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Acute Infectious Purpura Fulminans with Anticentromere Antibodies

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Abstract Purpura fulminans (PF) is a rare, life-threatening syndrome characterized by disseminated intravascular coagulation (DIC) and endovascular thrombosis resulting in a characteristic pattern of cutaneous purpura. There have been no reports of the combination of PF and anti-centromere antibody (ACA). A 70-year-old woman with a 2-day history of lumbago was transported from a local medical facility to our hospital due to right hydronephrosis due to ureterolithiasis and urosepsis. She had systemic lupus erythematosus (SLE) and schizophrenia. On arrival, she had consciousness disturbance and was in a shock state with cyanotic extremities. She was additionally diagnosed with renal failure, DIC and ACA positivity after examinations. She was treated with vasopressor, antibiotics and ureter stent placement. However, she developed unstable circulation, which necessitated tracheal intubation and continuous hemodiafiltration. Urine and blood cultures showed Escherichia coli. However, the cyanosis of all of her extremities changed to necrosis and she died on day 8 due to multiple organ failure. This is the first case of acute infectious PF with ACA positivity. As ACA is known to be a risk factor for digital necrosis, the present case suggests that in addition to a decrease of protein C or S, ACA may contribute to the development of PF.

Keywords: *purpura fulminans, anticentromere antibody, pyelonephritis*

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1. Introduction

Purpura fulminans (PF) is a rare, life-threatening syndrome characterized by disseminated intravascular coagulation (DIC) and endovascular thrombosis resulting in a characteristic pattern of cutaneous purpura. [1,2] PF is thought to result from dysfunction of the body's natural anticoagulant mechanisms, particularly abnormalities in the function of protein C (PC) and associated proteins as protein S (PS), and antithrombin (AT). PC is a vitamin K-dependent serine protease that negatively regulates coagulation and has anti-inflammatory and cytoprotective properties. The plasma levels of PC, PS, and AT antigen, which works as an anticoagulant, were significantly lower in affected patients. [3] In addition, among elderly individuals, asplenic or immunosuppressed patients are more likely to develop acute infectious PF in response to infection. PF tends to occur as a result of infection by endotoxin-producing Gram-negative bacteria but can also occur secondary to infection with Gram-positive and anaerobic organisms or viruses in adults.

While, anti-centromere antibody (ACA) is a type of anti-nuclear antibody (ANA) detected by indirect immunofluorescence displaying a centromeric pattern. ACA has been considered to be specific for limited cutaneous systemic sclerosis. [4] However, ACA and digital necrosis without sclerodactyly and sclerosis of the internal organs has been reported as a distinct entity from scleroderma with sclerosis. [5,6] Digital necrosis also occurs in PF. However, there has been no reports of the combination of PF and ACA. We herein report a case of acute infectious PF with ACA positivity.

2. Case Report

A 70-year-old woman with a 2-day history of right lumbago was transported from a local medical facility to our hospital by physician-staffed helicopter due to right hydronephrosis due ureterolithiasis, uroseptic shock. She had systemic lupus erythematosus (SLE) and schizophrenia, and was treated with methylprednisolone (5 mg), brexpiprazole (2 mg), aripiprazole (6 mg), and haloperidol (1 mg). Tests for antinuclear antibodies had been negative for 10 years. On arrival, her vital signs were as follows: Glasgow Coma Scale, E3V4M6; blood pressure, 90/50 mmHg under 0.1 μg/kg/min of noradrenalin; heart rate, 88 beats per minute; respiratory rate, 17 breaths per minute; body temperature, 36.6°C. A physical examination revealed cyanotic change at all extremities, with palpable radial and dorsal pedis arteries. There were no other remarkable findings due to consciousness disturbance. The patient's blood test results are shown in Table 1. She was positive for antinuclear

antibodies and ACA. Whole body computed tomography revealed calcification of the bilateral kidneys with right hydronephrosis and the dirty fat sign. She was diagnosed with right hydronephrosis due to ureterolithiasis, calculous pyelonephritis with septic shock, renal failure, and DIC, and was treated with vasopressor, antibiotics (linezolid and meropenem), an increased steroid dose and indwelling ureteral stent placement. However, her unstable circulation deteriorated and tracheal intubation was performed with mechanical ventilation and continuous hemodiafiltration on day 2. Urine and blood cultures grew Escherichia (E) coli. However, the cyanosis of all extremities progressed to necrosis (Figure 1) on day 6. She died due to multiple organ failure on day 8.

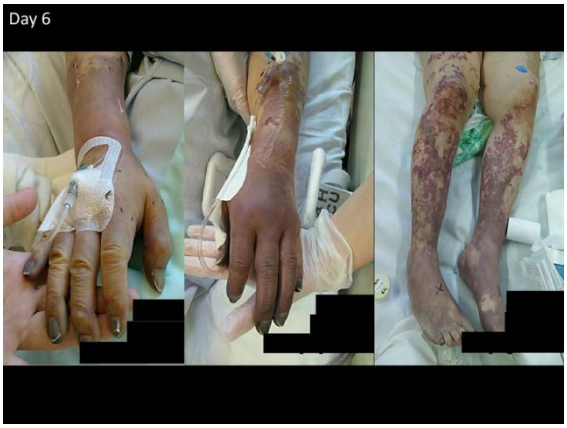

Figure 1. All extremities of the patient on day 6

All extremities had purpura and digital necrosis was present.

Table 1.

variables	level	unit
total protein	5.3	g/dL
albumin	2.5	g/dL
total bilirubin	0.9	IU/L
aspartate aminotransferase	43	IU/L
alanine aminotransferase	15	IU/L
creatinine phosphokinase	111	IU/L
amylase	72	IU/L
glucose	119	mg/dL
lactate dehydrogenase	286	IU/L
blood urea nitrogen	51.5	mg/dL
creatinine	3.52	mg/dL
uric acide	8.6	mg/dL
sodium	135	mEq/L
potassium	4.9	mEq/L
chloride	106	mEq/L
c-reactive protein	23.26	mg/dL
white blood cell count	25.3	μL
hemoglobin	8.8	g/dL
platelet	9.7	$\times 10^4/\mu L$
prothrombin time international normalized ratio	1.42	
activated partial thromboplastin time	39.7	sec
control	25.8	sec
fibrinogen	345	mg/dL
fibrinogen degradation products	187.7	mg/mL
pH	7.257	
pCO_2	32.3	Torr
pO_2	302	Torr
lactate	3.2	mmol/L
base excess	-11.8	mmol/L
antinuclear antibody	x320	
centromeres antibody	x320	
protein S antigen	61	%
protein C antigen	22	%

3. Discussion

This patient had DIC with necrosis of all extremities after developing calculous pyelonephritis due to E. coli infection and died of multiple organ failure. These findings are compatible with PF, as reported in a previous case. [7] While the present case was also positive for ACA. To our best knowledge, this is the first report of a patient with acute infectious PF with positive ACA.

In the present case, autoimmune disease was risk factor for the development of PF. [8,9,10] Most reported cases were associated with antiphospholipid antibody positivity, which can induce venous and/or arterial thrombosis by platelet activation and the production of procoagulants, such as von Willebrand factor. [11] The skin appears to be an important target organ in antiphospholipid antibody syndrome, including livedo reticularis, digital gangrene, or extensive cutaneous necrosis resembling PF. Unfortunately, we did not measure the patient's antiphospholipid antibody level. Digital necrosis can occur in patients with ACA positivity. [5,6] ACA might be related to the factors that are thought to be responsible for arteriole occlusion, such as enhanced platelet activation, endothelial damage, increased soluble mediators of vasoconstriction, or a hypercoagulation state. [5,12] Although these are hypotheses and further investigation is required for validation, the present case suggests that, in addition to a decrease in protein C or S, ACA may contribute to the development of PF.

4. Conclusion

This is the first case of a case of acute infectious PF with ACA positivity. The present case suggests that in addition to a decrease of protein C or S, ACA may contribute to the development of PF.

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