever, abdominal pain, dyspnea, weakness and confusion. The abdominal pain and high fever had first occured after a cystocele operation 5 months earlier and were interpreted as post-operative

intraabdominal infection. Her symptoms recurred despite intravenous antibiotic treatment. Symptoms and signs of peripheral polyneuropathy and congestive heart failure developed later and right pleural effusion was found upon further examination.

The patient was in a somnolent state with a body temperature of 38.1°C and a blood pressure of 160/110 mmHg bilaterally. Physical examination revealed tachypnea, tachycardia, peripheral cyanosis, bilateral cervical venous dilatation, positive hepato-jugular reflux, midsystolic ejection murmur and third heart sound heard on precordium, ecchymosis around the umblicus, generalized abdominal tenderness without defence and rebound tenderness, hepatomegaly, percussable spleen, erythema and tenderness of the left crura, muscular weakness more prominent at the distal extremities that severely impeded her movements, peripheral sensory neuropathy and bilateral decreased deep tendon reflexes.

In laboratory examination, the patient's erythrocyte sedimentation rate was 24 mm/h and a complete blood count showed total leukocytes 23,000/mm^3, neutrophils 22,000/mm^3, lymphocytes 1,000/mm^3, hemoglobin 111 g/L, hematocrits 35%, erythrocyte mean corpuscular volume 89 fL, and thrombocytes 83,000/mm^3. Serum biochemical analysis revealed sodium 128 mmol/L, potassium 3.3 mmol/L, alanine aminotransferase 130 IU/L, aspartate aminotransferase 72 IU/L, gamma glutamyl transferase 88 IU/L, albumin 21.1 g/L, and gamma globulin 18.1 g/L. Sinus tachycardia with inverted T waves on all derivations was seen on electrocardiography. Urine sediment was abundant with red blood cells and was thought to be related to the patient's intraurethral catheter. Left atrial dilatation, decreased left ventricular systolic function with 2 mural thrombi and moderate mitral valve insufficiency were seen on echocardiography. The patient's left ventricular ejection fraction was 32%. Hypoperfusion in the inferior-basal segments of the left ventricule was seen in a Thallium-201 scan. Percutaneous transfemoral coronary angiography was normal; blood cultures were sterile. Intravenous unfractionated heparin 5,000 units bolus and 1,000 units/h infusion was begun. Right hemiplegia and coma developed after the first day of the heparin infusion. No intracranial hemorrhage was found on cranial computed tomography. Cranial magnetic resonance imaging (MRI) indicated multiple cerebral and cerebellar infarcts and suspicious contrast differences on the left transverse and sigmoid sinuses, possibly related to impeded blood flow or thrombus formation. After 3 days of heparin treatment, the patient regained consciousness. Anticoagulant treatment was continued with warfarin. Neurologic examination showed right hemiparesis, bilateral motor and sensory polyneuropathy and decreased deep tendon reflexes, and electromyography revealed mononeuropathy multiplex with severe axonal degeneration. During the warfarin treatment, prothrombin time was 18.2 sec, activated partial thromboplastin time was 78 sec and lupus anticoagulant was negative. Anticardiolipin IgG was 27 GPL U/mL (normal: < 13.3 GPL U/mL) and anticardiolipin IgM was 3.6 MPL U/mL (normal: < 9.8 MPL U/mL). Antiphospholipid syndrome was diagnosed. Serum anti-nuclear antibody, anti-double-stranded DNA antibody and anti-neutrophil cytoplasmic antibody were all negative. Cranial and abdominal MRI angiography showed decreased left transverse sinus calibration, absent flow in the left sigmoid sinus and left proximal jugular vein, and decreased blood flow with thrombus formation in the abdominal aorta. Sural nerve biopsy was performed and we identified severe axonal neuropathy with perivascular inflammation related to Wallerian degeneration caused by ischemic neuropathy.

Discussion

High fever, postoperative abdominal pain, leukocytosis with neutrophilic predominance, thrombocytopenia and later rapid progression of multiorgan failure suggest sepsis and disseminated intravascular coagulation [2]. In the present case, however, serum levels of fibrinogen and fibrin degradation products were normal and there were no fragmented erythrocytes seen on a peripheral blood smear.

Hypoxemia and peripheral cyanosis were deemed to be related to severe heart failure due to the dilated cardiomyopathy seen on echocardiography. Intramural thrombus formation might depend on the presence of a myocardial contractility disorder. Although hypoperfusion was found in the inferior-basal segments on a Thallium-201 scan, the patient's coronary angiography was normal. Collagen/vascular diseases with myocardium involvement such as systemic lupus erythematosus and polyarteritis nodosa were used in differential diagnosis.

Ischemic vasculitic involvement of the vaso nervorum is responsible for 50% of cases with axonal degeneration in patients with polyarteritis nodosa, rheumatoid arthritis, systemic lupus erythematosus or mixed connective tissue

diseases. Other rare disorders are mixed cryoglobulinemia, Sjögren's syndrome, Wegener's granulomatosis, amyloidosis and hypereosinophilic syndromes [3]. After the identification of multiple venous thrombosis in our patient's central nervous system and abdominal aorta, diseases with an increased tendency to thrombosis were suspected. Antiphospholipid syndrome, systemic lupus erythematosus, thromboangitis obliterans, Behçet's syndrome, Wegener's granulomatosis and hyperhomocysteinemia are known disorders with an increased tendency to arterial and venous thrombotic events. We rejected these possibilities, however, because our patient's serum autoantibodies were negative and no symptoms or signs of Behçet's syndrome or thromboangitis obliterans were found. Her serum homocystein level was normal, though her serum anticardiolipin antibody IgG was elevated.

Anticardiolipin antibodies are strongly associated with an increased tendency to thrombosis and elevated serum levels are seen in antiphospholipid syndrome, systemic lupus erythematosus, primary Sjögren's syndrome, rheumatoid arthritis, temporal arteritis and other connective tissue diseases, some viral, bacterial and parasitic infections, lymphoproliferative disorders, chronic liver diseases and with the use of certain drugs [4]. In our patient, antiphospholipid syndrome was diagnosed based on our clinical and laboratory findings.

Disseminated microvascular thrombosis in catastrophic antiphospholipid syndrome can result in multiorgan failure and increased morbidity and mortality [5]. Acute cerebrovascular accident, chronic dementia, cognitive disorders, psychosis, chorea, epilepsy and transverse myelitis can be seen in cases of central nervous system involvement. Although these conditions are predominantly related to focal central nervous system thrombo-occlusive events, an interaction between anticardiolipin antibodies and central nervous system cellular elements may also be responsible for some of these disorders [6]. In the case of our patient, both central nervous system involvement and peripheral polyneuropathy were found. Perivascular inflammation of the vaso nervosum and axonal degeneration were seen in sural nerve biopsy, possibly caused by microvascular thrombotic events in the vaso nervorum due to ischemic neuropathy and axonal degeneration. It is important to note that peripheral nervous system involvement is rarely seen in antiphosholipid syndrome [7].

Cardiac involvement consists valvular lesions and vegetations, intramural thrombi, coronary artery disease and cardiac failure. Dilated cardiomyopathy is known to be related to microthrombi in the absence of valvular lesions or coronary artery disease [8, 9]. Intramural thrombus formation might be caused by dilated cardiomyopathy and/or an increased tendency to thrombosis. Mesenteric ischemia and renal arterial stenosis could explain our patient's abdominal pain and hypertension.

In conclusion, like a primary disorder, secondary antiphospholipid syndrome can involve many organ sys-

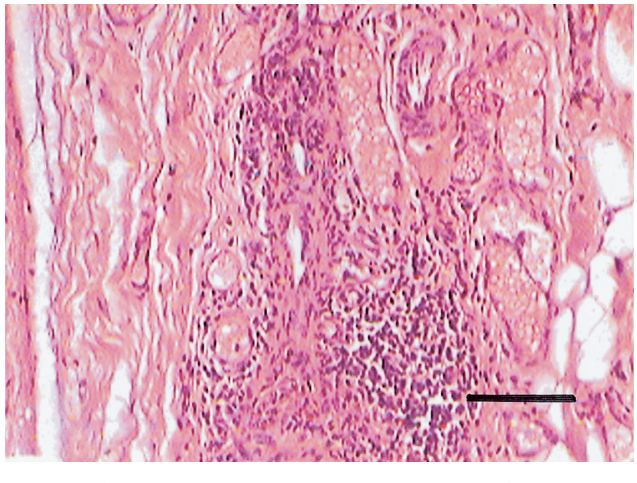

Fig. 1 Perivascular and transmural mononuclear infiltration in an epineurial vessel. Longitudinal paraffin section 10×10. Bar indicates 200 μm.

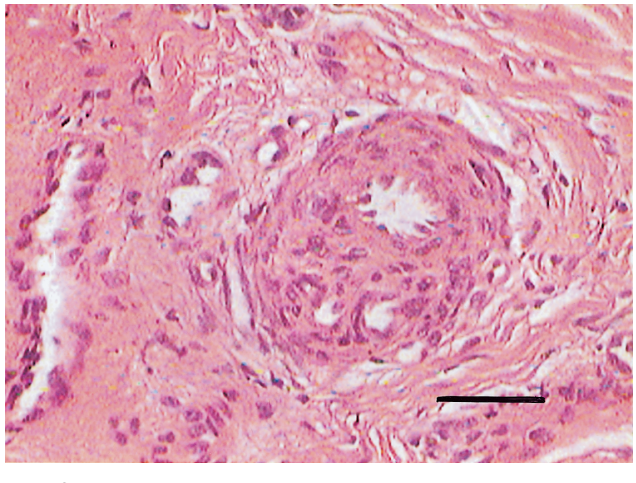

Fig. 2 Epineurial vessel showing recanalization. Transverse paraffin section 20×10. Bar indicates 100 μm.

Table I Laboratory examination results*

Hgb	111 g/L	Total Protein	56.7 g/L
Hct	35%	Albumin	21.1 g/L
MCV	89 fL	γ-globulin	18.1 g/L
WBC	23000/mm^3	Glucosuria	Negative
PMNL	22000/mm^3	Proteinuria	Negative
Lymphocytes	1000/mm^3	Urine sedimentation	Microscopic hematuria
PLT	83000/mm^3	PT	18.2 sec (Warfarin tx)
BUN	7.854 mmol/L	aPTT	78 sec
Creatinine	88.4 μmol/L	Lupus anticoagulant	Negative
Na	128 mmol/L	ACL IgG	27 GPL U/mL
K	3.3 mmol/L	ACL IgM	3.6 MPL U/mL
Cl	96 mmol/L	ANA	Negative
ALT	130 IU/L	Anti ds DNA	Negative
AST	72 IU/L	ANCA	Negative
GGT	88 IU/L	ESR	24 mm/h
ALP	216 IU/L	Serum homocystein	8.7 μmol/L

ACL IgG, anti cardiolipin antibody IgG; ACL IgM, anticardiolipin IgM; ALP, alkaline phosphatase; ALT, alanine amino transferase; ANA, anti-nuclear antibody; ANCA, anti-neutrophil cytoplasmic antibody; Anti ds DNA, anti-double-stranded DNA; aPTT, activated partial thromboplastin time; AST, aspartate aminotransferase; BUN, blood-urine-nitrogen; Cl, chloride; ESR, erythrocyte sedimentation rate; γ-globulin, gamma-globulin; GGT, gamma-glutamyl transferase; Hgb, hemoglobin; Hct, hematocrits; K, potassium; MCV, mean corpuscular volume; Na, sodium; PLT, platelets; PMNL, polymorphonuclear leukocytes; PT, prothrombin time; WBC, white blood cells.

*Laboratory examination of the patient revealed neutrophilic leukocytosis, mild elevation of liver transaminases, hypoalbuminemia and increased aPTT and serum ACL IgG levels consistent with antiphospholipid syndrome.

tems such as the cardiovascular and central nervous systems. It is important to note that peripheral nervous system involvement is rarely seen in cases of secondary antiphospholipid syndrome. Oral anticoagulation is the treatment of choice. In our patient, symptoms and signs were improved with warfarin alone, and after two years of clinical follow-up, no recurrence was reported under this treatment.

References

1. Virchow R: Thrombosis and emboli. Translated by Matzdorff AC and Bell WR. Science History Publications, Canton (1998).
2. Wenzel RP: Treating sepsis. N Engl J Med (2002) 347: 966–967.
3. Said G: Necrotizing peripheral nerve vasculitis. Neurol Clin (1997) 15: 835–48.
4. Love PE and Santoro SA: Antiphospholipid Antibodies: Anticardiolipin and the lupus anticoagulant in systemic lupus erythematosus (SLE) and in non-SLE disorders. Prevalence and clinical significance. Ann Intern Med (1990) 112: 682–698.
5. Asherson RA, Cervera R, Piette JC, Font J, Lie JT, Burcoglu A, Lim K, Munoz-Rodrigez FJ, Levy RA, Boue F, Rossert J and Ingelmo M: Catastrophic antiphospholipid syndrome. Clinical and laboratory features of 50 patients. Medicine (Baltimore) (1998) 77: 195–207.
6. Brey RL and Escalante A: Neurlogical manifestation of antiphospholipid antibody syndrome. Lupus (1998) 7: 67–74.
7. Honczarenko K, Ostanek L, Grzelec H, Fabian A, Fiedorowicz-Fabrycy I and Fryze C: Neurological deficits in patients with primary and secondary anticardiolipin syndrome. Neurol Neurochir Pol (2001) 35: 395–404.
8. Lockshin M, Tenedios F, Petri M, McCarty G, Forastiero R, Krilis S, Tincani A, Erkan D, Khamashta MA and Shoenfeld Y: Cardiac disease in the antiphospholipid syndrome: Recommendations for treatment. Committee consensus report. Lupus (2003) 12: 518–23.
9. Lauwerys BR, Lambert M, Vanoverschelde JL, Cosyns JP and Houssiau FA: Myocardial microangiopathy associated with antiphospholipid antibodies. Lupus (2001) 10: 123–5.