Cutaneous polyarteritis nodosa: A rare isolated cutaneous vasculitis

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ABSTRACT

Cutaneous polyarteritis nodosa (CPAN) is a rare form of cutaneous vasculitis that involves small and medium sized arteries of the dermis and subcutaneous tissue without systemic involvement. It presents with tender subcutaneous nodules, digital gangrene, livedo reticularis and subcutaneous ulcerations. The diagnosis is by skin biopsy and characteristic pathologic feature is a leukocytoclastic vasculitis in the small to medium-sized arterioles of the dermis. We report a rare case of benign cutaneous PAN in a 14-year-old girl who presented with history of fever, subcutaneous nodules with cutaneous ulcer and digital gangrene. The skin biopsy showed leukocytoclastic vasculitis with fibrinoid necrosis in the dermal vessels. She received treatment with steroids and lesions resolved completely over a period of month.

Key words: Cutaneous polyarteritis nodosa, livedo reticularis, subcutaneous nodules, leukocytoclastic vasculitis, methotrexate

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INTRODUCTION

Cutaneous polyarteritis nodosa (CPAN) is an uncommon and rare form of cutaneous vasculitis. It involves small and medium sized arteries of the dermis and subcutaneous tissue.[1] It should be differentiated from systemic polyarteritis nodosa (PAN) due to the different clinical course and management of the two conditions.[2] The etiopathogenesis of cutaneous polyarteritis nodosa remains unclear. It is characterized by tender subcutaneous nodules, livedo reticularis and subcutaneous ulcerations. The diagnosis is based on skin biopsy, as there are no specific serological tests. The treatment is with steroids, cyclophosphamide or other immunosuppressant though there is no effective definitive therapy.

CASE REPORT

A fourteen-year-old girl presented with history of fever, painful subcutaneous nodules with ulcerations in both the lower limbs for two months, and digital gangrene of the right index finger for one-month duration. There was no history of purpura, Raynaud's phenomenon, recurrent oral ulcers, hair loss or malar rash. The history of throat pain, jaundice or past tuberculosis was negative. The general physical examination showed normal vitals with multiple subcutaneous ulcers predominantly distributed over both the lower limbs [Figures 1a and b] and bluish black discoloration of distal phalanx of the index finger. The laboratory investigations are shown in Table 1. The renal function and liver function tests were normal. The peripheral smear showed elevated total count and Anti-streptolysin O (ASLO) titer was elevated. The throat and urine culture showed no growth of bacteria. The ultrasonography of the abdomen and echocardiography of the heart were normal. The deep incisional skin biopsy taken from the subcutaneous nodule revealed leukocytoclastic vasculitis of the dermal vessels [Figures 2a and b]. The patient was treated with methyl prednisolone (three pulses doses of 750 mg/day) followed by oral prednisolone of 1 mg/kg/day. She also received a course of oral penicillin for antecedent streptococcal throat infection. The skin lesions completely healed over a period of six months with scarring [Figures 3a and b], and patient was on regular follow up for one and half year after which she lost to follow up and treatment.

She presented to us again in July 2010 (three years after the initial episode in December 2007) with similar complaints of bluish black

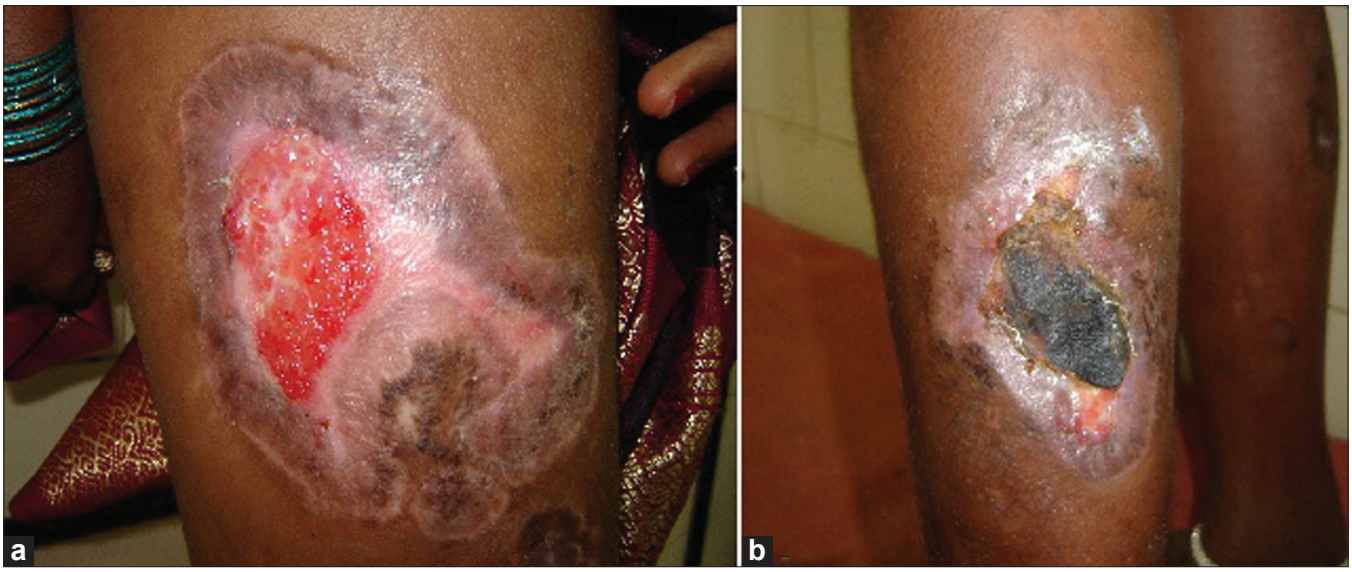

Figure 1: Photograph shows healing subcutaneous ulcer over thigh (a) and leg (b)

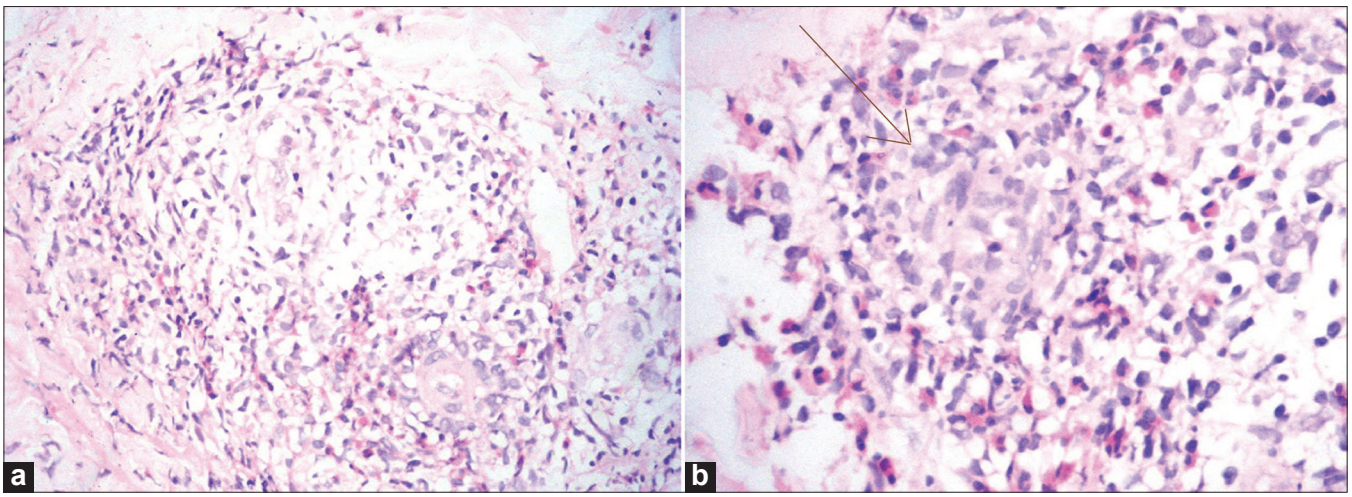

Figure 2: [H and E, ×400] shows normal epidermis and the dermis with inflammatory infiltrate, eosinophils and neutrophils (a) superficial dermis with destruction of the vessel walls by inflammatory infiltrate (b) (arrow)

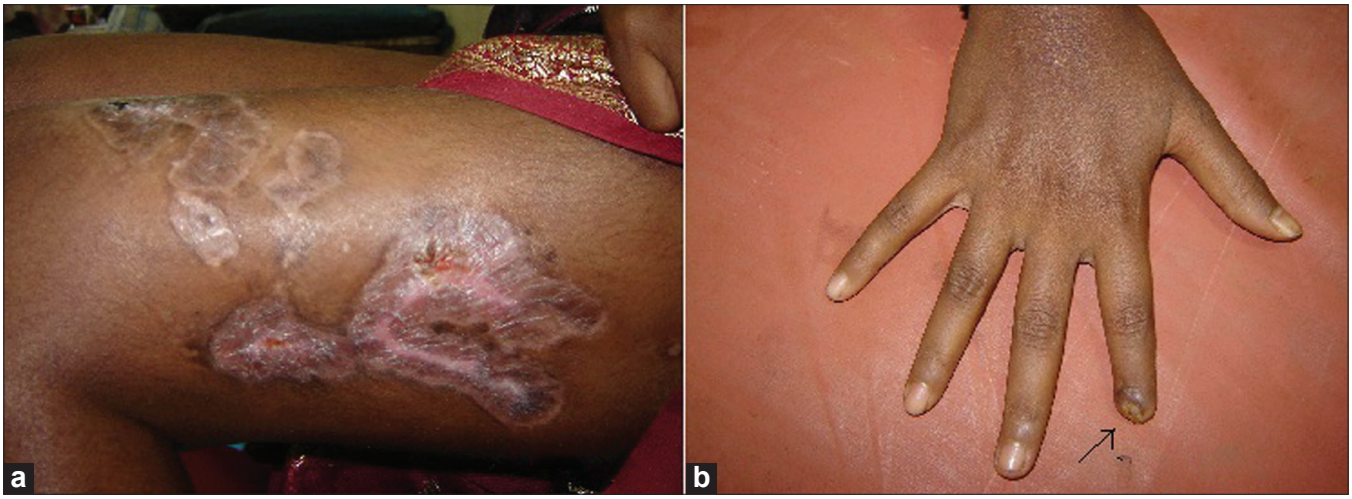

Figure 3: Photograph shows healed subcutaneous ulcer over thigh with scarring (a) and healed gangrene of finger (b) (i.e., autoamputated distal phalanx)

Table 1: Immunological profile and other laboratory investigations done for the patient in the study

Test	Report
ASLO	400 Todd units (elevated)
ANA	Negative
ANCA	Negative
APLA (IgG, IgM)	Negative
Anti-β2GPI	Negative
Lupus anticoagulant (KCT)	Negative
Rheumatoid factor	Negative
Serum cryoglobulins	Negative
Serum electrophoresis	Normal pattern
hsCRP	Elevated (63 mg/dl)
HIV	Negative
HBsAg	Negative
HCV	Negative
VDRL	Negative
Serum homocysteine level	Normal

ASLO: Anti-streptolysin O, ANA: Anti-nuclear antibody, ANCA: Anti-neutrophil cytoplasmic antibody, APLA: Anti-phospholipid antibody, Anti-β2GPI: Anti-β2 glycoprotein I, hsCRP-high sensitivity C-reactive protein, VDRL: Venereal disease research laboratory, HCV: Hepatitis C virus, HBsAg: Hepatitis B surface antigen, HIV: Human immunodeficiency virus

discoloration of left middle finger and subcutaneous nodules. The skin biopsy was repeated which showed leukocytoclastic vasculitis of the dermal vessels suggestive of CPAN. There was no systemic involvement by clinical examination and investigations. The ASLO titer was normal. The patient was treated with injection cyclophosphamide 750 mg/meter square (6 pulse doses every month) and advised to continue steroids (prednisolone 30 mg/day) and methotrexate 7.5 mg/week. Her symptoms completely resolved in two weeks time. The patient is on regular follow up in our immunology clinic and there is no further episode of relapse till date.

DISCUSSION

Lindberg described cutaneous polyarteritis nodosa (CPAN) first in 1931.[3] The precise etiology of CPAN remains unknown, but immune complex mediated disease plays a role in etiopathogenesis. There is high prevalence of IgM antiphosphatidylserine–prothrombin complex among patients with CPAN. These immunoglobulins are presumed to activate the classical complement pathway to cause CPAN.[4] Several infectious and noninfectious conditions have been associated both with initiation and relapse of the disease. The streptococcal infection has been commonly implicated.[5] Others infectious agents implicated are parvovirus B19, mycobacterium, hepatitis viruses B and C.[6,7] The noninfectious conditions associated with CPAN are connective tissue diseases (systemic lupus erythematosus, rheumatoid arthritis), Wegener's granulomatosis and Churg-Strauss syndrome.

In CPAN, lesions are limited to skin, adjacent muscles, nerves and joints. The characteristic manifestations are tender subcutaneous nodule, livedo reticularis, and ulceration, mostly localized on the lower extremity.[8] Gangrene and necrosis of fingers is a very uncommon finding.[9] The subcutaneous tender, erythematous nodules (usually 0.5-3 cm in diameter) may disappear spontaneously or undergo ulceration. Other findings include petechiae, purpura, cutaneous necrosis, auto amputations, and local extracutaneous manifestations like arthralgia, myalgia, constitutional symptoms (such as fever, malaise) and peripheral neuropathy (mononeuropathy and mononeuritis multiplex).

There are no specific clinical and laboratory findings. The diagnosis is based on clinical features of isolated skin involvement and confirmed by histopathological findings. A deep incisional biopsy, including subcutaneous tissue, is necessary for the accurate diagnosis of the disease. The characteristic pathologic feature is a leukocytoclastic vasculitis in the small to medium sized arterioles of the deep dermis or hypodermis with or without associated fibrinoid necrosis.[8] Both CPAN and systemic PAN share the same histopathologic features of necrotizing arteritis of small and medium sized vessels. Immunological testing does not appear helpful in confirming the diagnosis of CPAN, however, negative results help to exclude other systemic vasculitis.

Corticosteroids remain the mainstay of treatment for CPAN and are used in most severe cases.[10] The exact duration of treatment is uncertain. Immunosuppressive agents such as cyclophosphamide, azathioprine, or methotrexate, can been used in cases unresponsive to steroid therapy.[8,10] The non-steroidal anti-inflammatory (NSAIDs) drugs are used only in the milder form of CPAN, and antibiotics are used in cases of antecedent streptococcal throat infections. In cases resistant to systemic steroids and immunosuppressive therapy, studies have shown that intravenous immunoglobulin can be successfully used.[11] There are some reports that vasodilators[9] and antithrombotic agents are effective, especially for ulcers and gangrene associated with CPAN. Though CPAN has chronic, relapsing benign course there are reports of it evolving into systemic PAN.[12]

Our case presented with pure cutaneous manifestations without systemic involvement. The diagnosis was confirmed by histopathologic examination of skin biopsy. She had one episode of relapse three years after the initial episode. Initial episode was treated with steroids alone and following relapse she received six pulse doses of cyclophosphamide and presently she is on regular follow up with drugs, prednisolone (30 mg/day) and methotrexate (7.5 mg/week).

In conclusion, CPAN is a rare and benign cutaneous vasculitis of unknown etiology with chronic and relapsing course distinct

from systemic PAN. However, these patients should be kept on close regular follow up for its evolution into systemic PAN.

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