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A 31-year-old woman with painful black palms: Thrombosis or vasculitis?

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Abstract

Both of vaso-occlusive incidence of antiphospholipid syndrome (APS) or vasculitis secondary to systemic lupus erythematosus (SLE) can lead to gangrene, which requiring the urgent and appropriate therapeutic approach. However, it is sometimes difficult to achieve the differential diagnosis, especially when a tissue biopsy is difficult to obtain or is clinically contraindicated. Herein we report and discuss such a female patient who suffered rare progressive gangrene of palm skin and successfully treated with aggressive anticoagulation and immunosuppressive therapy.

Keywords

antiphospholipid syndrome syndrome (APS) • systemic lupus erythematosus(SLE) • thrombosis • vasculitis • treatment

A 31-year-old woman was admitted because of gangrene in both palms for a month. The lesions were red macules at the onset but merged gradually and developed into thick necrotic plaques finally, with unbearable pain (Figure 1A). She received anticoagulation treatment with low-molecular-weight heparin (LMWH) and tramadol for pain relief, but her symptoms were not improved. Therefore, she was admitted to the in-patient ward from the emergency room for further study.

Four years ago, she was diagnosed with Budd-Chiari syndrome and thrombocytopenic purpura by a hematologist of her local hospital, because of sudden and devastating jaundice, ascites, thrombocytopenia, and anemia. Contrast computerized tomography (CT) of the abdomen revealed inferior vena cava thrombosis. Bone marrow smear showed megakaryocyte maturation disorder. She was treated with inferior vena cava stent implantation and warfarin anticoagulant treatment combined with glucocorticoids (GCs). After these therapies, her ascites disappeared, liver function improved, and her platelets and anemia partially improved. Her GCs were tapered and stopped 1 year ago. Four months later, she had experienced seizures four times. Head CT showed lacunar infarction. She was diagnosed with lacunar cerebral infarction and treated with oral antiepileptic drugs combined with warfarin. Five days before she came to the emergency room, she stopped warfarin because her international normalized ratio (INR) test was 3.6.

When she was in the emergency room, her laboratory tests (Table 1) showed mild normocytic anemia (100 g/L), thrombocytopenia (61,000/μL), and elevated reticulocyte percentage (5.1%). Lactate dehydrogenase (LDH), and indirect bilirubin (IBIL) were slightly elevated.

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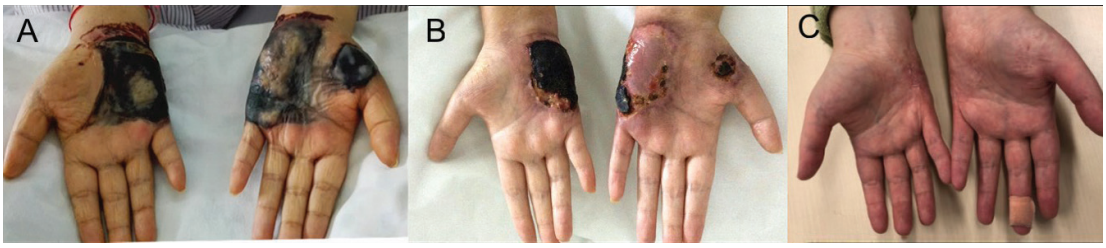

Figure 1: The recovery process of palms' gangrene. A. Gangrene occurred in both palms at admission. B. Improvement of palms after one-month treatment. C. Palms recovered from gangrene after one year of treatment.

*Table 1: Laboratory data**

Variable	Reference range, Adjusted for age and sex	Day of admission	Day of discharge	Follow-up
Hemoglobin (g/dL)	110–150	100	130	143
Reticulocytes (%)	0.8–2.0	5.15		
White cell count (per mm3)	3.5–9.5	4.14	8.32	6.25
Platelet count (per mm3)	100–350	61	118	144
Prothrombin time (sec)	10.4–12.6	13	28.5	27.7
APTT (sec)	22.7–31.8	45.7	41.5	36.7
d-Dimer (mg/L fibrinogen equivalent unit)	0–0.55	0.61	0.16	0.15
INR	0.86–1.14	1.16	2.37	2.51
Erythrocyte sedimentation rate (mm/h)	0–20	18	2	7
C-reactive protein (mg/L)	0–3.0	1.25	1.34	2.71
Alanine aminotransferase (U/L)	7–40	40	25	30
LDH (U/L)	0–250	255	229	344
Total bilirubin (mg/dL)	5.1–22.2	18.6	9.7	15.9
Direct bilirubin (mg/dL)	0.0–6.8	6.9	2.8	3.8
Creatinine (μmol/L)	45–82	62	53	68
Urine red blood cells (cells/μL)	0–15.9	21	neg	neg
24-hour urinary protein (g/24 h)	0.0–0.2	0.5	0.4	0.4
Immunoglobulin G (g/L)	7.00–17.0	4.14	6.02	5.65
Complement 3 (mg/dL)	0.73–1.46	0.492	0.669	1.14
Complement 4 (mg/dL)	0.1–0.4	0.065	0.081	0.13
ACL (pL-IgG U/mL)	<12	79	116	81.5*
Anti-β2-GP1 (RU/mL)	<20	169	120	66.5**
LA	<1.2	1.67	1.32	1.3
ANA	<1:40	1:80	1:80	1:80

APTT, activated partial thromboplastin time; ACL, anticardiolipin antibody; ANA, antinuclear antibody; anti-β2-GP1, anti-beta 2 glycoprotein 1; INR, international normalized ratio; LA, lupus anticoagulant; LDH, lactate dehydrogenase. Case records of the Peking Union Medical College Hospital.
*ACL-IgG GPLU/mL, reference range <16.0. ACL-IgA and IgM were negative.
**Anti-β2-GP1-IgG AU/mL, reference range <8.0; anti-β2-GP1-IgA and IgM were negative.

Urine test showed slight hematuria (21 cells/μL) and mild proteinuria (0.5 g/24 h). Antinuclear antibody (ANA) was positive at 1:80 dilution, in a speckled pattern. Coombs test was positive. Serum complement 3(C3) and C4 were decreased. All antiphospholipid antibodies, including lupus anticoagulant (LA), anticardiolipin antibody (ACL), and anti-beta 2 glycoprotein 1 (anti-β2-GP1) were positive. Protein C and protein S were in the normal range. Anti-extractable nuclear antigen (ENA), antineutrophil cytoplasmic antibody, rheumatoid factor, and cryoglobulin test were negative.

The diagnosis of antiphospholipid syndrome (APS) was confirmed, probably secondary to systemic lupus erythematosus (SLE). After admission, she was treated with, methylprednisolone 500 mg pulse therapy for 3 days, then prednisone 50 mg/day. She was also given intravenous cyclophosphamide(CYC) 0.4 g per week and hydroxychloroquine (HCQ) 0.2 g twice a

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day, as well as calcium and vitamin D. Meanwhile, she was treated with anticoagulants (low molecular weight heparin followed by warfarin; her INR ranged between 2.5 and 3.0), painkiller, vasodilation, and supportive treatment. The field of gangrene shrank gradually. Finally, the necrotic plaques were broken away from the underlying tissue (Figure 1B). She had a rapid improvement in anemia and thrombocytopenia and was discharged.

This patient has been followed up regularly for >6 years. Now, she takes 5 mg prednisone daily, mycophenolate mofetil (MMF) 750 mg daily, 0.3 g of HCQ per day, and warfarin. Her condition is stable. Her hands fully recovered with very few scars left (Figure 1C).

Discussion

The patient is a young woman with a chronic course of the disease. She suffered thrombocytopenia, multiple thromboses, and ischemic events, including inferior vena cava thrombosis, lacunar cerebral infarction, and gangrene of palms skin. As antiphospholipid antibodies LA, ACL, and anti-β2-GP1 were all positive, the diagnosis of APS could be confirmed according to the international classification criteria for APS.[1] SLE is the most common cause of secondary APS. According to 2012 SLICC criteria,[2] this patient could be classified as SLE. Lupus vasculitis occurs in up to 56% of patients with SLE, whereas vaso-occlusive complications could be found in up to 15% of lupus patients.[3] However, the differential diagnosis between primary APS and SLE is difficult in some cases. Renal biopsy could help to differentiate these entities, but for patients who were treated with long-term anticoagulation, kidney biopsy is contra-indicated, just like this case. Palm skin is a very rare site of gangrene in APS because palms have abundant blood supply from the ulnar artery and radial artery, converging into the superficial palmar arch and deep palmar arch. Her condition did not improve with anticoagulation alone, so underlying lupus vasculitis was suspected. Aggressive therapy with methylprednisolone pulse therapy, combined with immunosuppressive agents on the top of antithrombotic/anticoagulant treatment, is effective in most cases of lupus vasculitis.[4] In this case, the patient's condition improved remarkably with almost full recovery of her palm skin gangrene, supporting the diagnosis of lupus vasculitis.

In conclusion, we described a rare case of a young female SLE patient complicated with APS, which presented as progressive gangrene of palm skin. She was successfully treated with aggressive anticoagulation and immunosuppressive therapy with a rapid, complete response and a very good long-lasting response. Aggressive treatment is critical for a favorable outcome.

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Conflict of Interest

The authors declare no conflicts of interest.

Ethical Statement

There are no ethical related issues to this article.

Informed Consent

Informed consents have been obtained. The patient has given her consent for her images and other clinical information to be reported in the journal.

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