CHICAGO DERMATOLOGIC SOCIETY

Key location(s): Extremities **CASE 7**

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History of Present Illness

17 year-old African-American male presented with a painful, dusky lesion on his left forefoot that he attributed to trauma after jumping off his jail bunk bed three days prior to evaluation. He also noted similar lesions on the first digit of his right foot, right thigh, and left buttock. Upon further questioning, he reported similar skin lesions that resolved five months prior to admission and multiple episodes of loose stools that started four weeks before evaluation.

Past Medical History

None

Medications/Allergies

None/NKDA

Social History

Incarcerated
Marijuana

Review of Systems

The patient denied fevers, chills, nausea, vomiting, abdominal pain.

Physical Exam

Skin: Left forefoot: well-defined deep purple to black minimally indurated plaque with proximal retiform purpura and purpuric satellite lesions
Right foot, first digit: non-inflammatory retiform purpuric patches
Right lateral thigh: 10 x19cm non-inflammatory retiform purpuric patch

Pulses: Left Lower extremity: strong posterior tibial and dorsalis pedis pulses
Right lower extremity: strong posterior tibial and dorsalis pedis pulses

Laboratory Data

The following labs were remarkable/abnormal:

Prothrombin time	18 seconds	[11.6 – 14.4 seconds]
Partial thromboplastin time	43.2 seconds	[24.8 – 34.4 seconds]
INR	1.54	
D-dimer	>20 µg FEU/mL	[.22– 0.49 µg FEU/ mL]
Fibrinogen	196 mg/dL	[178 – 454 mg/dL]
Alkaline phosphatase	495 U/L	[50 – 120 U/L]
GGT	432 U/L	[3 – 60 U/L]
AST	37 U/L	[0 – 40 U/L]
ALT	77 U/L	[5 – 35 U/L]
p-ANCA	1:10	
c-ANCA	<1:10	
Caridiolipin Antibody	7.2 U/mL	[0- 20.0 U/mL]

Beta 2 glycoprotein	8.1 U/mL	[0 – 20.0 U/mL]
Protein C function	67%	[85 - 193%]
Protein S function	54%	[63 - 140%]
Prothrombin mutation	Negative	
Factor V Leiden mutation	Negative	
ANA screen	Negative	

Histopathology

RIGHT MEDIAL FOOT PUNCH BIOPSY:
Acral skin with focal mild perivascular neutrophilic infiltrates and extravasated erythrocytes; no vasculitis or thrombus seen

DIRECT IMMUNOFLUORESENCE: Negative

RIGHT LATERAL THIGH PUNCH BIOPSY:
Subcutaneous thrombotic vasculitis with fat necrosis and full thickness epidermal necrosis

Radiology

Left foot X-ray: mild soft tissue swelling

MRI/MRCP abdomen: mild intrahepatic and extrahepatic biliary ductal dilatation, associated with beaded appearance of the right and left hepatic ducts. Findings reflect sequela of sclerosing cholangitis

Arterial Doppler Ultrasound bilateral lower extremities: no evidence of vascular compromise

Venous Doppler Ultrasound bilateral lower extremities: no evidence of thrombosis

Colonoscopy

Mild active colitis with rare acute cryptitis, chronic inflammation, and fibrosis in lamina propria. Morphologic changes suspicious for inflammatory bowel disease.

Diagnosis

Benign cutaneous polyarteritis nodosa (CPAN) associated with inflammatory bowel disease and antiphospholipid syndrome

Treatment and Course

The patient was started on heparin in the ED for presumed vascular occlusion. Concern for underlying inflammatory process prompted additional treatment with IV methylprednisolone. Despite treatment, after approximately two weeks from initial evaluation, his left forefoot appeared more necrotic and after skin demarcation a transmetatarsal amputation was performed. Additionally, a second skin biopsy showed subcutaneous arterial vessel vasculitis consistent with cutanteous polyarteritis nodosa. Colonoscopy and liver biopsy were performed and showed changes suspicious for ulcerative colitis and primary sclerosing cholangitis.

After a multidisciplinary meeting, the patient was transitioned to oral azathioprine, asacol, enoxaparin, and prednisone to treat both vasculitis and inflammatory bowel disease. He was noncompliant with his outpatient appointments. On readmission four months later, he had new painful, dusky lesions on both his left upper and lower extremities. Repeat cardiolipin antibody was found to be grossly elevated at 148.268

U/mL, and lesional skin biopsy showed thrombotic vasculitis of small to medium cutaneous vessels. This coupled with the extent, configuration, and rapid progression of lesions suggested a dual diagnosis of CPAN and antiphospholipid syndrome (APLS). He was discharged on cyclophosphamide and enoxaparin with no known recurrence to date.

Discussion

Benign cutaneous polyarteritis nodosa is an underdiagnosed vasculitis that affects small and medium sized vessels of the dermis and subcutaneous tissue. Extracutaneous manifestations can occur and include fever, malaise, arthralgias, myalgias, and neuropathy. This is a distinct entity from systemic polyarteritis nodosa, which can affect multiple organ systems. Classically CPAN patients develop livedo reticularis, tender subcutaneous nodules, or cutaneous ulcerations. Petechiae, purpura, cutaneous necrosis, and autoamputation can also occur.

The etiology is unknown but recently it has been reported that CPAN may be caused by an immune response between prothrombin and apoptotic endothelial cells leading to the development of anti-phosphatidylserine-prothrombin complex antibodies (anti-PS/PT) and subsequent complement activation. Both micovascular occlusion and vasculitis may be closely related in the pathogenesis of this disease. Kawakami et al. studied the presence of antibodies associated with APLS in CPAN and found 13 (81.3%) of the 16 patients were positive for IgM anti-PS/PT; control subjects were negative. Three (18.8%) of the 16 CPAN patients had positive cardiolipin antibodies, which was notably elevated in our patient. The presence of these antibodies may serve as markers for CPAN and can aid in early diagnosis and treatment.

CPAN in the setting of inflammatory bowel disease (IBD) is well recognized though fairly uncommon. Daoud et al examined 79 patients with CPAN and found five cases associated with IBD (four patients with Crohn's disease and one with ulcerative colitis). In the study, 10% of the patients with CPAN-induced skin ulcers also had co-existing IBD. In a review of 16 patients with both CPAN and Crohn's disease skin biopsy specimens showed necrotizing arteritis, resolving vasculitis, granulomatous arteritis, or normal pathology. Skin manifestations included livedo reticularis, painful subcutaneous nodules, ulcers, and erythema.

References

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